BENZYL ETHERS OF METHYL α-D-GLUCOPYRANOSIDE

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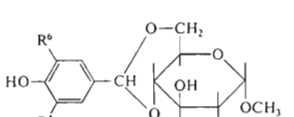
Methyl 4-O-(3-methoxy-4-hydroxybenzyl) and methyl 4-O-(3,5-dimethoxy-4-hydroxybenzyl)-α-D-glucopyranoside and their 6-O-isomers were prepared as model substances for the ether lignin-saccharide bond by reductive cleavage of corresponding 4,6-O-benzylidene derivatives. Kinetic study of acid-catalyzed hydrolysis of the compounds prepared was carried out by spectrophotometric determination of the benzyl alcoholic groups set free, after their reaction with quinonemonochloroimide, and it showed the low stability of the *p*-hydroxybenzyl ether bond.

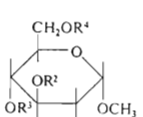
In connection with the study of the properties of the ether bonds of lignin with polysaccharides in wood on model compounds we prepared phenolic variants of substituted 4-O and 6-O-benzyl ethers of methyl α-D-glucopyranoside the aromatic component of which represents a guaiacyl and syringyl structure as the two main structural types of the lignin macromolecule units. For the synthesis of these substances reductive cleavage of corresponding 4,6-O-benzylidene derivatives was used, applying a procedure by which we prepared 4-methoxybenzyl ethers in our preceding study[1].

Hydrogenolysis of methyl 4,6-O-(4-hydroxy-3-methoxybenzylidene)-α-D-glucopyranoside (*I*) with $LiAlH_4$–$AlCl_3$ and subsequent fractional crystallization afforded methyl 4-O- (*II*) and syrupy 6-O-(4-hydroxy-3-methoxybenzyl)-α-D-glucopyranoside (*III*). In a similar manner 4-O (*IV*) and 6-O-(3,5-dimethoxy-4-hydroxybenzyl) (*V*) derivatives of methyl-α-D-glucopyranoside were prepared from methyl 4,6-O-(3,5-dimethoxy-4-hydroxybenzylidene)-α-D-glucopyranoside (*VI*). The structure of the substituted benzyl derivatives isolated was confirmed on the basis of the chemical shift of the methyl group in the ^{1}H-NMR spectra[2] of corresponding 2,3,6-tri-O-methyl (*VII*, *VIII*) and 2,3,4-tri-O-methyl derivatives (*IX*, *X*). The properties of the prepared substances are given in Table I.

From present knowledge on the properties of *p*-methoxybenzyl ethers of saccharides[1] it follows that they are easily hydrolysable under the conditions of mild acid-catalyzed hydrolysis, in contrast to the stability of unsubstituted saccharidic benzyl ethers. For a kinetic study of the stability of *p*-hydroxybenzyl ethers *II* – *V* we applied the method based on the reaction of liberated benzyl alcohol groups with quinonemonochloroimide and subsequent spectrophotometric determination of the coupling product of the reaction. This method was worked out by Gierer[3] for the determina-

tion of the content of benzyl alcoholic groups in the lignin macromolecule. Under the conditions used for the kinetic study of the hydrolysis of *p*-hydroxy-substituted benzyl ether of saccharides the ether-bound benzyl alcoholic group as well as the hydroxyl groups of the saccharide moiety of the models are inactive against the effect of quinonemonochloroimide.This method proved well reproducible and also suitable for the study of the stability of benzyl ether bonds in isolated lignin–saccharide fractions[4].





I, $R^5 = OCH_3$, $R^6 = H$
VI, $R^5 = R^6 = OCH_3$

II, $R^1 = R^2 = R^4 = H$, $R^3 = 3\text{-}CH_3O4\text{-}OHC_6H_3CH_2$
III, $R^1 = R^2 = R^3 = H$, $R^4 = 3\text{-}CH_3O4\text{-}OHC_6H_3CH_2$
IV, $R^1 = R^2 = R^4 = H$, $R^3 = 3,5\text{-}(CH_3O)_24\text{-}OHC_6H_2CH_2$
V, $R^1 = R^2 = R^3 = H$, $R^4 = 3,5\text{-}(CH_3O)_24\text{-}OHC_6H_2CH_2$
VII, $R^1 = R^2 = R^4 = CH_3$, $R^3 = 3,4\text{-}(CH_3O)_2C_6H_3CH_2$
VIII, $R^1 = R^2 = R^3 = CH_3$, $R^4 = 3,4\text{-}(CH_3O)_2C_6H_3CH_2$
IX, $R^1 = R^2 = R^4 = CH_3$, $R^3 = 3,4,5\text{-}(CH_3O)_3C_6H_2CH_2$
X, $R^1 = R^2 = R^3 = CH_3$, $R^4 = 3,4,5\text{-}(CH_3O)_3C_6H_2CH_2$

The rate constants of acid-catalyzed hydrolysis of benzyl ethers *II* – *V* are given in Table I. Under mild conditions all substances studied are easily hydrolysable at the same rate. Comparison of these data with the rate constants for *p*-OCH_3--substituted benzyl ethers[1] indicates a 3 to 4-times higher hydrolysis rate of *p*-OH--substituted derivatives, which depends on the higher polar effect of the substitution of the aromatic component of the prepared models. The observed different properties of the *p*-OH or *p*-OCH_3 benzyl ether bond in comparison with the known stability of unsubstituted benzyl ethers enable the utilization of compounds of this type for a temporary blocking of the hydroxyl groups of saccharides in various syntheses.

On the other hand, the results obtained complete the knowledge on the easy hydrolysability of the benzyl aryl ether bond in lignin. The properties of this bond with respect to acid-catalyzed hydrolysis were studied in detail on model compounds of dilignol type[5]. The differences in the properties of benzyl ethers (lignin–lignin bond) and benzyl alkyl ethers (lignin–saccharide bond) became manifest during the working up of models of both types in alkaline medium, where under the conditions of selective hydrolysis of *p*-hydroxybenzyl aryl ether bonds[6] the substituted

p-hydroxybenzyl ethers of saccharides prepared were not split. From these results it follows that a differentiation is possible as well as the determination of the amount of lignin–lignin and lignin–saccharide *p*-hydroxy-substituted benzyl ether structures in isolated lignin–saccharide fractions.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are uncorrected. Optical rotation was measured with a Perkin–Elmer 141 polarimeter in chloroform ($c = 1$). The ^{1}H-NMR spectra were obtained on a 80 HMz Tesla BS—482 instrument in deuteriochloroform. Thin-layer chromatography was carried out on silica gel PF_{254} Merck and column chromatography on silica gel Merck (0·063—0·1 mm) using the system A (chloroform–2-propanone 3 : 1) and B (chloroform–2-propanone 5 : 1).

Kinetics of the Hydrolysis of Ethers

A mixture of 1 ml of a 0·0015M solution of sample in water and 0·5 ml of buffer (KCl–HCl pH 1·1) was heated at 60°C (±0·1°) in sealed ampoules filled with nitrogen. At selected intervals

TABLE I
The Properties of the Substances Prepared

Compound	Formula (m.w.)	Calculated/Found % C	Calculated/Found % H	M.p., °C $[\alpha]_D^{25}$	$k \cdot 10^{-5}$ s^{-1}
II	$C_{15}H_{22}O_8$ (330·3)	54·53 54·60	6·71 6·60	129—130 +116	12·80
III	$C_{15}H_{22}O_8$ (330·3)	54·53 54·45	6·71 6·73	syrup +56	12·05
IV	$C_{16}H_{24}O_9$ (360·4)	53·32 53·25	6·71 6·65	131—133 +119	14·06
V	$C_{16}H_{24}O_9$ (360·4)	53·32 53·37	6·71 6·78	syrup +61	13·00
VII	$C_{19}H_{30}O_8$ (386·4)	59·05 58·99	7·82 7·75	syrup +53	—
VIII	$C_{19}H_{30}O_8$ (386·4)	59·05 59·16	7·82 7·87	syrup +102	—
IX	$C_{20}H_{32}O_9$ (416·3)	57·71 57·81	7·75 7·75	syrup +58	—
X	$C_{20}H_{32}O_9$ (416·3)	57·71 57·68	7·75 7·76	syrup +112	—

samples were withdrawn and – after cooling to room temperature – 7 ml of a 0·043M aqueous NaOH and 0·5% ethanolic solution of quinonemonochloroimide (0·01 ml) were added to the ampoule content. The content of the benzyl alcoholic groups set free was determined spectrophotometrically at 640 nm after 10 minutes' reaction. The calibration curves were determined from corresponding benzyl alcohols. Quinonemonochloroimide was prepared from 4-aminophenol[7].

Methyl 4-O-(4-Hydroxy-3-methoxybenzyl)-α-D-glucopyranoside (*II*) and Methyl 6-O-(4-Hydroxy-3-methoxybenzyl)-α-D-glucopyranoside (*III*)

Compound[8] *I* was hydrogenolysed using a procedure described in our previous paper[1]. From the crude product compound *II* was isolated in 29% yield by fractional crystallization from chloroform–2-propanone (1 : 1). ^{1}H-NMR: 6·70–7·40 (ss, 3 H, aromatic protons): 4·40–4·90 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·80 (s, CH_3O); 3·35 (s, CH_3O–1). The mother liquor was concentrated and compound *III* was isolated in 20% yield from the syrupy residue by column chromatography in system B. ^{1}H-NMR: 6·70–7·40 (ss, 3 H, aromatic protons); 4·40–4·80 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·78 (s, CH_3O); 3·33 (s, CH_3O–1).

Methyl 4-O-(3,5-Dimethoxy-4-hydroxy)phenyl-α-D-glucopyranoside (*IV*) and Methyl 6-O-(3,5-Dimethoxy-4-hydroxy)phenyl-α-D-glucopyranoside (*V*)

Reaction of compound[8] *VI* with $LiAlH_4$ (ref.[1]) and subsequent fractional crystallization from chloroform–acetone (1 : 1) afforded ether *IV* in 27% yield. ^{1}H-NMR: 6·70–7·40 (ss, 2 H, aromatic protons); 4·40–4·95 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·78–3·82 (ss, 2 CH_3O); 3·35 (s, CH_3O–1). Chromatographic separation of the concentrated mother liquor in system B gave compound *V* in 18% yield. ^{1}H-NMR: 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·78–3·92 (ss, 2 CH_2O); 3·38 (s, CH_3O–1).

Methyl 4-O-(3,4-Dimethoxybenzyl)-2,3,6-tri-O-methyl-α-D-glucopyranoside (*VII*)

Compound *VII* was obtained in 85% yield on treatment of *II* with methyl iodide and silver oxide in N,N-dimethylformamide. ^{1}H-NMR: 6·75–7·40 (ss, 3 H, aromatic protons); 4·40 to 4·95 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·82; 3·86 (ss, 2 CH_2O); 3·63 (s, CH_3O–3); 3·50 (s, CH_3O–2); 3·35 (s, CH_3O–1); 3·33 (s, CH_3O–6).

Methyl 6-O-(3,4-Dimethoxybenzyl)-2,3,4-tri-O-methyl-α-D-glucopyranoside (*VIII*)

Applying a similar procedure compound *VIII* was obtained from *III* in 82% yield. ^{1}H-NMR: 6·75–7·41 (ss, 3 H, aromatic protons); 4·36–4·80 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·82; 3·86 (ss, 2 CH_3O); 3·64 (s, CH_3O–3); 3·57 (s, CH_3O–4); 3·50 (s, CH_3O–2); 3·35 (s, CH_3O–1).

Methyl 4-O-(3,4,5-Trimethoxybenzyl)-2,3,6-tri-O-methyl-α-D-glucopyranoside (*IX*)

Methylation of *IV* afforded derivative *IX* in 76% yield. ^{1}H-NMR: 6·70–7·40 (ss, 2 H, aromatic protons); 4·40–4·93 (m, 3 H, benzyl, H–1); 3·30–4·00 (m, H–2,3,4,5,6,6′); 3·78; 3·82; 3·86 (ss, 3 CH_3O); 3·63 (s, CH_3O–3); 3·49 (s, CH_3O–2); 3·35 (s, CH_3O–1); 3·32 (s, CH_3O–6).

Methyl 6-O-(3,4,5-Trimethoxybenzyl)-2,3,6-tri-O-methyl-α-D-glucopyranoside (*X*)

Compound *X* was obtained in 81% yield on methylation of *V*. ^{1}H-NMR: 6·70—7·40 (ss, 2 H, aromatic protons); 4·40—4·85 (m, 3 H, benzyl, H—1); 3·30—4·00 (m, 3 H, benzyl, H—1); 3·78; 3·82; 3·86 (ss, 3 CH_3O); 3·64 (s, CH_3O—3); 3·58 (s, CH_3O—4); 3·50 (s, CH_3O—2); 3·35 (s, CH_3O—1).

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