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SYNTHESIS AND CONFIGURATION OF SOME DIALKENYLIDENE DERIVATIVES OF METHYL α-D-MANNOPYRANOSIDE

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ABSTRACT

New unsaturated acetals of methyl α-D-mannopyranoside have been obtained. On the basis of physical and chemical evidence, these compounds were shown to be methyl 2,3:4,6-di-*O*-alkenylidene-α-D-mannopyranosides. The configuration at the alkenylidene acetal carbon atoms has been determined.

INTRODUCTION

During the past twenty years, sugars have become available in large quantities, and detailed studies have been made of their chemical reactions in order to find products of commercial value. We have examined the acetalation of methyl D-hexopyranosides with unsaturated aldehydes (and the stereochemistry of the products), in the hope that these compounds might be used as starting materials for the synthesis of macromolecules.

In previous papers[1–3], the synthesis and structure of unsaturated 4,6-acetals of methyl α-D-glucopyranoside have been described. There was no indication of the formation of dialkenylidene derivatives; the *trans* disposition of HO-2 and HO-3 is unfavorable for cyclic acetal formation[4].

For methyl α-D-mannopyranoside (**1**), where HO-2 and HO-3 are *cis*, the formation of 2,3:4,6-di-*O*-alkenylidene derivatives was to be expected. In the presence of conc. sulphuric acid, copper sulphate, or zinc chloride as catalyst, saturated acetals of **1** have been obtained; examples include di-*O*-benzylidene[8–10], di-*O*-isopropylidene[11], di-*O*-propylidene[10,13], and di-*O*-furfurylidene[12] derivatives. The condensation of **1** with benzaldehyde at 150–155°/330 mmHg in an atmosphere of carbon dioxide gave[8] a mixture of a monobenzylidene and two isomeric dibenzylidene derivatives; the structures of these isomers have been assigned on the basis of n.m.r. data[5–7].

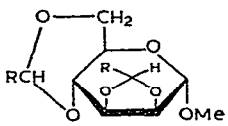
RESULTS AND DISCUSSION

The synthesis of unsaturated acetals of sugars presents difficulties, since the catalyst may react with the unsaturated aldehyde. Unsaturated acetals can be

prepared using toluene-*p*-sulphonic acid as catalyst and azeotropic removal of water. Thus, unsaturated acetals of **1** have been obtained (68–96% yield) by reaction of a 1:2–1:6.3 ratio of **1** with acrylaldehyde, metacrolein, crotonaldehyde, tiglaldehyde, cinnamaldehyde, and α-bromocinnamaldehyde. The products were dialkenylidene derivatives, and no traces of monoacetals were detected. Although two isomers of each methyl di-*O*-alkenylidene-α-D-mannopyranoside are possible, only after the condensation of α-bromocinnamaldehyde and **1** were two compounds isolated. The physical characteristics of some acetals are given in Table I.

TABLE I

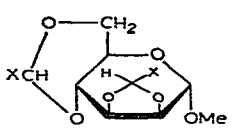
N.M.R. AND OTHER DATA FOR 2,3:4,6-DIACETALS OF METHYL α-D-MANNOPYRANOSIDE

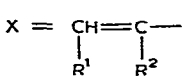


	R	*Isomer*	*M.p.* (*degrees*)	$[\alpha]_D^{20}$ (*CHCl*$_3$) (*degrees*)	*Yield* (%)	*P.m.r. data* (τ) *for acetal CH*	
						2,3-Acetal	*4,6-Acetal*
7a	$C_6H_5CH{=}CBr$	*endo*	154–156	−19	95.2	4.27	4.85
7b	$C_6H_5CH{=}CBr$	*exo*	93–94	−148	0.9	4.15	4.52
8a	$C_6H_5C{\equiv}C$	*endo*	190–191	+19	92.1	3.95	4.57
8b	$C_6H_5C{\equiv}C$	*exo*	105–106	−164	0.6	4.15	4.53
2a	C_6H_5	*endo*[a]	181–182	~0	21.8	4.16[b]	4.76[b]
2b	C_6H_5	*exo*[a]	97–98	−61	5.4	4.42[b]	4.84[b]
2a	C_6H_5	*endo*	180–181	~0	97.0	3.75	4.42
2b	C_6H_5	*exo*	96–98	−61	2.0	4.07	4.52

[a]Data taken from ref. 8. [b]Data taken from ref. 7.

The i.r. spectra of the acetals confirmed the absence of hydroxyl groups, and the characteristic absorptions at 1020–1180, 3040–3060, 1660–1680, and 905–999 cm^{-1} are assigned to O–C–O–C– and olefinic stretching vibrations, respectively. The strong absorption at 2230–2245 cm^{-1} for **8a** and **8b** is due to the C≡C stretching vibration. The n.m.r. spectra of the diacetals showed the presence of the methoxyl protons, HC–O, H_2C–O, and olefinic protons (**3**–**7**, **9**). The spectra of di-*O*-crotonylidene (**3**), di-*O*-methacrylidene (**4**), and di-*O*-tiglylidene (**5**) derivatives, for





3 $R^1 = Me, R^2 = H$ **6** $R^1 = Ph, R^2 = H$
4 $R^1 = H, R^2 = Me$ **7** $R^1 = Ph, R^2 = Br$
5 $R^1 = Me, R^2 = Me$ **9** $R^1 = R^2 = H$

example, contained signals for Me at τ 8.18–8.2, and those of the di-*O*-cinnamylidene (**6**), di-*O*-(α-bromocinnamylidene) (**7**), and di-*O*-(3-phenyl-2-propynylidene) (**8**) derivatives had signals for aromatic protons at τ 2.4–2.75.

Hydrolysis of each unsaturated acetal by 0.1M hydrochloric acid gave **1**, thereby confirming the absence of isomerisation during acetal formation.

The chemical and spectral data for the diacetals described above indicates them to be methyl 2,3:4,6-di-*O*-alkenylidene-α-D-mannopyranosides.

It has been established[5] by n.m.r. spectroscopy that if the acid-catalysed condensation of an aldehyde with a diol gives a six-membered acetal ring, then the alkyl or aryl group at the acetal carbon atom is equatorial. For a five-membered acetal ring *cis*-fused to a pyranoid ring, the formation of two isomers may be expected. The n.m.r. method (Table I) has been used to establish the configuration of the two isomers (**7a,b**) of methyl 2,3:4,6-di-*O*-(α-bromocinnamylidene)-α-D-mannopyranoside and those (**8a,b**) of methyl 2,3:4,6-di-*O*-(3-phenyl-2-propynylidene)-α-D-mannopyranoside.

For comparison purposes, the data for the isomeric methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranosides[8] (**2a,b**) are included in Table I.

The data in Table I show that **2** obtained (97% yield) by the azeotropic method has the same properties as the *endo*-isomer **2a**, obtained by Robertson[8]. The *exo*-isomer was obtained in low yield (2%). The differences in melting point and $[\alpha]_D$ values for the members of the *endo,exo* pairs **2ab**, **7ab**, and **8ab** are of similar magnitude. Also, the n.m.r. spectra of **7a**, **7b**, **8a**, and **8b** were compared with the n.m.r. spectra of **2a** and **2b** (Table I). According to Foster and co-workers[5–7], for solutions of the isomers of **2a** and **2b** in *p*-dioxane, the proton signals at τ 4.76 and 4.84 can be assigned to the 4,6-benzylidene group, and the signals at τ 4.46 and 4.16 to the 2,3-benzylidene groups having *exo* and *endo* benzyl-protons, respectively. By analogy (see n.m.r. data in Table I), the isomers **8a** and **8b** are assigned the *endo* and *exo* orientations of the acetal protons of the 5-membered ring.

When acrylaldehyde, metacrolein, crotonaldehyde, tiglaldehyde, and cinnamaldehyde reacted with **1**, only one product (**9**, **4**, **3**, **5**, **6**) was obtained in high yield. In contrast to **7** and **8**, the second isomers of **3**, **4**, **5**, **6**, and **9** were not detected. Comparing the properties of these compounds with those of the isomers (**7ab**, **2ab**) having known *endo* and *exo* configurations of the 2,3-acetal, it may be assumed that these unsaturated acetals have an *endo* configuration.

EXPERIMENTAL

I.r. and n.m.r. spectra were recorded with UR-20 and Varian S-100 XL instruments, respectively. N.m.r. spectra were measured on solutions in $CDCl_3$ or CCl_4, with internal Me_4Si.

Preparation of unsaturated acetals of methyl α-D-mannopyranoside (**1**). — A mixture of **1** (26 mmol, 5.06 g) and 52–164 mmol of freshly distilled, unsaturated aldehyde in benzene or heptane containing toluene-*p*-sulphonic acid (0.04 g) and

hydroquinone (0.05 g) was subjected to azeotropic distillation (Dean–Stark). After **1** had all dissolved (3–7 h), a small amount of pyridine was added and the solvent was then removed under reduced pressure. Extraction of the syrupy residue with cold acetone left unreacted **1**. The extract was concentrated, and the syrupy residue was washed with 0.1M KOH and distilled water, and then crystallised from ethanol (50 ml). A further yield of product was obtained by concentration of the mother liquor.

The following compounds were thus prepared.

Methyl 2,3:4,6-di-*O*-acrylidene-α-D-mannopyranoside (**9**, 68.4%), m.p. 117–118°, $[\alpha]_D^{20}$ +11.5° (*c* 3.5, chloroform). N.m.r. data: τ 6.7 (s, 3 H, OMe), 6.37–6.62 (m, 3 H), 5.62–6.07 (m, 3 H), 5.05–5.25 (q, 3 H), 3.92–5.0 (m, 6 H) (Found: C, 57.8; H, 6.7. $C_{13}H_{18}O_6$ calc.: C, 58.1; H, 6.6%).

Methyl 2,3:4,6-di-*O*-methacrylidene-α-D-mannopyranoside (**4**, 72.4%), m.p. 102–103°, $[\alpha]_D^{20}$ +13° (*c* 4.6, chloroform). N.m.r. data: τ 8.18 (d, 6 H, 2 Me), 6.48 (s, 3 H, OMe), 6.2–6.4 (m, 3 H), 5.9 (d, 1 H), 5.68–5.8 (m, 1 H), 5.4–5.62 (m, 1 H), 5.02 (s, 1 H), 4.9–5.0 (m, 3 H), 4.78 (s, 2 H), 4.42 (s, 1 H) (Found: C, 59.5; H, 7.7. $C_{15}H_{22}O_6$ calc.: C, 60.2; H, 7.7%).

Methyl 2,3:4,6-di-*O*-crotonylidene-α-D-mannopyranoside (**3**, 86%), m.p. 106–108°, $[\alpha]_D^{20}$ ~0° (*c* 4, chloroform). N.m.r. data: τ 8.25 (q, 6 H, 2 Me), 6.72 (s, 3 H, OMe), 6.25–6.6 (m, 3 H), 5.7–6.25 (m, 3 H), 5.1–5.3 (2 H), 3.9–4.95 (m, 5 H) (Found: C, 59.9; H, 7.7. $C_{15}H_{22}O_6$ calc.: C, 60.2; H, 7.7%).

Methyl 2,3:4,6-di-*O*-tiglylidene-α-D-mannopyranoside (**5**, 72%), m.p. 104–106°, $[\alpha]_D^{20}$ +10° (*c* 2.4, chloroform). N.m.r. data: τ 8.37 (q, 12 H, 4 Me), 6.72 (s, 3 H, OMe), 6.42–6.62 (m, 3 H), 5.62–6.12 (m, 3 H), 5.27 (d, 2 H), 4.72 (s, 1 H), 4.1–4.65 (m, 2 H) (Found: C, 62.5; H, 8.0. $C_{17}H_{26}O_6$ calc.: C, 62.1; H, 8.1%).

Methyl 2,3:4,6-di-*O*-cinnamylidene-α-D-mannopyranoside (**6**, 95.6%), m.p. 165–166°, $[\alpha]_D^{20}$ −72.5° (*c* 2, chloroform). N.m.r. data: τ 6.65 (s, 3 H, OMe), 6.2–6.45 (m, 3 H), 5.4–6.0 (m, 3 H), 5.05 (d, 1 H), 4.75–4.9 (m, 1 H), 3.65–4.5 (m, 3 H), 3.3–3.42 (d, 1 H), 3.07–3.17 (m, 1 H), 2.55–2.8 (m, 10 H) (Found: C, 71.1; H, 6.1. $C_{25}H_{26}O_6$ calc.: C, 70.9; H, 6.4%).

Methyl 2,3:4,6-di-*O*-(α-bromocinnamylidene)-α-D-mannopyranoside (**7a**, 95.2%), m.p. 154–156° (from ethanol–acetone), $[\alpha]_D^{20}$ −19° (*c* 3.6, chloroform). N.m.r. data: τ 6.62 (s, 3 H, OMe), 6.1–6.45 (m, 3 H), 5.22–5.8 (m, 3 H), 5.05 (s, 1 H), 4.85 (s, 1 H), 4.25 (s, 1 H), 2.3–2.72 (m, 12 H) (Found: C, 51.6; H, 4.2. $C_{25}H_{24}Br_2O_6$ calc.: C, 51.1; H, 4.2%).

When the mother liquors of **7a** were stored at 0°, **7b** separated as a syrup. Crystallisation from ethanol–carbon tetrachloride gave material (0.9%) having m.p. 92–94°, $[\alpha]_D^{20}$ −148° (*c* 1.4, chloroform). N.m.r. data: τ 6.6 (s, 3 H, OMe), 6.0–6.4 (m, 3 H), 5.2–5.8 (m, 3 H), 5.05 (s, 1 H), 4.52 (s, 1 H), 4.15 (s, 1 H), 2.3–2.7 (m, 12 H) (Found: C, 51.8; H, 4.3%).

The *endo* (**2a**) and *exo* (**2b**) isomers of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside were made as described by Robertson[8], and by the azeotropic method. From 10 g of **1** and 15 ml of benzaldehyde in benzene (100 ml), the *endo*, *exo*

mixture was obtained (97%). Recrystallization from ethanol gave **2a**, m.p. 180–181°, $[\alpha]_D^{20}$ ~0° (*c* 3.4, chloroform). N.m.r. data: τ 6.68 (s, 3 H, OMe), 5.4–6.1 (m, 6 H), 5.05 (s, 1 H), 4.42 (s, 1 H), 3.75 (s, 1 H). From the mother liquors of **2a**, **2b** was obtained (2%) having m.p. 96–98° (from ethanol–light petroleum), $[\alpha]_D^{20}$ −61° (*c* 2.5, chloroform). N.m.r. data: τ 6.62 (s, 3 H, OMe), 5.4–6.4 (m, 6 H), 5.0 (s, 1 H), 4.52 (s, 1 H), 4.07 (s, 1 H).

Elimination of hydrogen bromide from **7ab**. — Methyl 2,3:4,6-di-*O*-(3-phenyl-2-propynylidene)-α-D-mannopyranosides (**8ab**) were obtained from 2.2 g of **7a** or **7b** and 10.4 g of KOH, dissolved in acetone. After standing for 48 h at room temperature, the acetone was removed, the residue was dissolved in chloroform, and the solution was repeatedly washed with distilled water, then dried ($MgSO_4$), and concentrated. Crystallisation of the syrupy residue gave **8a** (from ethanol) and **8b** (from carbon tetrachloride): **8a** (92.1%) had m.p. 190–191°, $[\alpha]_D^{20}$ +19° (*c* 2.1, chloroform). N.m.r. data: τ 6.63 (s, 3 H, OMe), 6.12–6.5 (m, 3 H), 5.4–5.86 (m, 3 H), 5.05 (s, 1 H), 4.57 (s, 1 H), 3.95 (s, 1 H), 2.45–2.75 (m, 10 H) (Found: C, 71.7; H, 5.3. $C_{25}H_{22}O_6$ calc.: C, 71.4; H, 5.3%). **8b** (0.6%) had m.p. 105–106°, $[\alpha]_D^{20}$ −164° (*c* 1.1, chloroform). N.m.r. data: τ 6.62 (s, 3 H, OMe), 5.4–6.4 (m, 6 H), 5.05 (s, 1 H), 4.53 (s, 1 H), 4.15 (s, 1 H), 2.4–2.8 (m, 10 H) (Found: C, 71.3, H, 5.2%).

Removal of acetal groups by acid hydrolysis. — A solution of unsaturated methyl α-D-mannopyranoside acetal (3 g) in 25 ml of 0.1M alcoholic HCl was heated for 45 min in a boiling-water bath. The solution was filtered with decolourizing carbon and concentrated under reduced pressure at 45°. Crystallisation of the residue from ethanol gave **1**, m.p. 190–191°, $[\alpha]_D$ +78° (*c* 2, water).

REFERENCES

1 Z. JEDLIŃSKI AND J. MAŚLIŃSKA, *Rocz. Chem.*, 36 (1962) 1057.
2 Z. JEDLIŃSKI AND J. MAŚLIŃSKA, *Tetrahedron*, 19 (1963) 1171.
3 Z. JEDLIŃSKI AND J. MAŚLIŃSKA, *Rocz. Chem.*, 38 (1964) 979.
4 J. MAŚLINSKA-SOLICH AND Z. JEDLIŃSKI, *Rocz. Chem.*, 39 (1965) 617.
5 A. B. FOSTER, A. H. HAINES, J. HOMER, J. LEHMANN, AND L. F. THOMAS, *J. Chem. Soc.*, (1961) 5005.
6 N. BAGGETT, K. W. BUCK, A. B. FOSTER, AND J. M. WEBBER, *J. Chem. Soc.*, (1965) 3401.
7 N. BAGGETT, K. W. BUCK, A. B. FOSTER, M. H. RANDALL, AND J. M. WEBBER, *Proc. Chem. Soc.*, (1964) 118.
8 G. J. ROBERTSON, *J. Chem. Soc.*, (1934) 330.
9 W. ALBERDA VAN EKENSTEIN AND J. J. BLANKSMA, *Rec. Trav. Chim.*, 25 (1906) 153.
10 J. HONEYMAN AND J. W. W. MORGAN, *J. Chem. Soc.*, (1954) 744.
11 R. G. AULT, W. N. HAWORTH, AND E. L. HIRST. *J. Chem. Soc.*, (1935) 527, 1012.
12 H. BREDERECK, *Ber.*, 68 (1935) 777, 2299.
13 J. C. IRVINE AND J. P. SCOTT, *J. Chem. Soc.*, 103 (1913) 575.