Preparation of some D-glucofuranosides from unprotected D-glucose

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O-glycosidation of 3-(4-methoxyphenyl) propyl alcohol, benzyl alcohol and vanillin with totally unprotected D-glucose, performed in a heterogeneous media and promoted by anhydrous ferric chloride, afforded competent D-glucofuranosides as the major and D-glucopyranosides as the minor products of the reaction.

Keywords: O-glycosidation, synthesis of D-glucofuranosides.

INTRODUCTION

Recently Ferrieres et al.1,2 reported O-glycosylation of some long chain alcohols with totally unprotected uronic acids and some neutral carbohydrates, performed in heterogeneous media and promoted by anhydrous ferric chloride, which afforded alkyl D-glycofuranosiduronic acids and alkyl D-glycofuranosides, respectively, in high yields. These glycofuranosides are becoming increasingly important as surfactants3, liquid crystals4 and building blocks for glycofuranosyl donors in oligosaccharide synthesis.5,6 They can be obtained through a convenient one-pot synthesis. No other aryl and alkyl D-glycosides have been prepared so far by the application of the above rapid and simple method.

RESULTS AND DISCUSSION

In connection with the study of the possibility of modifying lignin by the glycosidation, some new water-soluble biodegradable derivatives of lignin were prepared by the previous described methodology.7 The objective of this paper was to apply this method to the lignin model monomeric compounds, to prepare benzyl, 3-(4-methoxyphenyl) propyl, and (2-methoxy-4-formyl)-phenyl D-glucosides by an one pot reaction according to Scheme 1, as described in the experimental part.

The reaction of the 3-(4-methoxyphenyl) propyl alcohol with D-glucose and anhydrous ferric chloride in dry 1,4-dioxane at room temperature for 24 h afforded the exclusive formation of the kinetically favoured glucofuranoside in high yields (32 %
yield) as a mixture of anomers of $\text{5}$ and $\text{5}$ in the ratio 1:1.8. The pyrano conformed glucosides were not present in the reaction mixture. Similarly, when the reaction of benzyl alcohol with the D-glucose was performed under the same reaction conditions, benzyl - and -D-glucofuranosides $\text{1}$ and $\text{1}$ were obtained as the major products and benzyl -D-glucopyranoside $\text{2}$ as the minor product of the reaction. The mixture of glucosides $\text{1}$ and $\text{1}$ were isolated by extraction with ethyl acetate and purified by column chromatography. TLC of the reaction mixture showed the existence of the -anomer of pyranoside in traces, which was not isolated. The total yield of glucosides in the reaction was 28 % and the the -/ -furanosides ratio (1:1.5).

Unlike the previous reactions, the glycosidation of the phenolic group of (2-methoxy-4-formyl)-phenylalcohol (vanillin) with the D-glucose under the same reaction conditions afforded only 4-formyl-2-methoxyphenyl -D-glucofuranosides $\text{3}$ and 4-formyl-2-methoxyphenyl -D-glucopyranoside $\text{4}$ (in a ratio of furano/pyrano of approximately 1:1). When the reaction time was prolonged, the reaction was not unambiguous and pure. TLC showed that the reaction mixture contained some secondary products, which were not identified.

All the D-glucofuranosides were obtained with a preference of the -anomer. After work up, both anomers of $\text{1}$, $\text{3}$ and $\text{5}$ were separated by column chromatography. The structure of all compounds was established by NMR spectroscopy. The $^1\text{H}$ and $^{13}\text{C}$-NMR spectra of $\text{1}$, $\text{1}$, $\text{3}$ and $\text{5}$ allowed the complete assignment of the signals.
for both anomers. The singlet for H-1 and the lowest field signal for C-1 (106.2–107.8 ppm for 1, 3 and 5) are characteristic of the -configuration while the -anomer is characterized by a $J_{1,2}$ value (4.1–4.7 Hz) and an upfield resonance for the anomic carbon (100.5 ppm for 1 and 101.3 ppm for 5). In addition, there is a difference of ca. 6 ppm between the resonance of the anomic carbon C-1 of the conformation of 2 in -D-pyranoside (101.8 ppm) and that of 1 in -D-furanoside (107.0 ppm). The furano conformation results in an upfield ppm shift of C-6 (62.7 ppm pyranoside, and 63.9 ppm furanoside). There are differences in the chemical shifts of C-4 (ca. 73 ppm of pyranoside, and 80 ppm of furanoside). All the chemical shifts and spin-spin coupling values are in good agreement with those corresponding to known values for D-glucofuranosides and pyranosides.8,9

Conventional esterification of 1 and , and 5 and with a mixture of acetic anhydride and pyridine, after purification of the crude products by column chromatography, afforded derivatives, the configuration and conformation of which were chromatography, afforded derivatives, the configuration and conformation of which were not changed.

In conclusion, the glycosylation method described by Ferrieres1,2 for the direct synthesis of either long chain alkyl O-furanosides or O-pyranosides from neutral carbohydrates is also useful for other alcohols, and phenols. Several of these glycosides are required for studies of lignin-saccharidic bonds as model substances. Also, the surface tension of these new derivatives allow them to be consider as prospective biodegradable surfactants.7

EXPERIMENTAL

General

Melting points were determined on a Kofler hot-stage. Optical rotations were measured using a Perkin-Elmer automatic polarimeter, model 141. The $^1$H and $^{13}$C-NMR spectra were recorded in chloroform-d using a Bruker AM-300 spectrometer ($^1$H 300 MHz, $^{13}$C 75 MHz). Thin-layer chromatography-analysis were conducted on coated non-activated glass plates. Detection was effected with a 10% solution of sulphuric acid in ethanol at 110 ºC. The eluents for column chromatography were: a = dichloromethane:methanol 5:1, b = chloroform:methanol 5:1, c = chloroform:heptane 10:1, d = dichloromethane:methanol 7:1. All chemicals were commercially available and 1,4-dioxane was dried over sodium/benzophenone and distilled.

General procedure for the preparation of benzyl and phenyl D-glucofuranosides from D-glucose

To a suspension of D-glucose (1.8 g 10 mmol) in dry 1,4-dioxane (50 ml) were added the appropriate alcohol (20 mmol) at room temperature. Excess solid anhydrous FeCl$_3$ (40 mmol) was added, and the mixture was stirred at room temperature. After 24 h the reaction media was concentrated and quenched by the addition of an equal volume of water followed by vigorous shaking. After several extractions (3 20 ml) with ethyl acetate the combined organic layers was washed with 3 %aq. HCl (20 ml), H$_2$O (30 ml), dried (MgSO$_4$) and concentrated under reduced pressure. The crude oil was purified by column chromatography eluting with 10:1 ethyl acetate–methanol.

Benzyl D-glucofuranoside (1) and benzyl β-D-glucopyranoside (2)

The glucosylation of benzyl alcohol (2.2 g) afforded 0.24 g (9%) of 1, 0.38 g (14%) of 1 and 0.14 g (5%) of 2; TLC (system b): $R_f$ 0.36 (1), 0.32 (1) and 0.42 (2);
The glycosylation of vanillin (3.1 g) afforded 0.32 g (10%) of 4 and 0.52 (4). TLC (system d): Rf 0.43 (3) and 0.52 (4).

3: syrup, \( \text{D}^{20} = 65.5 \) (c 1.0 water). \( \text{H-NMR} \) (, D2O): 7.20 – 7.15 (m, 3H arom.); 5.88 (s, 1H, H-1); 4.21 – 4.17 (m, H-3, 4); 4.07 (br s, 1H, H-2); 3.91 – 3.89 (m, 1H, H-5); 3.85 (s, H, OCH3); 3.81 (dd, 1H, J6,5 = 11.5 Hz, 6'; 3.66 (dd, 1H, J6,5 = 3.6 Hz, H-6').

13C-NMR (, D2O): 187.2 CHO; 132.4, 130.2; 129.9 C arom; 106.2 C; 87.4 C-2; 84.2 C-2; 75.8 C-3; 70.7 C-5; 65.2 C-6; 56.6 OCH3. Anal: Calcd. for C13H18O6 (270.28): C, 57.77; H, 6.71. Found: C, 57.42; H, 6.78.

(2-Methoxy, 4-formyl)-phenyl \( \beta \)-D-glucofuranoside (3) and (2-methoxy, 4-formyl)-phenyl \( \beta \)-D-glucofuranoside (4)

The glycosylation of vanillin (3.1 g) afforded 0.32 g (10%) of 3 and 0.28 g (9%) of 4; TLC (system c): Rf 0.43 (3) and 0.52 (4).

3: syrup, \( \text{D}^{20} = 65.5 \) (c 1.0 water). \( \text{H-NMR} \) (, D2O): 7.20 – 7.15 (m, 3H arom.); 5.88 (s, 1H, H-1); 4.21 – 4.17 (m, H-3, 4); 4.07 (br s, 1H, H-2); 3.91 – 3.89 (m, 1H, H-5); 3.85 (s, H, OCH3); 3.81 (dd, 1H, J6,5 = 11.5 Hz, 6'; 3.66 (dd, 1H, J6,5 = 3.6 Hz, H-6').

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(2-Methoxy, 4-formyl)-phenyl \( \beta \)-D-glucofuranoside (3) and (2-methoxy, 4-formyl)-phenyl \( \beta \)-D-glucofuranoside (4)

The glycosylation of vanillin (3.1 g) afforded 0.32 g (10%) of 3 and 0.28 g (9%) of 4; TLC (system c): Rf 0.43 (3) and 0.52 (4).

3: syrup, \( \text{D}^{20} = 65.5 \) (c 1.0 water). \( \text{H-NMR} \) (, D2O): 7.20 – 7.15 (m, 3H arom.); 5.88 (s, 1H, H-1); 4.21 – 4.17 (m, H-3, 4); 4.07 (br s, 1H, H-2); 3.91 – 3.89 (m, 1H, H-5); 3.85 (s, H, OCH3); 3.81 (dd, 1H, J6,5 = 11.5 Hz, 6'; 3.66 (dd, 1H, J6,5 = 3.6 Hz, H-6').

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s, 1H, H-2); 3.87 (m, 1H, H-5); 3.75 (dd, 1H, \( J_{6,5} = 11.3 \) Hz, \( J_{6,5} = 3.4 \) Hz, H-6'); 3.74 (s, 3H, OCH3); 3.65 (dd, 1H, \( J_{6,5} = 6.4 \) Hz, H-6); 3.37 (m, 2H, COOCH2CH2CH2); 2.54 (t, 2H, \( J = 7.7 \) Hz, COOCH2CH2CH2); 1.82 (m, 2H, COOCOCH2CH2CH2)

3-\( \text{OCH3} \) propyl 2,3,5,6-tetra-acetyl-\( \text{D-glucofuranoside} \) (6)

Esterification of 5 and 5 in the same manner as above gave 7 and 7 in 85 % and 80 % yield, respectively.

7 : syrup, TLC (system c); \( R_f /c98 = +63 \) (c 1 chloroform). \( ^{1} \)H-NMR ( , CDCl3): 7.39 – 7.28 (m, 5H arom); 5.41 (d, \( J_{5,6} = 9.4 \) Hz, H-3); 5.27 (m, \( J_{3,4} = 9.7 \) Hz, \( J_{6,5} = 5.0 \) Hz, H-5); 5.09 (s, 1H, H-1); 5.03 (s, 1H, H-2); 4.63 (dd, 1H, \( J_{6,5} = 12.0 \) Hz, \( J_{6,5} = 2.2 \) Hz, H-6'); 4.47 (d, \( J_{3,4} = 9.6 \) Hz, H-4); 4.14 (dd, 1H, H-6); 2.16 – 2.05 (4 s, 12H, 4 COOCH3). \( ^{13} \)C-NMR ( , CDCl3): 170.4, 169.9, 169.3 OCOCH3; 137.9, 128.4, 127.1 C arom; 105.4 C-1; 80.3 C-4; 78.1 C-2; 73.1 C-3; 69.7 C-5; 62.9 C-6; 20.7, 20.6, 20.5, 20.4 OCOCH3. Anal: Calcd. for \( \text{C24H32O11} \) (496.51): C, 58.06, H, 6.50. Found: C, 58.12, H, 6.48.

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D-GLUCOFURANOSIDES SYNTHESSES

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IZVOD

DODIJAĆE NEKIH D-GLUKOFURANOZIDA OD NEZAŠTIćENIH D-GLUKOZE D. JONIAK i M. POLAKOVA

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O-Glukozidacija 3-(4-metoksifenil)propil alkohola, benzil alkohola i vanilina potpuno neshtaćenom D-glikozom, izvedena u heterogenoj sredini i promovisana anhidivanim feni-hloridom, daje odgovarajuće D-glikofuranonizde kao glavne i D-glikopyranonizde kao sporedne proizvode reakcije.

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