Synthesis of some cyclic acetals of methyl α-D-glucopyranoside as model compounds of lignin—saccharide complex

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Cyclic acetals have been prepared from methyl α-D-glucopyranoside and anisaldehyde, vanillin, veratrylaldehyde and syringaldehyde by zinc chloride-catalyzed condensation. The stability of the 4,6-*O*-acetal structure towards the action of 30% acetic acid has been investigated. It has been found that the differences in the acid instability of the extremely acid-labile compounds can be accounted for by the polar effects of the substituents on the aromatic ring.

In order to study the character of linkages between lignin and saccharides model compounds containing acetal bonds were synthesized. This is one of the possible type of bonds considered to be present in lignin—saccharide complex of plants [1, 2].

Some cyclic acetals of methyl α-D-glucopyranoside and aromatic aldehydes and ketones *e.g.* salicylaldehyde, *p*-tolualdehyde [3], cinnamaldehyde [4], benzophenone, and acetophenone [5] were prepared by previous authors. Here we report on the synthesis, some properties and the determination of the structure of 4,6-*O*- cyclic acetals derived from methyl α-D-glucopyranoside and some aromatic aldehydes bearing different substituents on the aromatic ring.

Experimental

Melting points were determined on a Kofler hot stage. Optical rotations were measured on a Perkin—Elmer automatic polarimeter Model 141. Methyl α-D-glucopyranoside (commercial product) was dried at 100°C for 12 hours before use. Vanillin, syringaldehyde, veratrylaldehyde, and *p*-methoxybenzaldehyde were commercial products, dried over phosphorus pentoxide for 24 hours. Zinc chloride was freshly fused and finely powdered under benzene. Thin-layer chromatography on Silica gel PF 254 (Merck, A. G., Darmstadt) and column chromatography on Silica gel 60 (Merck, A. G., Darmstadt) (0.05—0.2 mm) was carried out with: *A*. chloroform—benzene—methanol 6 : 4 : 1, *B*. chloroform—ether 10 : 1, and *C*. chloroform—methanol 8 : 1 (v/v). Detection was by charring with 5% sulfuric acid in ethanol.

Preparation of acetals (I—IV)

Methyl α-D-glucopyranoside (1 molar equivalent), the respective aldehyde (3 molar equivalents), and zinc chloride (1 molar equivalent) were stirred under reflux for 24—36 hours. The mixture was filtered rapidly and the organic solvent removed. The residue was dissolved in saturated solution of sodium hydrogen carbonate and the resulting solution extracted with ether to remove most of the unchanged aldehyde. Subsequent

extraction with chloroform (3 times) gave the crude product which was purified by column chromatography in system *A*, and the pure acetal was crystallized from chloroform—petroleum ether. The physical constants and analytical figures of acetals and their derivatives are summarized in Table 2. The acetals are well soluble in methanol, ethanol, pyridine, benzene, chloroform, less in ether and water, and are not soluble in petroleum ether and *n*-heptane.

Preparation of the methyl derivatives of acetals (V—VII)

The acetal (0.4 g) was stirred with silver carbonate (1.6 g) and methyl iodide (0.7 g) at room temperature for 8 hours during which time fresh portions of methyl iodide (2 × 0.7 g) were added. The mixture was stirred for additional 24 hours, diluted with chloroform, filtered, and the product was purified by column chromatography in system *B*.

Preparation of acetal acetates (VIII—XI)

The acetal (0.4 g) in pyridine (0.7 ml) was treated at room temperature with acetic anhydride (0.7 ml) for 24 hours, whereafter the mixture was poured onto crushed ice. The separated white solid product was filtered, washed with ice water, dried, and crystallized from chloroform—petroleum ether.

Hydrolysis of acetals

A sample of the acetal (10 mg) was dissolved in 30% (v/v) acetic acid and left at room temperature. The course of the hydrolysis was monitored in 1 minute intervals by thin-layer chromatography in system *A* [5]. The time needed for the complete disappearance of the starting acetal is given in Table 3.

Similar hydrolysis of methyl ethers *V—VII* (0.5 g) gave, after removal of the aldehyde by column chromatography in system *C*, methyl 2,3-di-*O*-methyl-α-D-glucopyranoside which was in all respects identical with the authentic sample.

Results and discussion

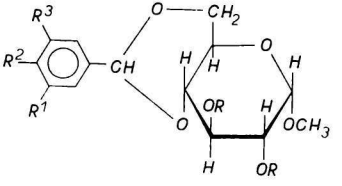
The yields of cyclic 4,6-*O*-acetals obtained from methyl α-D-glucopyranoside and vanillin, anisaldehyde, syringaldehyde, and veratrylaldehyde, compared with similar zinc chloride-catalyzed reactions, were noticeably lower. Although an excess of the aldehyde was used, the yields, which were in the range of 9—20%, could not be improved either by increasing the reaction temperature or by extending the reaction times. The stability of the formed acetal bond depends, *inter alia*, on the polar effect of substituents [3, p. 237] on the aromatic ring of the respective aldehyde. For instance, *p*-methoxybenzylidene acetal is ten times more acid labile than benzylidene acetal [6]. Another methoxyl group in the *m*-position to the carbonyl group exhibits little effect upon the stability of an acetal.

The elemental analyses of the prepared acetals showed that these are equimolar compounds of the aldehyde and methyl α-D-glucopyranoside. To confirm the structure the acetals were methylated using Purdie method.

Methylation of the vanillilidene and veratrylidene acetal of methyl α-D-glucopyranoside gave the same compound. Mild acid hydrolysis of *O*-methyl ethers of cyclic acetals gave,

Table 1

List of the prepared acetals and their derivatives



No.	Compound	R^1	R^2	R^3	R
I	Methyl 4,6-*O*-anisylidene-α-D-glucopyranoside	—H	—OMe	—H	—H
II	Methyl 4,6-*O*-vanillilidene-α-D-glucopyranoside	—OMe	—OH	—H	—H
III	Methyl 4,6-*O*-syringylidene-α-D-glucopyranoside	—OMe	—OH	—OMe	—H
IV	Methyl 4,6-*O*-veratrylidene-α-D-glucopyranoside	—OMe	—OMe	—H	—H
V	Methyl 4,6-*O*-anisylidene-2,3-di-*O*-methyl-α-D-glucopyranoside	—H	—OMe	—H	—Me
VI	Methyl 2,3-di-*O*-methyl-4,6-*O*-veratrylidene-α-D-glucopyranoside	—OMe	—OMe	—H	—Me
VII	Methyl 2,3-di-*O*-methyl-4,6-*O*-(3,4,5-trimethoxybenzylidene)-α-D-glucopyranoside	—OMe	—OMe	—OMe	—Me
VIII	Methyl 2,3-di-*O*-acetyl-4,6-*O*-anisylidene-α-D-glucopyranoside	—H	—OMe	—H	—Ac
IX	Methyl 2,3-di-*O*-acetyl-4,6-*O*-(3-methoxy-4-acetoxybenzylidene)-α-D-glucopyranoside	—OMe	—OAc	—H	—Ac
X	Methyl 2,3-di-*O*-acetyl-4,6-*O*-(3,5-dimethoxy-4-acetoxybenzylidene)-α-D-glucopyranoside	—OMe	—OAc	—OMe	—Ac
XI	Methyl 2,3-di-*O*-acetyl-4,6-*O*-veratrylidene-α-D-glucopyranoside	—OMe	—OMe	—H	—Ac

Table 2

Characteristics of the prepared compounds

No.	Formula	*M* (calc.)	Calculated/found % C	% H	Yield [%]	M.p. [°C]	$[\alpha]_D^{24}$ *c* = 1, methanol
I	$C_{15}H_{20}O_7$	312.31	57.68 57.51	6.45 6.40	17	201–202	+88
II	$C_{15}H_{20}O_8$	328.31	54.90 54.81	6.14 6.18	9	181–182	+66
III	$C_{16}H_{22}O_9$	358.33	53.63 53.72	6.19 6.11	18	208	+68
IV	$C_{16}H_{22}O_8$	342.33	56.12 55.93	6.48 6.53	20	192	+73
V	$C_{17}H_{24}O_7$	340.30	59.98 60.06	7.11 7.02	72	148–149	+70
VI	$C_{18}H_{26}O_8$*	370.38	58.36 58.35	7.07 7.12	62	132	+71
	$C_{18}H_{26}O_8$**	370.38	58.36 58.30	7.07 7.00	68	132–133	+71
VII	$C_{19}H_{26}O_9$	398.39	56.99 57.04	7.06 7.00	65	120–121	+65
VIII	$C_{19}H_{24}O_9$	396.39	57.56 57.53	6.10 6.12	95	136–137	+64
IX	$C_{21}H_{26}O_{11}$	454.41	55.50 55.44	5.76 5.72	90	66–68	+42
X	$C_{22}H_{28}O_{12}$	484.44	54.54 54.51	5.82 5.86	92	72–74	+40
XI	$C_{20}H_{26}O_{10}$	426.40	56.33 56.33	6.14 6.20	96	139	+53

* Compound prepared by methylation of *II*.
** Compound prepared by methylation of *IV*.

Table 3

Time needed for complete hydrolysis of the acetals with 30% acetic acid

Compound	*I*	*II*	*III*	*IV*	*V*	*VI*	*VII*
Time [min.]	28	14	38	38	40	95	7.5 hrs.

in all cases, the corresponding aldehyde and methyl 2,3-di-*O*-methyl-α-D-glucopyranoside identical in all respects with an authentic standard. This showed that the prepared compounds are cyclic monoacetals having the acetal ring attached to the C-4 and C-6 position of methyl α-D-glucopyranoside. Methylation analysis showed also that during the preparation process no changes occurred either in the pyranoid structure or on the anomeric centre. The prepared acetals and their derivatives are listed in Tables 1, 2.

The relative stability of the prepared acetals towards the action of acid was investigated, similarly as by *Evans et al.* [5], by the determination of the time needed for complete hydrolysis of the acetal with 30% acetic acid. The results obtained (Table 3) confirmed

the extreme acid-lability of the prepared acetals *I*—*IV*. The differences in the stability of the individual acetals towards the action of the applied acid can be attributed to the polar effects of the substituents on the aromatic ring.

The hydrolysis of acetals *O*-methyl ethers *V*—*VIII* was carried out in a similar manner. Taking into account the time needed for complete splitting off of the acetal residue it can be concluded that the *O*-methyl ethers of acetals are relatively less acid-labile than the corresponding hydroxy compounds.

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