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Carbohydrate Research 284 (1996) 241–248

CARBOHYDRATE RESEARCH

Note

Preparation of mono-*O*-isopropylidene derivatives of methyl α-D-glucoseptanoside [1]

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Received 27 March 1995; accepted 8 December 1995

Keywords: Septanosides; Acetals; NMR; Conformations

Methyl α-D-glucoseptanoside (**1**) may be prepared from methyl 2,3:4,5-di-*O*-isopropylidene-α-D-glucoseptanoside (**2a**) by acid-catalyzed hydrolysis. Compound **2a** has been prepared using several procedures: by the reaction of D-glucose with an acidified mixture of acetone and methanol [1] (see Experimental for the details of this method), by heating methyl 4,6-*O*-isopropylidene-α-D-glucopyranoside with pyridinium chloride [2], or by methylation of 2,3:4,5-di-*O*-isopropylidene-D-glucoseptanose, which may be isolated in low yield from the reaction of D-glucose with acetone [3] or prepared by a procedure involving D-glucose diethyl dithioacetal as a starting compound [4]. Earlier work showed that acid-catalyzed hydrolysis of **2a** gives initially methyl 4,5-*O*-isopropylidene-α-D-glucoseptanoside (**3a**) together with **1**. Longer hydrolysis times yielded **1** (in moderate yield) and D-glucose [3].

A more detailed study of the hydrolysis of **2a** has revealed the presence of two other products in the hydrolysis mixture, namely, methyl 2,3-*O*-isopropylidene-α-D-glucoseptanoside (**4a**) and methyl 3,4-*O*-isopropylidene-α-D-glucoseptanoside (**5a**) (see below for identification). The presence of **5a** in the hydrolysis mixture indicates that one or both of **3a** and **4a** have undergone isomerization. Similar isomerization of 1,6-anhydro-3,4-*O*-isopropylidene-β-D-talopyranose to give the 2,3-acetal by treatment with aqueous acid has been reported [5].

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[1] Septanose Carbohydrates, Part 4. For Part 3, see ref. [12].

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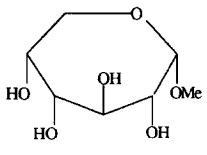
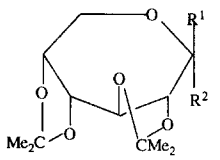
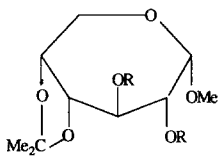
PII S0008-6215(96)00023-7



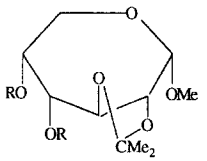
1



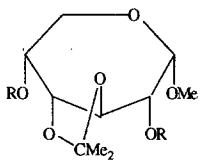
2a R^1 = H R^2 = OMe
2b R^1 = OMe R^2 = H



3a R = H
3b R = Ac
3c R = Bz



4a R = H
4b R = Ac
4c R = Bz



5a R = H
5b R = Ac
5c R = Bz

The poor yield of **1** obtained by dioxane–aqueous acid hydrolysis of **2a** prompted a search for conditions leading to a higher yield of **1**. In one procedure, hydrolysis was stopped after a high proportion of **3a** had been formed. Treatment of this product with dilute aqueous acid gave **1** in 85% yield (based on **3a**). A somewhat simpler procedure involves the use of methanol and aqueous acid. By stopping hydrolysis when only traces of D-glucose had been produced and continuing hydrolysis after crystallization of **1**, the glycoside was obtained in 80% yield after two passes.

Acetonation of methyl α-D-glucoseptanoside.—Using 2,2-dimethoxypropane (DMP) and *p*-toluenesulfonic acid in *N,N*-dimethylformamide (DMF) [6,7] and ensuring that the DMF was free of dimethylamine by treating it with phosphorus pentaoxide [8], **1** gave a mixture of four products when slightly more than one equivalent of DMP was used. Separation was effected by column chromatography using GLC and TLC to monitor elution. The first compound to be eluted was identified as the diacetal (**2**). Next eluted was **4a**, obtained as a mobile syrup. The 4,5-*O*-isopropylidene derivative **3a** was the next compound eluted, followed by the major component of the reaction mixture, **5a**, which crystallized readily from ethyl acetate. The structures of **4a** and **5a** were established by their E.I. mass spectra and by the ^{1}H NMR spectra (see Tables 1 and 2) of the derived diacetates **4b** and **5b**. The ratios of the three monoacetals formed by treatment of **1** with DMP and *p*-toluenesulfonic (PTSA) acid in DMF were determined by GLC of the acetates as 1:2:8 for **4b**, **3b**, and **5b**. From a preparative scale reaction, a 65% yield of **5a** was obtained by crystallization.

Characterization of **3a** as the crystalline diacetate **3b** and dibenzoate **3c** has been reported [3]. Syrupy **4a** yielded a liquid diacetate and a crystalline dibenzoate **4c**. The crystalline 3,4-acetal, **5a**, was characterized as the crystalline diacetate **5b** and dibenzoate **5c**.

Other acetonation procedures which were examined with the aim of increasing the

Table 1
^{1}H NMR chemical shifts (ppm)

Compound	Solvent	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	OCH_3	CMe_2		OAc	
3b [a]	$CDCl_3$	4.674	4.851	5.725	4.367	4.349	3.850	3.496	3.426	1.414	1.331	2.082	2.078
3b	C_6D_6	4.624	5.075	6.195	4.230	4.038	3.886	3.423	2.969	1.127	1.342	1.645	1.709
4b	$CDCl_3$	4.928	3.888	4.557	5.421	5.065	4.048	3.358	3.463	1.417	1.414	2.116	2.008
4b	C_6D_6	4.772	3.633	4.854	5.735	5.285	4.055	3.258	3.088	1.396	1.279	1.663	1.658
4c	$CDCl_3$	5.028	4.047	4.817	5.828	5.420	4.285	3.570	3.518	1.456	1.450		
5b	$CDCl_3$	4.420	5.294	4.513	4.020	5.357	4.232	3.751	3.404	1.423	1.386	2.156	2.139
5b	C_6D_6	3.814	5.547	4.782	3.563	5.252	3.919	2.928	3.038	1.409	1.297	1.785	1.675
5c	$CDCl_3$	4.635	5.569	4.812	4.226	5.707	4.380	3.939	3.400	1.421	1.273		

[a] Values obtained by iterative analysis using the program PANIC (Bruker).

yield of the 2,3-acetal **4a** were unsuccessful. These included treatment of **1** with acetone and anhydrous copper(II) sulfate or mineral acid and reaction of **1** with DMP and copper(II) sulfate. With this last procedure, only **2a** and **5a** were detected by TLC. A similar result was obtained when **1** was treated with excess of DMP and PTSA in DMF. Clearly, **3a** and **4a** are consumed in the formation of **2a**, but **5a** is not affected.

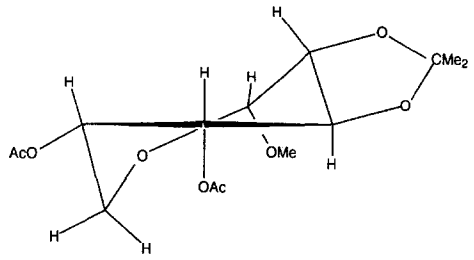
Conformation of **4b**.—A probable conformation of **4b** in solution has been determined by comparing the torsional angles between hydrogen atoms of the various chair and twist-chair conformations with those values estimated from the observed coupling constants. The values of $J_{5,6a}$, $J_{5,6b}$, and $J_{6a,6b}$ (8.5, 1.3, and 13.2 Hz, respectively) are consistent with a synclinal orientation of H-5 to one of the C-6 hydrogens and antiperiplanar to the other or with H-5 eclipsed with H-6a. These orientations exist in the conformations extending from $^{O}C_{3,4}$ to $^{2}C_{5,6}$ in the chair/twist-chair pseudorotational itinerary [9] of the septanoid ring, that is, conformations $^{O}C_{3,4}$, $^{1,2}TC_{6,O}$, $^{4,5}C_1$, $^{O,1}TC_{2,3}$, and $^{2}C_{5,6}$. The $^{O}C_{3,4}$ conformation may be excluded because the dihedral angle between H-4 and H-5 ($\Phi_{4,5}$, 120°) would be expected to give rise to a value of $J_{4,5}$ smaller than that observed (6.4 Hz). Similarly, $^{4,5}C_1$ may be excluded by the value of $J_{4,5}$ (5.0 Hz, not consistent with $\Phi_{4,5} = 0°$), and a $\Phi_{4,5}$ of 66° in $^{2}C_{5,6}$ is not compatible with $J_{4,5}$. Of the two twist-chair conformations, $^{1,2}TC_{6,O}$, in which $\Phi_{5,6b}$ is close to 90°, accounts

Table 2
^{1}H NMR coupling constants (Hz)

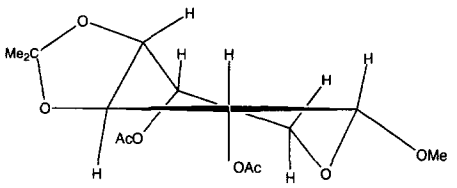
Compound	Solvent	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	Others
3b [a]	$CDCl_3$	2.70	10.69	8.32	7.26	10.57	4.09	12.59	$J_{1,3}$ 0.48; $J_{1,6a}$ 0.61; $J_{4,6b}$ 0.83
3b	C_6D_6	2.71	10.77	8.45	6.95	10.87	3.93	12.33	$J_{1,3}$ 0.39; $J_{1,6a}$ 0.61; $J_{4,6b}$ 0.76
4b	$CDCl_3$	2.22	10.02	6.52	5.10	8.68	1.32	13.23	$J_{1,3}$ 0.53; $J_{1,6a}$ 0.56; $J_{4,6b}$ 1.64
4b	C_6D_6	2.25	9.99	6.71	5.14	8.64	1.29	13.13	$J_{1,3}$ 0.47; $J_{1,6a}$ 0.68; $J_{4,6b}$ 1.46
4c	$CDCl_3$	2.32	9.98	6.60	5.18	8.67	1.32	13.14	$J_{1,3}$ 0.55; $J_{1,6a}$ 0.71; $J_{4,6b}$ 1.51
5b	$CDCl_3$	3.65	7.43	9.72	2.46	1.81	2.75	14.10	$J_{3,5}$ 0.49
5b	C_6D_6	3.73	7.45	9.75	2.47	1.66	2.60	14.05	$J_{3,5}$ 0.51
5c	$CDCl_3$	3.82	7.69	9.62	2.54	2.04	3.20	14.20	$J_{3,5}$ 0.45

[a] Values obtained by iterative analysis using the program PANIC (Bruker).

more easily for the small value of $J_{5,6b}$. This conformation also accounts for the ^4J coupling of H-4 and H-6b as these are close to a W arrangement. We note that this conformation was proposed for both **2a** and **3b** in solution and is the conformation found for **2a** in the solid state [10]. The ease of formation of **2a** from **1** in acidified acetone may be accounted for by the diacetal having the same conformation as its two monoacetal precursors, **3a** and **4a**.



$^{1,2}TC_{6,0}$ Conformation of **4b**



$^{4,5}TC_{6,0}$ Conformation of **5b**

Conformation of **5b**.—Proton spin coupling constants for **5b** and 5-*O*-acetyl-1,2:3,4-di-*O*-isopropylidene-α-D-glucoseptanose (**6**) are almost identical, indicating that **5b** and **6** adopt the same conformation in solution. Since it has been concluded [3] that **6** exists in the $^{4,5}TC_{6,O}$ conformation in solution, we propose this conformation for **5b**. This is also the solid state [11] and solution [3] conformation of methyl 2,3,4,5-tetra-*O*-acetyl-α-D-glucoseptanoside (**1b**)

1. Experimental

General methods.—Optical rotations were determined using 2-cm cells in a Bendix NPL Automatic Polarimeter 143C equipped with a JANUS digital voltmeter. Melting points were determined on a Kofler hot-stage and are uncorrected. IR spectra were recorded using a Pye Unicam SP1000 Infrared Spectrophotometer and liquid paraffin for the mulls. NMR spectra were obtained using a Bruker CXP-300 (300 MHz) or AM-500 (500 MHz) spectrometer, with tetramethylsilane as an internal reference. Digital resolution in the transformed spectrum was generally ca. 0.06 Hz. Mass spectra were recorded using an AEI-MS12 single focussing mass spectrometer. Silica gel supported on microscope slides was used for TLC, visualization being achieved by charring on a hot plate after spraying the slide with H_2SO_4 in EtOH. Adsorbents used for column chromatography were Peter Spence Type H alumina and Mallinkrodt 100-mesh silicic acid. GLC was carried out on a custom-built instrument fitted with glass-lined insert and flame-ionization detector. Glass columns used were 120 cm packed with 2% poly(ethylene glycol) succinate on Chromosorb W (EGS) and 240 cm packed with 1.5% LAC-IR-296 on Chromosorb W (LAC). Ether refers to diethyl ether and, unless otherwise stated, light petroleum refers to the fraction boiling at 60–80 °C.

*Methyl 2,3:4,5-di-*O*-isopropylidene-α- and -β-*D*-glucoseptanosides* (**2a** *and* **2b**).—To a stirred, cooled (10 °C) mixture of MeOH (3 L) and acetone (12 L) was added concd H_2SO_4 (600 mL) at such a rate that the temperature remained below 20 °C. D-Glucose (1 kg), ground using a hammer mill, was added to the mixture at ca. 20 °C and stirring continued for 12 h. The reaction mixture was kept at 22 °C for 8 days, after which it was cooled to ca. 4 °C and neutralized using gaseous ammonia. This caused the deeply coloured solution to become lightly coloured. After precipitated salts had been removed by filtration and washed with acetone, filtrate and washings were concentrated, and the syrupy residue was divided into three. Each portion of residue was shaken with water (2 L), benzene (500 mL), and light petroleum (1 L), and the organic phase washed with water (2 × 100 mL). After extracting the aqueous phase plus washings with 1:2 benzene–light petroleum (1 L) and washing the extract with water (2 × 100 mL), the total organic extracts were dried ($MgSO_4$) and concentrated, finally using a mechanical pump on the rotary evaporator (pressure ca. 0.5 mm, bath 60 °C), to give a deeply colored, mobile liquid, **A** (418 g). A solution of **A** in light petroleum (600 mL) was added to a column of alumina (3 kg packed in light petroleum, 7 cm × 76 cm) and the column was developed with light petroleum. After a residue test on the eluate proved positive, 1-L fractions were collected, the eluent being changed to 1:19 ether–light petroleum after fraction 3 and to 1:9 ether–benzene after fraction 4. Elution was monitored by GLC. Fraction 1 contained only compounds of short retention time, including 1,2:3,4:5,6-tri-*O*-isopropylidene-1-methoxy-D-glucitol [1]. Evaporation of fractions 2 to 5, containing compounds of short retention time and **2a**, gave 193.8 g of mobile syrup, **B**. Evaporation of fractions 6 to 12, containing **2a** and **2b**, gave 91.9 g of syrupy products, **C**. A solution of syrup **B** in light petroleum (500 mL) was added to a column of silicic acid (1 kg packed in 1:19 ether–light petroleum, 7 cm by 49 cm) and the column was developed with light petroleum. After colored material appeared in the eluate, 500-mL fractions were collected. The following ether–light petroleum eluents were used: after fraction 4, 1:19; 8, 1:9; 23, 1:4; 24, 1:1. Fractions 1 to 10 contained 57.5 g of fast-moving compounds. Concentration of fractions 11 to 28 gave 101 g of syrupy products which yielded **2a** after dilution with 30–40 °C light petroleum and seeding. Recrystallization of the crude **2a** from 30–40 °C light petroleum gave colourless crystals of **2a** (36.2 g); mp 64–65 °C. The filtrates were chromatographed over silicic acid (650 g) using ether–light petroleum as above. Crystalline **2a** (7.8 g) was obtained from appropriate fractions. Further crops of impure **2a** from the filtrate were combined with **2a** obtained from syrup **E** (see below).

Syrup **C** was diluted with a small volume of light petroleum, and seeding with **2b** gave crystals. Recrystallization of this product from light petroleum gave almost colourless crystals of **2b** (26.2 g); mp 69–70 °C. The residue left on evaporation of the filtrates was dissolved in light petroleum (100 mL) and this solution was added to a column of silicic acid (350 g packed in 1:19 ether–light petroleum). After elution of a mixture of **2a** and **2b** (42.2 g, syrup **D**) with 1:19 ether–light petroleum, fractions containing **2b** alone were eluted with 1:2 ether–light petroleum. The syrup (11.5 g) left on concentrating these fractions was diluted with light petroleum and seeded with crystals of **2b** to give colourless **2b** (8.9 g). Chromatography of syrup **D** (diluted with 200 mL of light petroleum) over silicic acid (400 g, activated at 100 °C for 6 h, packed

in 1:19 ether–light petroleum) gave 27.1 g of syrup (**E**) containing **2a** (eluted with 1:9 ether–light petroleum) and 12.1 g syrup (**F**) containing **2b** (eluted with 1:1 ether–light petroleum). Syrup **F** yielded colourless crystals of **2b** (7.6 g) from light petroleum; total yield of **7b**, 42.7 g (2.8%). Syrup **E** was diluted with a small amount of 40–60 °C light petroleum, seeded with **2a**, and refrigerated. The crystals produced were combined with impure **2a** (above) and recrystallized from 40–60 °C light petroleum to give colourless **2a** (19.7 g); total yield of **2a**, 63.7 g (4.2%).

In subsequent preparations, a reaction time of 5 days was found to give similar yields of **2a** and **2b**. In other preparations, equivalent amounts of 1,2:5,6-di-*O*-isopropylidene-α-D-glucofuranose were used instead of D-glucose: this avoided the need to prepare finely divided D-glucose and eliminated the lengthy stirring period. Comparable yields were obtained.

Methyl 4,5-O-isopropylidene-α-D-glucoseptanoside (**3a**).—Hydrochloric acid (0.05 M, 100 mL) was added to a solution of methyl 2,3:4,5-di-*O*-isopropylidene-α-D-glucoseptanoside (**2a**) (10 g) in 1,4-dioxane (100 mL). After the reaction mixture had been kept at 30°C for 3 days, TLC using 1:9 EtOH–EtOAc showed **2a** with R_f 0.9, **3** with R_f 0.6, and methyl α-D-glucoseptanoside (**1**) with R_f 0.15 to be present. Two other components, **4a** (R_f 0.75) and **5a** (R_f 0.4) were also present. Concentration of the neutralized reaction mixture (Amberlite IRA-400, HCO_3^- form) gave a residue which was shaken with 1:4 benzene–light petroleum (50 mL) and water (50 mL). The organic phase was washed with water (10 mL) and concentrated to give **2a** (2.6 g). The residue left on concentration of the combined aqueous extracts was dissolved in EtOH, benzene was added, and the solution concentrated. Seeding a solution of the residue in EtOH (10 mL) yielded **1** (1.1 g). An ethyl acetate solution of the residue left on concentration of the filtrate was added to a column of silicic acid (75 g) packed in 1:4 EtOAc–light petroleum. After **2a** (0.1 g) had been eluted with the same solvent mixture, **3a** and **4a** (total 3.7 g) were eluted with 1:1 EtOAc–light petroleum; **5a** (0.17 g) and **1** (0.70 g) were eluted with EtOAc and 1:4 EtOH–EtOAc, respectively. The mixture of **3a** and **4a** was dissolved in warm 1:1 EtOAc–light petroleum and seeded to yield 2.8 g of **3a** (45% based on consumed **2a**). Recrystallization of **3a** from EtOAc–light petroleum gave stout needles; mp 90–91 °C; $[\alpha]_D^{22}$ +119.4° (*c* 2.1, water); lit. [3] mp 86–87 °C, $[\alpha]_D^{22}$ +136.5° (*c* 0.9, $CHCl_3$).

Methyl α-D-glucoseptanoside (**1**).—(a) A solution of methyl 4,5-*O*-isopropylidene-α-D-glucoseptanoside (**3a**) (10 g) in 0.05 M HCl (100 mL) was kept at 20 °C. After 4 days, only a trace of **3a** was detected using TLC. Neutralization of the reaction mixture (Amberlite IRA-400, HCO_3^-) and concentration gave a residue from which a mixture of benzene and EtOH was evaporated. Crystallization from EtOH gave **1** (5.4 g), and more **1** (1.7 g) crystallized from the filtrate after concentration. Total yield of **1**: 85%. GLC analysis of an acetylated sample of the final mother liquor showed that the diacetate of **5a** accounted for 35% of the volatile products.

(b) To a solution of **2a** (68.5 g, 0.25 mol) in MeOH (600 mL) at 30 °C was added 0.1 M HCl (300 mL). After 4 h, a further 200 mL of 0.1 M HCl was added and the homogeneous mixture was kept at 30 °C for 48 h. A solution in EtOH of the residue left on concentration of the neutralized (resin) reaction mixture gave 17.70 g of **1**, with a further 4.9 g of **1** from the filtrate after addition of EtOAc. Recrystallization of the crude

glycoside from EtOH–EtOAc gave 21.5 g of **1**, mp 139–140 °C; lit. [3] mp 140–141 °C. Concentration of the filtrates gave a residue which was dissolved in MeOH (25 mL). After the addition of 0.05 M HCl (200 mL), the hydrolysis mixture was kept at 25 °C for 70 h. Workup as before gave 17.6 g of **1**. Treatment of the filtrate with MeOH (10 mL) and 0.05 M HCl (100 mL) for 24 h at 25 °C gave a further 3.4 g of **1** after an aqueous solution of the products was chromatographed over 50 mL of Dowex resin (200–400 mesh, HO^- form) to remove glucose. Total yield of **1**: 42.5 g (87.6%).

Acetonation of methyl α-D-glucoseptanoside.—(a) *Using 2,2-dimethoxypropane and p-toluenesulfonic acid.* Methyl α-D-glucoseptanoside **1** (5.0 g) was dissolved in 50 mL of freshly distilled DMF (from CaH_2) with warming. After cooling to 22 °C, DMP (3.35 g, 1.25 molar equiv) and *p*-toluenesulfonic acid monohydrate (0.2 g) were added. After 12 h at 22 °C, TLC (1:9 EtOH–EtOAc) showed the presence of diacetonide **2a** (R_f 0.9), methyl 4,5-*O*-isopropylidene-α-D-glucoseptanoside (**3a**, R_f 0.6), and two other components, **4a** (R_f 0.75) and **5a** (R_f 0.4). No starting material (R_f 0.15) was detected. Water (50 mL) was added and, after neutralization (resin), the solution was concentrated under reduced pressure and DMF was removed by codistillation with xylene (2 × 50 mL). A solution of the residue in ca. 5 mL of benzene was added to a column of silicic acid (60 g) packed in 1:4 EtOAc–light petroleum. Diacetonide **2a** (0.71 g) was eluted with the same solvent mixture; **3a** and **4a** were eluted with 1:1 EtOAc–light petroleum (total 1.45 g). Elution with EtOAc gave **5a** (3.96 g). Crystallization of **3a** from the mixture with **4a**, using EtOAc–light petroleum and chromatography of the mother liquors, gave **4a** (0.50 g), **3a** (0.85 g), and 0.1 g of mixture.

Compound **4a** was isolated as a syrup and, from the NMR data (Tables 1 and 2) of its diacetate (**4b**), was identified as methyl 2,3-*O*-isopropylidene-α-D-glucoseptanoside. After short-path distillation (100 °C bath) under vacuum (0.05 mm Hg), **4a** gave $[\alpha]_D^{23}$ +154.6° (*c* 1.1, $CHCl_3$); *m/z* 219 (M − 15). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.3; H, 7.7. Found: C, 51.4; H, 7.6.

The syrupy diacetate **4b** was similarly purified (120 °C bath, 0.05 mm Hg) to give $[\alpha]_D^{20}$ +121.4° (*c* 0.8, $CHCl_3$); IR (film) 1760 cm^{-1} (C = O); *m/z* 303 (M − 15). Anal. Calcd for $C_{14}H_{22}O_8$: C, 52.8; H, 7.0. Found: C, 53.0; H, 7.6.

Benzoylation of **4a** with benzoyl chloride–pyridine gave a crystalline dibenzoate (**4c**) which crystallized from benzene–light petroleum; mp 184.5 °C; $[\alpha]_D^{22}$ +100.2° (*c* 0.8, $CHCl_3$); IR (mull) 1730 cm^{-1} (C = O). Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.2; H, 5.9. Found: C, 65.4; H, 5.9.

Compound **5a** was isolated as a solid and, from the NMR data (Tables 1 and 2) of its diacetate, was identified as methyl 3,4-*O*-isopropylidene-α-D-glucoseptanoside. Recrystallization of **5a** from EtOAc gave prisms; mp 132–133 °C; $[\alpha]_D^{22}$ −17.5° (*c* 1.1, H_2O); *m/z* 219 (M − 15). Anal. Calcd for $C_{10}H_{18}O_6$: C, 51.3; H, 7.7. Found: C, 51.2; H, 7.9.

Acetylation of **5a** yielded the diacetate (**5b**) which crystallized as needles from benzene–light petroleum; mp 85–86 °C; $[\alpha]_D^{22}$ +0.02° (*c* 6.4, $CHCl_3$); IR (mull) 1745 cm^{-1} (OAc); *m/z* 303 (M − 15). Anal. Calcd for $C_{14}H_{22}O_8$: C, 52.8; H, 7.0. Found: C, 52.9; H, 7.0.

Benzoylation of **5a** gave a dibenzoate (**5c**) which crystallized from ethyl acetate–light petroleum as prisms; mp 168 °C; $[\alpha]_D^{22}$ +25.3° (*c* 0.8, $CHCl_3$); IR (mull) 1725 cm^{-1} (C = O). Anal. Calcd for $C_{24}H_{26}O_8$: C, 65.2; H, 5.9; Found: C, 65.0; H, 5.8.

The proportion of components in the reaction mixture was determined using GLC of an acetylated sample. A small sample (ca. 20 μL) was treated with an equal volume of Ac_2O–pyridine on a steam bath and examined directly using GLC. On the LAC column (175 °C), the diacetonide (**2a**), 2,3-acetal diacetate (**4b**), 4,5-acetal diacetate (**3b**), 3,4-acetal diacetate (**5b**), and methyl α-D-glucoseptanoside tetraacetate gave retention times of 2.0, 4.2, 4.2, 8.1, and 15.2 min, respectively. On the EGS column (175 °C), **4b** and **3b** were well separated at 17.8 and 20.6 min, respectively. The proportions of **4b**, **3b**, and **5b** in the reaction mixture were, respectively, 1:2:8. The yield of **5a** was 65%, and a 77% yield was obtained when 1.45 molar equivalents of 2,2-dimethoxypropane were used, although the yields of **4a** and **3a** were lower.

(b) *Using anhyd $CuSO_4$ and acetone.* Methyl α-D-glucoseptanoside (**1**, 60 mg) was suspended in dry acetone (1.0 mL) and the mixture was stirred vigorously with anhyd $CuSO_4$ (60 mg). After 3 days, the mixture was concentrated, and the residue was treated with Ac_2O–NaOAc and examined directly by GLC: **2a**, 5%; **4b**, 5%; **3b**, 6%; **5b**, 28%; and the tetraacetate of **1**, 56%.

(c) *Using anhyd $CuSO_4$ and 2,2-dimethoxypropane.* Finely ground **1** (1.0 g) was stirred with anhyd $CuSO_4$ (0.2 g) and 2,2-dimethoxypropane (16 mL) until all the starting material has dissolved (4 days). The solid was removed by filtration and the filtrate was concentrated. The residue was shaken with water (40 mL), benzene (4 mL), and light petroleum (16 mL). Evaporation of the organic phase after washing with water (10 mL) gave **2a** (0.50 g). The combined aqueous solutions were evaporated and a mixture of benzene and EtOH was evaporated from the residue which gave needles of **5a** (0.62 g, 48%) from EtOAc. Examination of the minor products by GLC of an acetylated sample of the reaction mixture showed that **3b** and **4b** were minor components (2% each).

Acknowledgements

We are grateful to Messrs. C. Harwood and R. Linguard for the mass spectra, and to Dr. E. Challen and Mr. J. Sussman for microanalyses.

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