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THE SYNTHESIS, PROPERTIES AND STRUCTURES OF SOME UNSATURATED METHYL-α,D-GLUCOPYRANOSIDE ACETALS

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Abstract—A method for the synthesis of unsaturated methyl-α,D-glucopyranoside acetals has been developed. The structure and some properties of these acetals and their derivatives has been investigated.

THE acetals formed from unsaturated aldehydes such as citral,[1] cinnamaldehyde,[2] crotonaldehyde[3] and pentaerythritol with simple alcohols are known.

The unsaturated acetals of sugars have not been described and in a previous investigation[4] only the reaction product of methyl-α,D-glucopyranoside with crotonaldehyde was described. Sugar derivatives of this type may be given different structural formulae and the present work describes syntheses and the structural determination of unsaturated methyl-α,D-glucopyranoside acetals with cinnamaldehyde, crotonaldehyde and citral.

The synthesis of unsaturated acetals of sugars, presents difficulties, as in the majority of cases the catalyst react with the unsaturated aldehyde, or cause, polymerization of aldehyde. For this reason acetals could not be prepared from aldehydes and methyl-α,D-glucopyranoside in the presence of hydrogen chloride, zinc chloride or an ion exchanger but the azeotropic removal of water at elevated temperatures, and the use of anhydrous magnesium sulphate as catalyst, resulted in the desired compounds.

In comparison with the synthesis of saturated acetals, the reaction of methyl-α,D-glucopyranoside with unsaturated aldehydes, requires longer time, higher temperatures and the azeotropic removal of water. The structure of the reacting aldehyde is also important. The acetal of cinnamaldehyde can be obtained easily, in a 80% yield at 86–89° and with a 1:6 ratio of glucoside to aldehyde, while only a 37% yield of acetal is obtained from crotonaldehyde under similar reaction conditions and the synthesis of citrylidene acetal requires a temperature of 150°. The reactivity of the unsaturated aldehyde is weaker the longer the chain linkage, and stronger when a phenyl radical is present. Analysis of the acetals has shown that they are equimolar compounds of aldehyde and glucoside.

For the purpose of structural determination and resolution of free hydroxyl groups, the mono acetals were subjected to etherfication with methyl iodide, with formation of dimethyl ethers which by action of benzaldehyde in presence of $ZnCl_2$, according to Freudenberg *et al.*[5] resulted in the formation of 2,3 dimethyl-4,6 benzylidene-methyl-α,D-glucopyranoside, previously described.

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In the case of citrylidene acetal, proof of its structure was obtained by esterification of the free hydroxyl groups with acetic anhydride, removal of the citrylidene group with alcoholic hydrogen chloride and conversion of the diacetate by the action of trityl chloride to 2,3-acetyl-6-trityl-methyl-α,D-glucopyranoside.

The tests performed prove that the acetal group in the compounds is situated at the fourth and sixth carbons of methyl-α,D-glucopyranoside. At the same time, it has been established that during the reactions no configurational changes take place in the pyranoside ring and, therefore, the configuration at the first carbon is preserved.

A number of new acetal derivates have been prepared and the formulae shown in Fig. 1.

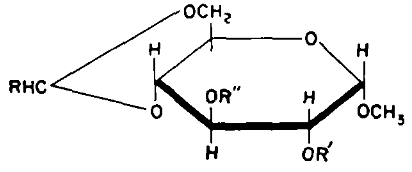

FIG 1

I.	$R{-}CH_3CH{=}CH{-}$	$R'{-}H$	$R''{-}H$
II.	$R{-}C_6H_5CH{=}CH{-}$	$R'{-}H$	$R''{-}H$
III.	$R{-}(CH_3)_2C{=}CH{-}(CH_2)_2\underset{\substack{\mid\\ CH_3}}{C}{=}CH{-}$	$R'{-}H$	$R''{-}H$
IV.	$R{-}CH_3CH{=}CH{-}$	$R'{-}CH_3{-}$	$R''{-}CH_3{-}$
V.	$R{-}CH_3CH{=}CH{-}$	$R'{-}CH_3CO{-}$	$R''{-}CH_3CO{-}$
VI.	$R{-}C_6H_5CH{=}CH{-}$	$R'{-}CH_3CO{-}$	$R''{-}CH_3CO{-}$
VII.	$R{-}CH_3CH{=}CH{-}$	$R'{-}C_6H_5CO{-}$	$R''{-}C_6H_5CO{-}$
VIII.	$R{-}C_6H_5CH{=}CH{-}$	$R'{-}C_6H_5CO{-}$	$R''{-}C_6H_5CO{-}$
IX.	$R{-}(CH_3)_2C{=}CH{-}(CH_2)_2\underset{\substack{\mid\\ CH_3}}{C}{=}CH{-}$	$R'{-}NO_2C_6H_4CO{-}$	$R''{-}NO_2C_6H_4CO{-}$
X.	$R{-}CH_3CH{=}CH{-}$	$R{-}CH_3C_6H_4SO_2{-}$	$R''{-}H{-}$
XI.	$R{-}C_6H_5CH{=}CH{-}$	$R'{-}CH_3C_6H_4SO_2{-}$	$R''{-}CH_3C_6H_4SO_2{-}$

EXPERIMENTAL

Unsaturated acetals of methyl-α,D-glucopyranoside

Equimolar quantities of glucoside and unsaturated aldehyde in benzene or xylene with addition of anhydrous $MgSO_4$ as catalyst were introduced into a flask fitted with a Dean-Stark water trap and reflux condenser. After 18–20 hr heating the catalyst was filtered off, the solvent removed under red. press., the residue dissolved in benzene and the acetals precipitated with pet ether and recrystallized. The acetals are soluble in alcohols, pyridine, benzene, chloroform, but insoluble in pet ether, n-heptane and water.

The following compounds were prepared:

4,6 *Crotonylidene-methyl-α,D-glucopyranoside* (I) was prepared from 50 g methyl-α,D-glucopyranoside and 105 g crotonaldehyde in benzene, yield 37%. Microcrystalline crystals m.p. 73–74°, $[\alpha]_D^{20} = +116{\cdot}8°$ (*c.* 1·65 in CH_3OH). (Found: C, 53·1; H, 7·3 $C_{11}H_{18}O_6$ requires: C, 53·6; H, 7·3%).

4,6 *Cinnamylidene-methyl-α,D-glucopyranoside* (II) was obtained from 25 g methyl-α,D-glucopyranoside and 115 g cinnamaldehyde in benzene; yield 80%, white small crystals, m.p. 119–121°, $(\alpha)_D^{25} +$ 91·4° (*c.* 2·0 in $CHCl_3$). Found: C, 62·2; H, 6·6 $C_{16}H_{20}O_6$ requires: C, 62·3; 6·5%.

4,6 *Citrylidene-methyl-α,D-glucopyranoside* (III) was obtained from 25 g methyl-α,D-glucopyranoside and 117 g citral in xylene; yield 90%, as a syrup; $(\alpha)_D^{25} + 108{\cdot}8°$ (*c.* 2·5 in $CHCl_3$). Found: C, 61·9; 8·7 $C_{17}H_{28}O_6$ requires: C, 62·2; H, 8·6%.

2,3 *Dimethyl-4,6 crotonylidene-methyl-α,D-glucopyranoside* (IV) was obtained from 2 g acetal (I) and 30 ml methyl iodide in the presence of Ag_2O as catalyst in a 62% yield which crystallized as white fine crystals m.p. 46–47°; $(\alpha)_D^{25} - 117{\cdot}4°$ (*c.* 1·0 in $CHCl_3$). Found: C, 57·0; H, 7·9. $C_{13}H_{22}O_6$ requires: C, 56·9; H, 8·0%.

2,3 *Diacetyl-4,6 crotonylidene-methyl-α,D-glucopyranoside* (V) and 2,3 *Diacetyl-4,6 cinnamylidene-methyl-α,D-glucopyranoside* (VI) were the esterification products of 2 g acetal (I, II) with 2·5 ml acetic anhydride in pyridine at room temp, yield 95%. 2,3 Diacetyl-4,6 crotonylidene-methyl-α,D-glucopyranoside is a syrup, $(\alpha)_D^{25}$ + 102·6° (*c.* 0·5). Found: C, 54·5; H, 6·8; $C_{15}H_{22}O_8$ requires: C. 54·5; H, 6·7%. 2,3 Diacetyl-4,6 cinnamylidene-methyl-α,D-glucopyranoside crystallized from methanol, m.p. 163–164°; $(\alpha)_D^{25}$ +78·2° (*c.* 1·8 in $CHCl_3$). Found: C, 61·3; H, 6·2; $C_{20}H_{22}O_8$ requires: C, 61·2; H, 6·2%.

2,3 *Dibenzoyl-4,6-crotonylidene-methyl-α,D-glucopyranoside* (VII) and 2,3 *Dibenzoyl-4,6 cinnamylidene-methyl-α,D-glucopyranoside* (VIII) 2 g of acetal (I, II) in 10 ml pyridine were treated with 2·8 ml benzoyl chloride at −10°, yield 50–60%. 2,3 Dibenzoyl-4,6 crotonylidene-methyl-α,D-glucopyranoside crystallized from ethanol m.p. 142–143°, $(\alpha)_D^{25}$ + 135·8 (*c.* 1·0 $CHCl_3$). Found: C, 65·8; H, 5·6; $C_{25}H_{26}O_8$ requires: C, 66·0; H, 5·7%. 2,3 Dibenzoyl-4,6 cinnamylidene-methyl-α,D-glucopyranoside, crystallized from ethanol, m.p. 174–176°, $(\alpha)_D^{25}$ +96·6° (*c.* 1·7 in $CHCl_3$). Found: C, 69·6; H, 5·4; $C_{30}H_{28}O_8$ requires: C, 69·7; H, 5·5%.

2,3 *Di-*p*-nitrobenzoyl-4,6-citrylidene-methyl-α,D-glucopyranoside* (IX) was produced from 3 g acetal (III) in pyridine and 12 g *p*-nitrobenzoyl chloride. The yellow crystalline product was recrystallized from ethanol, m.p. 76–78°, $(\alpha)_D^{25}$ + 132·3° (*c.* 0·6) in $CHCl_3$. Found: C, 59·7; H, 5·2; $C_{31}H_{34}O_{12}N_2$ requires: C, 59·4; H, 5·4%.

2-p-*Toluenesulphonyl-4,6 crotonylidene-methyl-α,D-glucopyranoside* (X) and 2,3 *Di-*p*-Toluenesulphonyl-4,6 cinnamylidene-methyl-α,D-glucopyranoside* (XI) were produced from the acetals (I, II) and *p*-toluenesulphonyl chloride in molar ratios of 1:2 and 1:6 respectively and at room temp. 2-*p*-Toluenesulphonyl-4,6 crotonylidene-methyl-α,D-glucopyranoside has a m.p. 49–51°, $(\alpha)_D^{25}$ + 66·9° (*c.* 1·6). Found: C, 54·3; H, 6·0; S, 6·7; $C_{18}H_{24}O_8S$ requires: C, 54·0; H, 6·0; S, 8·0%. 2,3 Di-*p*-Toluenesulphonyl-4,6-cinnamylidene-methyl-α,D-glucopyranoside, crystallized from ethanol, m.p. 102–104°, $(\alpha)_D^{25}$ +32·2 (*c.* 2·8 in $CHCl_3$). Found: C, 58·4; H, 5·3; $C_{30}H_{32}O_{10}S_2$ requires: C, 58·4; H, 5·2%.

2,3 *Dimethyl-4,6 benzylidene-methyl-α,D-glucopyranoside* obtained from acetals (I, II) was converted into the dimethyl derivative 4,6-benzylidene-methyl-α,D-glucopyranoside, according to the Freudenberg method and crystallized from petroleum, m.p. 121–122°, $(\alpha)_D^{20}$ + 97·2° (*c.* 1·0).

2,3 *Diacetyl-6-trityl-methyl-α,D-glucopyranoside*. The acetals were esterified with acetic anhydride and then heated to 40° in 20 ml alcoholic 1% solution of HCl. The solution was neutralized with Ag_2CO_3, trityl chloride added and the product after crystallization from ligroin yielded white crystals of the known 2,3 diacetyl-6-trityl-methyl-α,D-glucopyranoside m.p. 160–162°, $(\alpha)_D$ + 76·2°(*c.* 1·0 in $CHCl_3$).