SYNTHESIS AND TRANSFORMATIONS OF CARBOHYDRATE DERIVATIVES.

1. SYNTHESIS OF FURAN AND 5-NITROFURAN DERIVATIVES OF SOME THIOSEMICARBAZONES AND THIOSEMICARBAZIDES OF D-GLUCOSE AND L-ARABINOSE


N-Glycopyranosylthiosemicarbazones and their acetates were synthesized by the reaction of tetraacetylglycopyranosyl isothiocyanates with hydrazones of furan and nitrofuran aldehydes and also by reaction with hydrazine hydrate and subsequent treatment with the aldehydes. Acetates of glycopyranosyl-5-R-furoylthiosemicarbazides were obtained by acetylation of glycopyranosylthiosemicarbazides with furan- and 5-nitrofuranocarboxylic acid chlorides. The structures of the synthesized compounds were confirmed by thin-layer chromatography and the IR and PMR spectra and by the results of elementary analysis.

In order to increase the selectivity of the action, decrease the toxicity, and increase the solubilities in water of biologically active furan and 5-nitrofuran compounds [1, 2] we synthesized carbohydrate-containing derivatives of furan and 5-nitrofuran that are connected by means of thiosemicarbazide and thiosemicarbazone fragments.

We studied the reactions of 1-deoxy-2,3,4,6-tetra-O-acetyl-D-glucopyranosyl isothiocyanate (I) and 1-deoxy-2,3,4-tri-O-acetyl-L-arabinopyranosyl isothiocyanate (XIV) with hydrazine hydrate, hydrazones of 2-R-substituted formylfurans (R = H, NO2), and hydrazides of 5-R-substituted furan-2-carboxylic acids (R = H, NO2).

Compounds I and XIV were obtained by the action of ammonium thiocyanate or silver thio-

cyanate on the acetobromo sugar in an inert medium [3, 4]. They are readily identified from the characteristic absorption bands in the IR spectra of 2060-2140 cm⁻¹ (N=S) and at 1750 and 1240 cm⁻¹ (0OCOCH3).

Acetylglycosylthiosemicarbazides II and XV are formed in good yields when the glycosyl-
isothiocyanates are treated in the cold with hydrazine hydrate, while partial deacetylation of the desired products occurs in the presence of excess hydrazine hydrate. Two absorption bands at 3315-3465 cm⁻¹, which are related to the symmetrical and asymmetrical stretching vi-

brations of the amino group, are observed in the IR spectra of II and XV. In the PMR spectra of II and XV the protons of the amino group give a singlet at 4.6 ppm (2H), while the re-

main ing NH protons of the thiosemicarbazide part give singlets at 8.3 (IH) and 9.6 ppm (IH).

Glycosylthiosemicarbazide acetates II and XV form formylfuran and 5-nitroformylfuran glycosylthiosemicarbazone acetates (V-VIII and XVII-XXI) with formylfuran and 5-nitroformyl-

furan in alcohol media in the presence of acids (method A). The band that is characteristic for the amino group vanishes in the IR spectra of these compounds, and a band of an azomethine group appears at 1470-1485 cm⁻¹. In addition, NH (3320-3340 cm⁻¹) and CSH (1680 cm⁻¹) stretching vibrations and vibrations of the furan ring at 1510 and 1595 cm⁻¹ are observed in the spectra. Symmetrical vibrations of the C=O bond of the furan ring are observed at 1025-1035 cm⁻¹, while the asymmetrical vibrations are overlapped by the vibrations of the O-C group in the acetates. The nitro group in VII, VIII, XX, and XXI gives two characteristic intense absorption bands at 1360 and 1530-1560 cm⁻¹. The bands of the acetate groups of the carbonyl ring appear at 1750 (C=O) and 1240 cm⁻¹ (O=C). The pyranose ring in V-VIII and XVIII-XXI is characterized by an absorption band at 910-925 cm⁻¹. The deformation vibrations of the C(1)H bond at 885-894 cm⁻¹ are due to the β configuration of the aglycone.
In contrast to glycosylurazas and N-glycosides [5], the anomeric proton shows up in the form of a triplet ($J = 8.5-10$ Hz) in the PMR spectra of derivatives V-VIII and XVIII-XXI. This splitting is a consequence of spin–spin coupling of the anomeric proton with the protons attached to the C(2) atom and the 4'-N atom. The signal of the N'(4)-H proton is observed in the form of a broad doublet due to the quadrupole moment of the nitrogen atom. The magnitude of the $J_{\text{NH}}$ value of the proton anomers confirms the B configuration of the aglycone vis-à-vis the glycoside center for glycosylthiosemicarbazones V-VIII, XVII-XXI, and X-XIII [6].

The signals of the H$_B$ and H$_B'$ protons of the furan ring in V, VI, X, XI, XVIII, and XIX give doublets at 6.7-7.0 ppm. In the spectra of compounds that contain a nitro group in the 5 position (VII, VIII, XII, XIII, XX, and XXI) these signals are shifted to weaker field (7.40-7.80 ppm) due to its electronegative character, in agreement with the data in [7].

The use of diacetates instead of unstable formylfuran and 5-nitroformylfuran in the reaction with glycosylthiosemicarbazides II, XV, and IX in acidic media gives thiosemicarbazones V-XIII and XVIII-XXI in good yields. When the reaction is carried out at pH 2-3 with acetyl-glycosylthiosemicarbazides, it leads to partial deacetylation of the reaction products.

Glycosylthiosemicarbazones V-VIII and XVII-XXI were also obtained by the reaction of acetylglycosyl isothiocyanates I and XIV with furfural and 5-nitrofurancarboxylic acid chlorides (method B). The yields of the compounds were higher by method B than by method A.

The acetyl protective groups of VII, VIII, XX, and XXI are removed in absolute methanol in the presence of HClO$_4$ or HCl. However, we were unable to remove the protective groups by the Zemplen method [8] in absolute methanol in the presence of sodium methoxide because of the instability of the nitrofuran ring.

The addition of a carbohydrate fragment to the formylfuran and 5-nitroformylfuran thiosemicarbazones increases their solubility in water.

The bands of an acetate group (1750 cm$^{-1}$) vanish in the IR spectra of X-XIII, and a broad absorption band of a hydroxy group appears at 3350-3490 cm$^{-1}$.

A method for the preparation of 4-(acetyl-N-glycopyranosyl)-1-furoyl-3-thiosemicarbazides by direct reaction of glycosyl isothiocyanates with furan-2-carboxylic acid hydrazide is known [9]. We demonstrated that the compounds indicated above and 4-(acetylglycopyranosyl)-1-(5-nitro-2-furoyl)-thiosemicarbazides can be obtained by acylation of glycosylthiosemicarbazide acetates II and XV with furan- or 5-nitrofurancarboxylic acid chlorides in an inert solvent.