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Abstract

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SYNTHESES OF CERTAIN ARYL-*N*-GLYCOSIDES

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Numerous *N*-glycosides, highly diverse in their properties, constitute a relatively little-studied but very important group of sugar derivatives. The fact that most clearly illustrates the insufficiency of our knowledge in this area is the lack of precise information on the structure of most aryl- and alkyl-*N*-glycosides, in particular on the presence in their molecules of cyclic or open structures (of the Schiff-base type) ([1]); the question of tautomerism of *N*-glycosides is likewise exceptionally complex and confused ([1]).

At the same time, the theoretical and practical significance of *N*-glycosides is exceptionally great. It is sufficient in this connection to point to the group of pyrimidine- and purine-*N*-ribosides and deoxyribosides—nucleosides, which are structural components of nucleotides and nucleic acids. The very readily formed and readily hydrolyzed aryl- and alkyl-*N*-glycosides apparently play a role in the biological transformations of sugars upon interaction with amino compounds. In view of the ease of formation of the named glycosides, they are finding ever increasing use in the preparative isolation and identification of sugars ([2]).

The problem of creating medicinal substances—derivatives of amino compounds and sugars—has long attracted attention, since the introduction of a sugar residue into the molecule of a medicinal substance results in decreased toxicity and increased solubility ([3–5]), and sometimes in a substantial change in the character of its action ([6]).

In the course of work on the study of the properties of *N*-glycosides, we encountered the necessity of synthesizing a number of compounds of this class. Thus, in the literature, in particular in summary tables ([1]), there is an almost complete absence of information on *N*-galactosides and *N*-xylosides of *m*-substituted anilines, which are needed for evaluating the influence of the position of substituents in the benzene ring on the properties of *N*-glycosides. In attempts to synthesize derivatives of this kind, it was not possible to isolate crystalline products ([7]).

The present article describes the syntheses and the most important properties of *N*-galactosides of *m*-aminobenzoic acid, *m*-nitroaniline, *m*-toluidine, *o*-anisidine, and *p*-chloroaniline, as well as *N*-xylosides of *m*-nitroaniline and *o*-anisidine. To obtain the preparations, general methods for the synthesis of *N*-glycosides were used: the Weygand method ([8]) and the Sorokin method ([9]), in a number of cases with slight modifications. For purification of products with *m*-substituents, attempts at recrystallization did not give successful results (cleavage of the *N*-

glycosides occurred), and purification was carried out by successive washing of the precipitates with a mixture of ether and alcohol and with pure ether. By the usual method (action of acetic anhydride in pyridine ([10])), some acetates of the synthesized *N*-glycosides were obtained and partly characterized.

According to our data, the information available in the literature ([1]) gives an exaggerated impression of the instability of *N*-glycosides. According to our observations, *N*-glycosides, even those purified only by washing with solvents, are sufficiently stable under ordinary storage conditions (in a desiccator over $CaCl_2$). Thus, for example, the *N*-galactoside of *m*-aminobenzoic acid proved to be analytically pure even two years after its preparation.

Experimental Part

The starting sugars and amines* used were freshly recrystallized and freshly distilled.

N-D-Galactoside of *m*-nitroaniline. A mixture of 4.5 g (0.025 mole) of galactose, 4 g (0.029 mole) of *m*-nitroaniline, 1.5 ml of water, and 0.1 ml of glacial CH_3COOH was heated on a water bath for 1 hour; then 10 ml of alcohol was added, and the resulting solution was left in a refrigerator. After several days the precipitate that separated was filtered off and thoroughly washed with alcohol and ether. Attempts at recrystallization from alcohol gave a gelatinous precipitate. Therefore the washed product was dried without further purification in a desiccator over $CaCl_2$. Yield of yellow crystalline product 5.65 g (75.3%), m.p. 156–158°, $[\alpha]_D^{21} - 98.9^\circ$ (*C* 1.4151; pyridine).

Found, %:	C 48.19; 48.10; H 5.70; 5.75; N 9.06; 9.12
$C_{12}H_{16}O_7N_2$. Calculated, %:	C 48.00; H 5.33; N 9.33

Tetraacetate, m.p. 151–153° (from alcohol).

Found, %:	C 50.92; H 5.00
$C_{20}H_{24}O_{11}N_2$. Calculated, %:	C 51.28; H 5.13

N-D-Galactoside of *m*-toluidine. A mixture of 5 g of galactose, 4 g of *m*-toluidine, and 1.5 ml of water was heated on a water bath for 15 min; after cooling to room temperature, the solidified reaction mixture was dissolved in a mixture of 10 ml of alcohol and 20 ml of ether and left in a refrigerator. The precipitate that separated was filtered off and thoroughly washed with alcohol and ether. Yield of N-D-galactoside 5.06 g (67.7%), colorless crystals, m.p. 97–99°, $[\alpha]_D^{21} - 99.1^\circ$ (*C* 0.8133; pyridine).

Found, %:	C 57.34; H 7.19; N 5.25; 5.45
$C_{13}H_{19}O_5N$. Calculated, %:	C 57.99; H 7.06; N 5.21

N-D-Galactoside of *m*-aminobenzoic acid. To a solution of 3.5 g of galactose and 2.5 g of *m*-aminobenzoic acid in 40 ml of absolute CH_3OH was added a granule of fused $ZnCl_2$; the mixture was boiled for half an hour on a water bath, then evaporated in vacuo, and the residue was dissolved, while boiling, in 15 ml of absolute alcohol and left in a refrigerator. After several days the precipitate was filtered off and washed with a mixture of alcohol and ether, then with ether. Yield of product, faintly beige-colored, 2.65 g (48.6% of theory based on the starting amino acid); m.p. 99-100° (with decomposition), $[\alpha]_D^{20} - 57.0^\circ$ (*C* 0.6701; pyridine).

Found, %:	C 52.12; 52.13; H 5.90; 6.0; N 4.38; 5.58
$C_{13}H_{17}O_7N$. Calculated, %:	C 52.17; H 5.63; N 4.68

N-D-Galactoside of *o*-anisidine. A mixture of 1.9 g of galactose, 1.3 ml of *o*-anisidine, and 0.5 ml of water was heated on a water bath for half an hour; the solid mass obtained was dissolved by prolonged heating (45 min) in alcohol. After several days the precipitate was filtered off, washed abundantly with ether, and recrystallized twice from aqueous alcohol (30 ml of alcohol, 1 ml of water). Yield of colorless crystalline product 2 g (70.1%; in further work the yield was increased to 82.6%); m.p. 138-140° (with decomposition), $[\alpha]_D^{20} - 45.3^\circ$ (*C* 0.5098; pyridine).

Found, %:	N 4.93; 5.12
$C_{13}H_{19}O_6N$. Calculated, %:	N 4.93

N-D-Galactoside of *p*-chloroaniline. A suspension of 1.8 g of galactose and 1.27 g of *p*-chloroaniline in 10 ml of water was heated on a water bath for half an hour, then 20 ml of alcohol and 1 ml of water were added. With continued

in the liquid state, a colorless crystalline precipitate separated, which was filtered off and washed with alcohol and ether. Yield of the N-glycoside 84.7%; m.p. 178-179° (with decomp.), $[\alpha]_D^{21} - 103.95^\circ$ (*C* 1.3674; pyridine).

Found, %:	C 49.86; H 5.58; N 4.95; 5.05
$C_{12}H_{16}O_5NCl$. Calculated, %:	C 49.79; H 5.53; N 4.84

Tetraacetate, m.p. 157-158.5°.

Found, %:	N 3.14; 3.24
$C_{20}H_{24}O_9NCl$. Calculated, %:	N 3.06

N-D-Xyloside of *m*-nitroaniline. A mixture of 1.04 g of xylose, 0.96 g of *m*-nitroaniline, 0.4 ml of water, and 0.02 ml of CH_3COOH was heated on a water

bath until dissolved, then for another 10 min (15 min in all); 10 ml of alcohol was added, and the reaction mixture was again heated on a water bath until dissolution. On cooling, a precipitate of the N-xyloside separated, which was washed with alcohol and ether. Yield of product 0.71 g (38%); yellow crystals, m.p. 155–157° (with decomp.), $[\alpha]_D^{21} - 72.3^\circ$.

Found, %:	C 48.92; 48.93; H 5.34; 5.23; N 10.20; 10.31
$C_{11}H_{14}O_6N_2$. Calculated, %:	C 48.88; H 5.18; N 10.37

N-D-Xyloside of *o*-anisidine. 1.5 g of xylose, 1.4 ml of *o*-anisidine, and 0.5 ml of water were heated on a water bath for 6 min; then 1 ml of absolute alcohol was added to the mixture. The mass that solidified on cooling was diluted with ether after 24 hours. The yield of colorless crystals was quantitative. After recrystallization from absolute alcohol, m.p. 120–130° (with decomp.), $[\alpha]_D^{20} - 66.6^\circ$ (*C* 0.8126; pyridine).

Found, %:	C 56.45; 56.58; H 6.95; 6.84; N 5.72; 5.59
$C_{12}H_{17}O_5N$. Calculated, %:	C 56.47; H 6.67; N 5.49

Triacetate, m.p. 173.5–175° (from alcohol).

Found, %:	C 56.20; H 6.04
$C_{18}H_{23}O_8N$. Calculated, %:	C 56.69; H 6.03

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Note: Figure translations are in progress. See original paper for figures.