

Synthesis of D-glucose 3-O-ethers as models representing the α -ether type linkage between lignin and carbohydrates

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Reaction of sodium salt of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose with the corresponding substituted benzyl halides, followed by acid hydrolysis gave 3-*O*-anisyl- and 3-*O*-veratryl- D-glucose. It has been found during acid hydrolysis of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose 3-*O*-anisyl- and 3-*O*-veratryl derivatives that the stability of the ether linkage in these substances is comparable to that of the 1,2-*O*-isopropylidene acetal residue.

В работе описан способ приготовления 3-*O*-анизил- и 3-*O*-вератрил-*D*-глюкозы при помощи реакции натриевой соли 1,2:5,6-ди-*O*-изопропилиден- α -*D*-глюкофуранозы с соответствующим замещенным бензилгалогеном. При изучении кислотно-катализируемого гидролиза 3-*O*-анизил-1,2:5,6-ди-*O*-изопропилиден- α -*D*-глюкофуранозы и 1,2:5,6-ди-*O*-изопропилиден-3-*O*-вератрил- α -*D*-глюкофуранозы в условиях, подходящих для гидролиза изопропилиденовых групп, было найдено, что устойчивость эфирной связи приблизительно такая же, как устойчивость 1,2-*O*-изопропилиденовой ацетальной связи.

Model compounds having defined ether type linkages between the aromatic component and HO-3 of D-glucose, *i.e.* 3-*O*-benzyl-, 3-*O*-anisyl-, and 3-*O*-veratryl-D-glucoses have been prepared in order to study the α -ether type linkage between lignin and carbohydrates in plants. In connection with studies concerned with linkages between lignin and carbohydrates, *Freudenberg* [1] prepared guaia-cylglycerol- β -coniferyl ether.

Of the known sugar derivatives, 3-*O*-benzyl-D-glucose (*Ic*) represents the most simple model for the ether type linkage between lignin and carbohydrates. The substance was obtained in 90% yield *via* the procedure based on the reaction of sodium salt of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose with benzyl halide. The other models, 3-*O*-anisyl- (*IIc*) and 3-*O*-veratryl-D-glucose (*IIIc*) were prepared in a similar manner. The substances are models for lignin-carbohydrate

in ethanol—water 1:1, 70°C, 4 h) and the yields of the produced ethers were optimized.

The ethers *Iic* and *IIIc* present in the reaction mixtures together with D-glucose and the corresponding alcohol (t.l.c.) were isolated by column chromatography. The structure of the obtained substances was proved by p.m.r. spectral data.

An important conclusion follows from the obtained results, *i.e.* that the *p*-methoxysubstituted benzyl ethers show more pronounced acid lability compared to their nonsubstituted analogues, the latter being relatively acid-stable under similar conditions and may be split by catalytic hydrogenolysis [2].

The observed properties of the substituted benzyl ethers described herein are comparable to those of lignin dimers containing α -ether linkages, the stability of which was studied by *Gierer* [3], *Harkin* [4], and *Ciaramitaro* and *Steelink* [5].

Experimental

Melting points were determined on a Kofler hot-stage. Optical rotations were measured with a Perkin—Elmer automatic polarimeter, Model 141. P.m.r. spectra (80 MHz) for solutions in chloroform-*d* or chloroform-*d*—DMSO-*d*₆ were obtained using a Tesla BS 487 B spectrometer. Thin-layer chromatography was performed on neutral Silica gel PF₂₅₄ (Merck, A. G., Darmstadt). Preparative chromatography was done on columns (80 × 2.5 cm) of Silica gel (0.063—0.1 mm, Merck). The following systems were used for elutions: *A.* benzene—ethyl acetate 3:2; *B.* benzene—ethyl acetate 1:3; *C.* chloroform—acetone 8:1; *D.* chloroform—acetone 1:1.

3-O-Benzyl-1,2:5,6-di-O-isopropylidene- α -D-glucofuranose (Ia)

Compound (*Ia*) was prepared as described [6]. The p.m.r. data (chloroform-*d*): δ 7.80—7.00 (m, 5H, aromatic); 5.85 (d, H-1); 5.00—3.30 (m, 8H, benzyl, H-2,3,4,5,6,6'); 1.48, 1.40, 1.38, 1.28 (4s, 4Me).

3-O-Benzyl-1,2-O-isopropylidene- α -D-glucofuranose (Ib)

Compound (*Ib*) was obtained by selective hydrolysis [6] of *Ia*. The p.m.r. data (chloroform-*d*): δ 7.80—7.00 (m, 5H, aromatic); 5.89 (d, H-1); 5.00—3.30 (m, 8H, benzyl, H-2,3,4,5,6,6'); 1.45, 1.30 (2s, 2Me); 2.75 (d, 2H, OH).

3-O-Benzyl-D-glucose (Ic)

Compound (*Ic*) was obtained from *Ia* by hydrolysis [7]. The p.m.r. data (chloroform-*d*): δ 7.80—7.00 (m, 5H, aromatic); 5.00—4.40 (m, 3H, benzyl, H-1); 5.00—3.30 (m, H-2,3,4,5,6,6'); 3.25 (broad, 4H, OH).

3-O-Anisyl-1,2:5,6-di-O-isopropylidene- α -D-glucofuranose (IIa)

Anisyl chloride (24.3 g; 0.15 mole) was added to the sodium salt of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose [2] (42 g; 0.15 mole) and the mixture was heated with vigorous stirring for 16 h at 90°C. Petroleum ether (500 ml) was added after cooling, the mixture was filtered, the filtrate washed with water (5 \times 300 ml) and dried over anhydrous sodium sulfate. The crude product was purified by elution from a column of silica gel with solvent *A* to give pure *IIa* (81%; R_f 0.8) as a yellow sirup, $[\alpha]_D^{20} -17^\circ$ (*c* 1, chloroform). The p.m.r. data (chloroform-*d*): δ 7.40—6.75 (4s, 4H, aromatic); 5.89 (d, H-1); 5.00—3.30 (m, 8H, anisyl, H-2,3,4,5,6,6'); 3.80 (s, OMe); 1.50, 1.45, 1.39, 1.35 (4s, OMe).

For $C_{20}H_{28}O_7$ (380.44) calculated: 63.14% C, 7.41% H; found: 62.95% C, 7.37% H.

3-O-Anisyl-1,2-O-isopropylidene- α -D-glucofuranose (IIb)

Aqueous hydrochloric acid (0.2%; 100 ml) was added to the solution of *IIa* (2%; 100 ml) in ethanol and the mixture was kept at 30°C. The reaction was monitored by t.l.c. in solvent *C*. The solution was neutralized after 3 h with sodium carbonate and extracted with chloroform. The chloroform solution was dried over anhydrous sodium sulfate, concentrated and purified by elution from a column of silica gel with solvent *C*. The fractions containing material having R_f 0.55 were collected to give *IIb* (70%) as a yellow sirup, $[\alpha]_D^{20} -20^\circ$ (*c* 1, chloroform). The p.m.r. data (chloroform-*d*): δ 7.40—6.70 (4s, 4H, aromatic); 5.88 (d, H-1); 5.00—3.30 (m, 8H, anisyl, H-2,3,4,5,6,6'); 3.75 (s, OMe); 1.45, 1.30 (2s, 2Me); 2.75 (d, 2H, OH).

For $C_{17}H_{24}O_7$ (340.37) calculated: 59.98% C, 7.10% H; found: 59.90% C, 7.05% H.

3-O-Anisyl-D-glucose (IIc)

A 1% solution of *IIa* (2 g) in ethanol—water (1:1) containing hydrochloric acid (0.2%) was heated at 70°C for 4 h. The mixture was neutralized with sodium carbonate, concentrated to 100 ml and extracted with dichloromethane (5 \times 150 ml). The combined extracts were dried over anhydrous sodium sulfate, concentrated and chromatographed (solvent *D*). Fractions containing the component having R_f 0.15 (solvent *B*) were collected to give on concentration *IIc* (40%). Crystallization from chloroform—acetone (1:1) gave pure title substance melting at 134—135°C and having $[\alpha]_D^{20} 14 \rightarrow 26^\circ$ (*c* 1, ethanol). The p.m.r. data (chloroform-*d*—DMSO-*d*₆): δ 7.75—6.65 (m, 4H, aromatic); 5.00—4.40 (m, 3H, anisyl, H-1); 4.30—3.30 (m, 6H, H-2,3,4,5,6,6'); 3.75 (s, OMe); 3.32 (broad, 4H, OH).

For $C_{14}H_{20}O_7$ (300.31) calculated: 55.99% C, 6.71% H; found: 55.85% C, 6.65% H.

1,2:5,6-Di-O-isopropylidene-3-O-veratryl- α -D-glucofuranose (IIIa)

Reaction of sodium salt of 1,2:5,6-di-*O*-isopropylidene- α -D-glucofuranose with veratryl chloride in the manner described in the preparation of *IIa* gave *IIIa* (86%) as a yellow oil,

m.p. 70–71°C, $[\alpha]_D^{20} - 24^\circ$ (c 1, chloroform). The p.m.r. data (chloroform-d): δ 7.10–6.80 (s, 3H, aromatic); 5.92 (d, H-1); 5.00–3.30 (m, 8H, veratryl, H-2,3,4,5,6,6'); 3.89 (s, 2OMe); 1.50, 1.45, 1.39, 1.35 (4s, 4Me).

For $C_{21}H_{30}O_8$ (410.47) calculated: 61.44% C, 7.37% H; found: 61.36% C, 7.40% H.

1,2-*O*-Isopropylidene-3-*O*-veratryl- α -D-glucofuranose (*IIIb*)

Partial hydrolysis of *IIIa* in the manner described in the preparation of *IIIb* gave crude *IIIb* which was purified by elution from a column of silica gel (solvent *C*). The title substance (R_f 0.5, solvent *B*, $[\alpha]_D^{20} - 31^\circ$ (c 1, chloroform)) was obtained (75%) as a yellow oil. The p.m.r. data (chloroform-d): δ 7.10–6.80 (s, aromatic); 5.85 (d, H-1); 5.00–3.30 (m, 8H, veratryl, H-2,3,4,5,6,6'); 3.85 (s, 2Me); 1.45, 1.28 (2s, 2Me); 2.75 (s, 2H, OH).

For $C_{18}H_{26}O_8$ (370.40) calculated: 58.36% C, 7.07% H; found: 58.30% C, 7.00% H.

3-*O*-Veratryl-D-glucose (*IIIc*)

Hydrolysis of *IIIa* in a manner described in the preparation of *IIIc* gave crude sirupy *IIIc* (R_f 0.1, solvent *B*). After purification on a silica gel column with solvent *D* and crystallization from chloroform–acetone (1:1) the pure title substance (43%) melted at 136–138°C and had $[\alpha]_D^{20} + 8 \rightarrow 36.4^\circ$ (c 1, ethanol). The p.m.r. data (chloroform-d–DMSO- d_6): δ 7.15–6.65 (m, 3H, aromatic); 5.00–4.40 (m, 3H, veratryl, H-1); 5.00–3.30 (m, 6H, H-2,3,4,5,6,6'); 3.79 (s, 2OMe); 3.25 (broad, 4H, OH).

For $C_{15}H_{22}O_8$ (330.34) calculated: 54.53% C, 6.71% H; found: 54.49% C, 6.65% H.

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