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Abstract

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NEW SYNTHESES OF C-SUBSTITUTED CARBOHYDRATES

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By the usual route of organomagnesium synthesis it is possible to obtain C-substituted carbohydrates with relatively simple radicals (phenyl, tolyl, anisyl, etc.). Most of the complex C-derivatives of carbohydrates have been obtained by further treatment of products synthesized by the Grignard reaction. Thus, glycopyranosylarylamines were obtained by successive nitration and reduction of the corresponding glycopyranosyl derivatives ([1,2]).

We have attempted to broaden the range of radicals introduced into carbohydrates by the Grignard method. Of interest is the direct introduction into sugars of an aglycone containing an amino group. For this purpose amines with a protected (for example, methylated) amino group are suitable, since a free amino group reacts with the Grignard reagent. Aryl bromides containing an amino group in the para position to the halogen react with magnesium only in the presence of a catalyst. Therefore we obtained dimethylaminophenylmagnesium bromide by treating magnesium with a mixture of equivalent amounts of *n*-bromodimethylaniline and ethyl bromide. This product gave, with acetochloroglucose, *n*-glycopyranosyldimethylaniline, isolated as the tetraacetate in a yield of 25.4% of theory.

An attempt to combine glucose with dimethylaniline through dimethylaminophenyllithium proved less successful. In the reaction of acetobromoglucose with lithium dimethylaniline, only 1.6% of the final product was obtained. The use of organolithium compounds for the synthesis of C-substituted carbohydrates in other cases also did not give good results. In the reaction of phenyllithium with acetochloroglucose the yield of phenylglucose was only 9.4% of theory ([3]); the interaction of picolyllithium with acetobromoglucose did not lead at all to the formation of a C-derivative of glucose ([4]).

Glucopyranosyldimethylhydroquinone was obtained by us from acetochloroglucose and magnesium bromodimethylhydroquinone. The low yield of the product (18.8%) is explained by the poor solubility of the starting bromide in ether, as well as by steric hindrance. The synthesis of *n*-allylglucopyranosylbenzene presented no particular difficulties. In addition to the previously described rhamnose derivatives ([5]), from the interaction of acetochlororhamnose with α-iodothiophene and *n*-bromoanisole we obtained, in the form of acetates, syrupy structural formula

Figure 1: structural formula

rhamnopyranosylthiophene and crystalline rhamnopyranosylanisole. The latter was also obtained in the free form.

Experimental Part

***n*-Tetraacetyl-*D*-glucopyranosyldimethylaniline.** To a solution of *n*-dimethylaminophenylmagnesium bromide, prepared by the interaction of 7.86 g (0.32 mole) of magnesium with a solution of 32.75 g (0.16 mole) of *n*-bromodimethylaniline and 17.44 g (0.16 mole) of ethyl bromide in 100 ml of abs. ether, was added a solution of 5 g (0.013 mole) of chloroacetoglucose in 75 ml of abs.

ether. The reaction mixture was stirred for 2 hours at room temperature, then for another 5 hours with heating on a water bath. After completion of the reaction, 50 ml of water was added to the mixture with cooling; the aqueous layer was separated and evaporated to dryness, and the dry residue was acetylated with acetic anhydride in the presence of sodium acetate. The acetylated product was extracted with ether; the ether extracts were decolorized with charcoal and dried over calcium chloride.

The solid viscous mass obtained after evaporation of the ether was recrystallized from isopropyl alcohol, then from ethyl alcohol. This gave 1.6 g (25.4% of theory) of a crystalline substance in the form of white shiny needles, m.p. 169–170°, soluble in ether, chloroform, methanol, hot ethyl and propyl alcohols, insoluble in water and petroleum ether. Described for the first time.

Found, %: C 58.48; H 6.54; N 3.23
$C_{22}H_{29}O_9N$. Calculated, %: C 58.53; H 6.43; N 3.10

The structure of the substance is represented by the formula:

$$\mathrm{Ac} = \mathrm{CH_3CO}-$$

n-D-Glucopyranosyldimethylaniline. 1.3 g of *n*-tetraacetyl-D-glucopyranosyldimethylaniline was dissolved in 100 ml of absolute methanol; the solution was saturated with dry ammonia and left overnight. The syrup obtained after evaporation of the methanol was washed with ether and recrystallized from methyl acetate.

This gave 0.65 g (79.7% of theory) of a white crystalline substance with m.p. 88–90°, soluble in water, lower alcohols, and methyl acetate, insoluble in ether. Described for the first time.

structural formula

Figure 2: structural formula

Found, %:	N 5.18
$C_{14}H_{21}O_5N$. Calculated, %:	N 4.94

Tetraacetyl-D-glucopyranosyldimethylhydroquinone. To a solution of dimethylhydroquinonemagnesium bromide, obtained from 3.93 g (0.16 mole) of magnesium and 34.72 g (0.16 mole) of bromodimethylhydroquinone in 120 ml of absolute ether, was added a solution of 5 g (0.013 mole) of chloroacetoglucose in 75 ml of absolute ether. The reaction mixture was stirred for 5 hours with heating on a water bath. Further work-up was carried out in the usual manner.

After acetylation, 1.2 g (18.8% of theory) of a cream-colored crystalline product with m.p. 134–135° was obtained. The substance is soluble in ether, chloroform, and methanol, insoluble in water and petroleum ether. On destructive oxidation with alkaline permanganate, dimethylhydroquinonecarboxylic acid was obtained and identified. The substance is described for the first time.

Found, %:	C 56.28; H 6.13
$C_{22}H_{28}O_{11}$. Calculated, %:	C 56.41; H 5.98

On the basis of the synthesis conditions and the analytical data, the substance is assigned the formula:

n-Allyltetraacetyl-*D*-glucopyranosylbenzene. To a solution of *n*-allylphenylmagnesium bromide, prepared from 3.93 g (0.16 mole) of magnesium and 31.52 g (0.16 mole) of *n*-bromoallylbenzene in 70 ml of absolute ether, 5 g (0.013 mole) of chloroacetoglucose in 75 ml of absolute ether was added. The mixture was stirred at room temperature for 1 hour, then for 3 hours while heated on a water bath. Further treatment was carried out in the usual manner. 1.7 g (28.1% of theory) of a white crystalline substance was obtained, m.p. 88–90°, which dissolves in the usual organic solvents. Destructive oxidation with alkaline permanganate gave terephthalic acid. The substance decolorizes bromine water. Described for the first time.

Found, %: C 61.37; H 6.34

$C_{23}H_{28}O_9$. Calculated, %: C 61.60; H 6.25

The structure is represented by the formula:

n-Triacetyl-*L*-rhamnopyranosylanisole. To a solution of *n*-anisylmagnesium bromide, prepared from 5.52 g (0.23 mole) of magnesium and 43 g (0.23 mole) of *n*-bromoanisole in 100 ml of absolute ether, a solution of 8 g (0.023 mole) of structural formula: tetraacetyl-D-glucopyranosylbenzene bearing a para-allyl substituent

Figure 3: structural formula: tetraacetyl-D-glucopyranosylbenzene bearing a para-allyl substituent

structural formula: triacetyl-L-rhamnopyranosylanisole

Figure 4: structural formula: triacetyl-L-rhamnopyranosylanisole

chloroacetorhamnose in 100 ml of absolute ether was added. The reaction mass was stirred for 1 hour at room temperature, then for 3 hours while heated. Further treatment was carried out in the usual manner. After evaporation of the ether, 7.3 g of a viscous solid substance was obtained (74.1% of theory).

After recrystallization from isopropyl alcohol, 2.4 g of a snow-white crystalline substance with m.p. 106–107° was isolated. The syrup remaining after evaporation of the isopropyl alcohol was not investigated.

On destructive oxidation of the crystalline product, *n*-methoxybenzoic acid was obtained. The substance is soluble in ether, chloroform, methanol, insoluble in water and petroleum ether. Described for the first time.

Found, %: C 59.78; H 6.33
$C_{19}H_{24}O_8$. Calculated, %: C 60.00; H 6.31

The structural formula is as follows:

n-*L*-Rhamnopyranosylanisole. 1 g of *n*-triacetyl-*L*-rhamnopyranosylanisole was dissolved in 50 ml of absolute methanol; the solution was saturated with dry ammonia and left overnight. After evaporation of the methanol, the syrupy residue was washed with ether and recrystallized from benzene. 0.4 g (51% of theory) of a white crystalline substance with m.p. 121.5–123° was obtained, which dissolves in water, lower alcohols, and hot benzene, and is insoluble in ether and petroleum ether. Described for the first time.

Found, %: C 61.29; H 7.28
$C_{13}H_{18}O_5$. Calculated, %: C 61.41; H 7.08

α-Triacetyl-*L*-rhamnopyranosylthiophene. To a solution of thienylmagnesium iodide, prepared from 3.82 g of magnesium (0.16 mole) and 33.6 g

To α-iodothiophene in 70 ml of abs. ether, 5 g (0.016 mole) of chloroacetorhamnose was added gradually. After the usual workup, 0.92 g of syrup (16.1% of theory) was obtained, which could not be crystallized. On oxidation of the product with alkaline permanganate, α-thiophenecarboxylic acid was obtained. The substance is described for the first time.

structural formula: thiophene-substituted acetylated rhamnose derivative with labels OAc, AcO, CH_3, O, and S

Figure 5: structural formula: thiophene-substituted acetylated rhamnose derivative with labels OAc, AcO, CH_3, O, and S

$C_{16}H_{20}O_7S$. Found %: S 8.64
Calculated %: S 8.98

The following structural formula is assigned:

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