Carbohydrate Research, 74 (1979) 187–197

ACETALATION OF D-GLUCITOL: 2,3:5,6-DI-*O*-ISOPROPYLIDENE-D-GLUCITOL

JÁNOS KUSZMANN AND PÁL SOHÁR
Institute for Drug Research, H-1325 Budapest 4, P.O. Box 82 (Hungary)
(Received December 16th, 1978; accepted for publication, January 3rd, 1979)

ABSTRACT

The reaction of D-glucitol with acetone–zinc chloride gave a mixture of isopropylidene derivatives, from which the 2,3:5,6-diacetal (**12**) could be separated as its 1,4-dimesylate (**13**) or 1,4-ditosylate (**14**). The structure of **12** was proved by converting **14**, *via* the 1-mono-iodide, into the known 1-deoxy-D-glucitol, and by mass-spectrometric investigation of the 1-deoxy-4-*O*-methyl diacetal. The terminally situated acetal group in **12** can be selectively hydrolyzed, and, on treatment with base, the 5,6-dihydroxy derivative obtained gives a D-galactitol 4,5-epoxide derivative.

INTRODUCTION

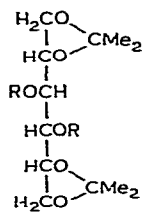
During our search for biological alkylating agents, we needed a large quantity of 1,2:5,6-di-*O*-isopropylidene-D-glucitol (**1**), which was prepared by a modification[1] of the synthesis described by Anderson *et al.*[2]. The crude mixture of the different isopropylidene compounds (obtained from D-glucitol on treatment with acetone in the presence of zinc chloride) was benzoylated, to yield crystalline 3,4-dibenzoate **2**, readily converted into **1** by methanolic sodium methoxide.

The corresponding 3,4-dimesylate **3** was similarly formed on mesylation of **1**. However, in an attempt to simplify the synthesis of **3** by directly mesylating, instead of benzoylating, the crude mixture of acetals, the crystalline di-*O*-mesyl derivative (**13**) so obtained differed from **3**; consequently, it must have been formed from another di-*O*-isopropylidene-D-glucitol isomer (**12**) present in the original mixture of the acetals.

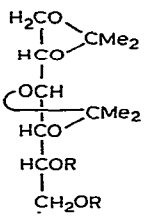
The new diacetal **12** could be obtained as a fairly homogeneous syrup from the acetal mixture by column chromatography. On mesylation, it gave the dimesyl ester **13**, and, on tosylation, the ditosylate **14**, which could also be obtained directly from the crude mixture of acetals. Compound **14** differed from the 3,4-ditosylate **4**, as well as from the known 1,2-ditosylate[3] **11**, excluding structure **9** for the new diacetal.

Anderson *et al.*[2] had indicated that a second di-*O*-isopropylidene derivative is present, besides the 1,2:5,6-diacetal **1**, in the crude reaction-mixture, but it was not obtained in crystalline state, and its structure was not established. Bonner *et al.*[4]

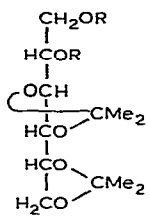
investigated in detail the formation of acetals from D-glucitol and acetone in the presence of zinc chloride; on the basis of g.l.c. data, they stated that two mono-, one tri-, and three di-*O*-isopropylidene isomers are present in the equilibrium mixture. Among these, they supposed that the 1,2:5,6- and 1,2:3,4-diacetals (**1** and **6**) are the major components; the corresponding 3,4:5,6-diacetal **9** could be detected (as a minor component) only after a prolonged reaction-time. They re-investigated the syrupy diacetal described by Anderson *et al.*[2] and assumed that it contained mostly uncrystallized **1**, as, after benzoylation, they separated the corresponding dibenzoate **2** in a yield of ~50%. From these results, it might be supposed that our new compounds should be the 5,6-di-*O*-mesyl (**7**) and 5,6-di-*O*-tosyl (**8**) derivatives of 1,2:3,4-di-*O*-isopropylidene-D-glucitol (**6**).



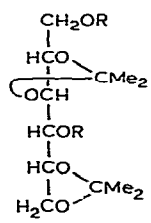
1 R = H
2 R = Bz
3 R = Ms
4 R = Ts
5 R = Ac



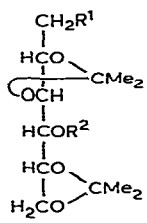
6 R = H
7 R = Ms
8 R = Ts



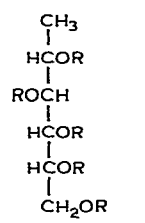
9 R = H
10 R = Ms
11 R = Ts



12 R = H
13 R = Ms
14 R = Ts



15 R^1 = I, R^2 = Ms
16 R^1 = H, R^2 = Ms
17 R^1 = R^2 = H
18 R^1 = I, R^2 = Ts
19 R^1 = H, R^2 = Ts



20 R = H
21 R = Ac

RESULTS AND DISCUSSION

From the ^{1}H-n.m.r. data (see Table I) for the di-*O*-mesyl derivative **13**, it became obvious that one mesyloxy group is in a terminal position, while the other is attached to a secondary carbon atom, and that the two groups are not vicinal. In the ^{1}H-n.m.r. spectrum of the di-*O*-mesyl derivative **13**, there appeared only one signal, of one-proton intensity, as a doublet of doublets (J = 2 and 5 Hz) at lower field (4.95 p.p.m.), separated from the other protons of the carbohydrate chain; consequently, only one of the two mesyloxy groups can be attached to a secondary carbon atom,

TABLE I

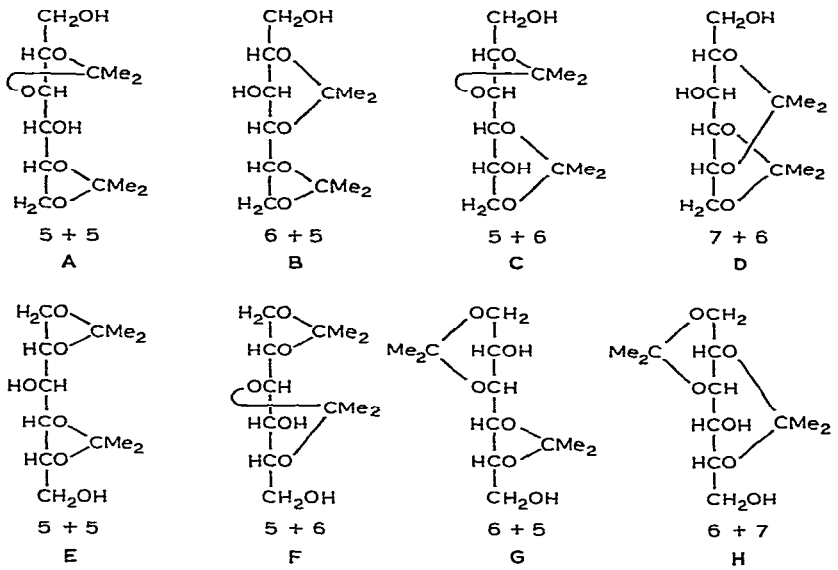
^{1}H-N.M.R. DATA[a] FOR COMPOUNDS **3–5, 12–19, 23, 24,** AND **27**

Compound	*CMe_2*	*H-1*	*H-6*	*H-2*	*H-5*	*H-3*	*H-4*	*Other protons*
3	1.40, 1.45, 1.50	←——225–280*m*—→				285——300*m*		3.20, 3.23*s* 2 mesyl-Me
4	1.25, 1.30	←——210–270*m*—→				275——300*m*		2.45*s* 2 tosyl-Me
5	1.35, 1.40	←——220–260*m*—→				300——320*m*		2.15*s* 2 acetyl-Me
12	1.35, 1.40, 1.45	←——215–255*m*——→						3.00*s* OH
13[b]	1.35, 1.45	←——230–275*m*——→					4.95[c]	3.20, 3.30*s* 2 mesyl-Me
14	1.20, 1.30	←——220–260*m*——→					4.70[c]	2.45*s* 2 tosyl-Me
15	1.40, 1.45	200–210*m*	←——230–260*m*——→				4.80[c]	3.20*s* mesyl-Me
16	1.40, 1.45	1.35[d]	←——210–270*m*——→				4.80[c]	3.15*s* mesyl-Me
17	1.40, 1.45	1.30[d]	←——190–260*m*——→					2.65*s* OH
18	1.30, 1.40	3.35[e]	←——225–265*m*——→				4.80[c]	2.45*s* tosyl-Me
19	1.25, 1.35	1.25[d]	←——210–265*m*——→				2.75[e]	2.45*s* tosyl-Me
23[b]	1.40	4.25*s*	←—200–250*m*—→		3.0*s*	200–250*m*	3.0*s*	3.20*s* mesyl-Me, 4.8*t* OH(J = 5)
24	1.45	←——215–285*m*——→			180–210*m*	215–285*m*	180–210*m*	3.10*s* 2 mesyl-Me
27	1.40, 1.45	1.30[d]	230–260*m*	190–225*m*	←——230–260*m*——→		190–225*m*	3.55*s* OMe

[a] δ scale; chloroform-*d* solution; multiplets and coupling constants are given in Hz. [b] Me_2SO-d_6 solution. [c] 2 *d* (J = 5 and 2). [d] *d* (J = 7). [e] *d* (J = 4).

while the other must be in a terminal position. The splitting of the corresponding signal into the doublet of doublets proved the neighboring positions of two secondary carbon atoms; consequently, the two mesyloxy groups cannot be vicinal.

The latter conclusion is in agreement with the finding of Anderson *et al.*[2] that their syrupy diacetal did not consume periodate, and that, consequently, the two free hydroxyl groups therein are not vicinal. These facts excluded the alleged structure **6** for the new diacetal, and, taking into consideration only isopropylidene derivatives possessing not larger than seven-membered rings, only eight possible, isomeric structures, **A–H** (see Scheme 1), remained. Four isomers (**A–D**) have OH-1 free, and four (**E–H**) have OH-6 free. For distinguishing between these two series, the primary mesyloxy group of the dimesyl ester **13** was exchanged by iodide, and the mono-iodide **15** formed was reduced to the corresponding deoxy compound **16**. The secondary mesyloxy group of the latter could not, however, be removed by lithium aluminum hydride, as, instead of **17**, only a mixture of unsaturated compounds was formed *via* elimination of methanesulfonic acid. For this reason, the di-*O*-tosyl derivative **14** was converted, in a similar reaction-sequence *via* the mono-iodide **18**, into the deoxy compound **19**. The tosyloxy group remaining could be removed with sodium amalgam, yielding the mono-hydroxy derivative **17**. Any side-reaction that might have taken place during this reaction could be excluded, as tosylation of **17** afforded the starting material **19** in quantitative yield. It should be mentioned that the tosyloxy groups of the ditosylate **11** could not be removed with sodium amalgam, as no reaction took place at room temperature, and, at the boiling point of the methanolic solution, only decomposition products were formed.



Scheme 1

Hydrolysis of **17** with acetic acid gave the known, crystalline 1-deoxy-D-glucitol[5–7] (**20**), which was further characterized as its pentaacetate[6,8,9] (**21**). From these results, the possible structure of the new diacetal was limited to the isomers **A–D**, as, on similar treatment, structures **E–H** should give 6-deoxy-D-glucitol (1-deoxy-L-gulitol), the antipode of which is known from the literature [10,11], and whose physical properties differ from those of **20**.

The location of the second mesyloxy group, as well as those of the two *O*-isopropylidene groups in **13** was proved by partial hydrolysis. In accordance with the literature[3], the terminal acetal-ring was much more sensitive towards hydrolysis than that attached to the secondary oxygen atoms; consequently, there was obtained a mono-*O*-isopropylidene derivative **22** which, on treatment with base, afforded the crystalline epoxide **23**. The presence of a free primary hydroxyl group in **23** was proved by mesylation, as, according to n.m.r.-spectral data, the dimesyl derivative **24** so obtained possessed two primary mesyloxy groups.

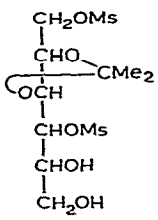
In the spectrum of **23** in Me_2SO-d_6, the proton of the hydroxyl group appears as a triplet ($J = 5$ Hz), proving its terminal location. On the other hand, the mesyloxy group must also be in a terminal position, as no signal of a partner proton of a secondary mesyloxy group appeared above 4.5 p.p.m. The same applies to the spectrum of **24**, in which both mesyloxy groups must be attached to primary carbon atoms, because of the lack of signals at values greater than 4.5 p.p.m.

The formation of a nonterminal, epoxide group from the dihydroxy compound **22** provided a further limiting factor as concerns structures **A–D**, as the **B** type of derivative does not fulfil the necessary requirements.

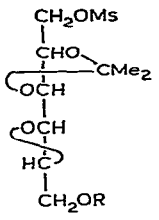
The **D** type of diacetal could also be excluded, as the epoxide which would be formed from the monoisopropylidene compound should, on mesylation, give a symmetrical 1,6-di-*O*-mesylallitol derivative that would have a quite different n.m.r. spectrum. As the D-galactitol configuration of **23** could not be proved directly, the L-iditol configuration (**26**), which would be formed from the corresponding 5-mesylate **25**, had to be excluded by further experiments.

Methylation of the 1-deoxy derivative **17** with methyl iodide–silver oxide afforded the monomethyl ether **27**, the mass-spectroscopic investigation of which unambiguously proved its structure. Besides the base fragment of *m/e* 115, representing the "upper" half of the molecule (**28**), the fragment of the terminal dioxolane ring appeared at *m/e* 101 (**29**), with an intensity of 30%, thus excluding the possibility of structure **C**, which contains a terminal dioxane ring; consequently, the corresponding methoxydioxolane fragment **30** should appear at *m/e* 145.

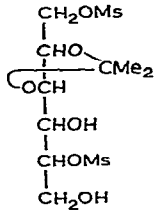
From these results, the structures of the two diacetals that are formed as major components by the acetalation of D-glucitol with acetone in the presence of zinc chloride correspond to 1,2:5,6- (**1**) and 2,3:5,6-di-*O*-isopropylidene-D-glucitol (**12**). A re-investigation of the acetalation products by g.l.c. revealed that at least 12 different acetals are present in the crude mixture, instead of the 6 reported by Bonner *et al.*[4]. From among these acetals, the proportion of **12** reached its maximum after 24 h.



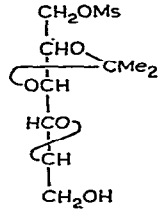
22



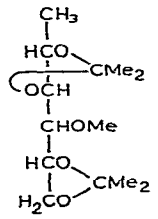
23 R = H
24 R = Ms



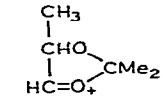
25



26

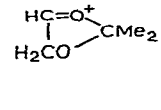


27



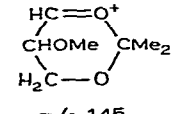
m/e 115

28



m/e 101

29



m/e 145

30

EXPERIMENTAL

General methods. — Melting points are uncorrected. All evaporations were conducted in a rotary evaporator under diminished pressure, after the organic solution had been dried with sodium sulfate. Light petroleum used had b.p. 60–80°. Optical rotations were determined in chloroform (*c* 1) if not stated otherwise. T.l.c. was effected on Kieselgel G with (*A*) ethyl acetate, ethyl acetate–carbon tetrachloride 1:1 (*B*), 1:3 (*C*), and 1:5 (*D*), and (*E*) 1:1 ethyl acetate–ethanol. For detection, 1:1 0.1M potassium permanganate–M sulfuric acid was used at 105°. Column chromatography was performed on Kieselgel 40 (63–200 μm). ^{1}H-N.m.r. spectra (60 MHz) were recorded at room temperature with a JEOL 60-HL spectrometer for solutions in chloroform-*d*, with tetramethylsilane as the internal standard. G.l.c. was conducted with a Hewlett–Packard 5720A-type gas chromatograph, using a glass column (1.6 m × 4 mm) packed with 5% of QF-1 on Gas-Chrom Q; temperature: 2°.min^{-1} from 150 to 220°; carrier: nitrogen gas at the rate of 45 mL.min^{-1}. Mass spectra were recorded with a Varian MAT SM-1 instrument.

I.r. spectra. — These were recorded, for KBr pellets, with a Perkin–Elmer 577 spectrometer. All spectra of isopropylidene acetals contained the characteristic bands of isopropylidene groups, at 1395–1385, 1380–1370, 1195–1170, and 1185–1155 cm^{-1}. The mesyl and tosyl derivatives showed bands at 1380–1330, 1180, and 565–505 cm^{-1}. The absorptions of the hydroxyl groups in compounds **12**, **17**, and **23** appeared at 3490, 3460, 3360, 1070, and 1040 cm^{-1}. The C–I band appeared at 510 cm^{-1} in the spectra of **15** and **18**. The epoxy bands appeared at 3400, 3035–3025, 1270, and 895

cm^{-1} in the spectra of **23** and **24**. The methoxyl bands of **27** could be detected at 2840 and 1080 cm^{-1}, and the ester bands of **5** at 1740, 1260–1220, and 1070 cm^{-1}.

1,2:5,6-Di-O-isopropylidene-3,4-di-O-(methylsulfonyl)-D-glucitol (**3**). — To a stirred solution of compound[1] **1** (13.1 g) in pyridine (30 mL) was added a solution of mesyl chloride (9.5 mL) in pyridine (20 mL) at −10°. The mixture was kept for 1 h at room temperature and then cooled to −5°; water (20 mL) was added at such a rate as to keep the temperature below 0°, and then the mixture was poured into water. The precipitate was filtered off, washed with water, and dried, to give, after recrystallization from methanol (50 mL), pure **3** (15.2 g, 72.5%), m.p. 114–116°, $[\alpha]_D^{20}$ +34.5°; R_F 0.40 (*C*).

Anal. Calc. for $C_{14}H_{26}O_{10}S_2$: C, 40.18; H, 6.26; S, 15.32. Found: C, 40.48; H, 6.33; S, 15.48.

1,2:5,6-Di-O-isopropylidene-3,4-di-O-p-tolylsulfonyl-D-glucitol (**4**). — To a solution of compound **1** (5.25 g) in pyridine (34 mL) was added tosyl chloride (8.4 g), and the mixture was kept for one week at room temperature, to give, after the usual processing, and recrystallization from ethanol (100 mL), pure **4** (8.1 g, 71.0%), m.p. 135–137°, $[\alpha]_D^{20}$ +37.3°; R_F 0.45 (*D*).

Anal. Calc. for $C_{26}H_{34}O_{10}S_2$: C, 54.72; H, 6.01; S, 11.24. Found: C, 54.98; H, 5.88; S, 11.26.

3,4-Di-O-acetyl-1,2:5,6-di-O-isopropylidene-D-glucitol (**5**). — A solution of compound **1** (1 g) in pyridine (3 mL) and acetic anhydride (1.5 mL) was kept for two days at room temperature, to give, after the usual processing, and recrystallization from methanol–water, pure **5** (1 g, 75.7%), m.p. 64–66°, $[\alpha]_D^{20}$ +25.5°; R_F 0.45 (*D*); lit.[2] m.p. 64–65°, $[\alpha]_D^{25}$ +26.1° (*c* 10).

2,3:5,6-Di-O-isopropylidene-D-glucitol (**12**). — D-Glucitol (36.4 g) was added to a stirred solution of zinc chloride (70 g) in acetone (350 mL) at room temperature. Stirring was continued until the hexitol had completely dissolved (~15 min). The solution was kept for 24 h at room temperature, and was then poured into a vigorously stirred, ice-cooled solution of potassium carbonate (90 g) in water (90 mL). The precipitate was filtered off, washed with acetone (3 × 150 mL), and discarded. Conc. ammonium hydroxide solution (2 mL) was added to the filtrate, and then it was evaporated. The residue was extracted with ethyl acetate (3 × 100 mL), and the extract evaporated, to give a syrupy mixture of the crude acetals (50 g).

A portion (10 g) of this mixture was purified by column chromatography, using solvent *B* for elution. On evaporation, the fractions having R_F 0.9 gave 1,2:3,4:5,6-tri-*O*-isopropylidene-D-glucitol (2.9 g, 24%), m.p. 44–46°, $[\alpha]_D^{20}$ +16.5° (*c* 6, MeOH), +4.5° (pyridine), +7.5° (chloroform); lit.[3] m.p. 46°, $[\alpha]_D^{18}$ +13.8° (*c* 6.1, MeOH), lit.[2] m.p. 48°, $[\alpha]_D^{25}$ +14.3° (*c* 10, EtOH); lit.[14] m.p. 45–46°.

On evaporation, the fractions having R_F 0.8 gave another (isomeric) tri-*O*-isopropylidene-D-glucitol (0.3 g) which, after recrystallization from methanol–water, had m.p. 115–118°, $[\alpha]_D^{20}$ −16.4° (pyridine), −6.3° (chloroform).

The fractions having R_F 0.4 gave, on evaporation, and recrystallization of the

residue from dibutyl ether, pure **1** (0.75 g, 7.15%), m.p. 93–94°; lit.[1] m.p. 93–94°, lit.[2] m.p. 95–95.5°.

On evaporation, the fractions having R_F 0.25 gave compound **12** (3.2 g, 30.5%), as a colorless syrup, $[\alpha]_D^{20}$ −15.5° (chloroform), $[\alpha]_D^{20}$ −9.5° (pyridine). The purity of **12** was checked by g.l.c. investigation of its diacetate, which showed, besides the main component (90%) with relative retention-time of 4.1, the presence of two other isomers (~5%) with relative retention-times of 4.5 and 5, compared to that of 1,2:3,4:5,6-tri-*O*-isopropylidene-D-glucitol as unity.

Anal. Calc. for $C_{12}H_{22}O_6$: C, 54.96; H, 8.46. Found: C, 54.75; H, 8.32.

2,3:5,6-Di-O-isopropylidene-1,4-di-O-(methylsulfonyl)-D-glucitol (**13**). — *Method a.* The crude mixture of the different isopropylidene derivatives (50 g), obtained as described for compound **12**, was dissolved in pyridine (250 mL), and treated at 0° with mesyl chloride (50 mL). The mixture was kept overnight at +5°, and then processed in the usual way, to yield, after evaporation of the chloroform solution and recrystallization of the semisolid residue from methanol, pure **13** (23 g, 27.5%), m.p. 149–151°, $[\alpha]_D^{20}$ +2°; R_F 0.30 (*C*).

Anal. Calc. for $C_{14}H_{26}O_{10}S_2$: C, 40.18; H, 6.26; S, 15.32. Found: C, 40.25; H, 6.20; S, 15.41.

Method b. D-Glucitol (36.4 g) was converted into the dibenzoate **2** as described in the literature[1]. The methanolic mother-liquor of **2** was concentrated to 80 mL, and the concentrate was treated (in the presence of phenolphthalein) at 50° with 5M aqueous sodium hydroxide solution (~40 mL) to faint alkalinity. During this treatment, the intense odor of methyl benzoate disappeared. The solution was then extracted with chloroform, and the extract evaporated to a syrup (15 g) which was mesylated as described in method *a*, yielding pure **13** (6.5 g, 7.8%), identical with that described in *a*.

2,3:5,6-Di-O-isopropylidene-1,4-di-O-p-tolylsulfonyl-D-glucitol (**14**). — The syrupy mixture (50 g) of the acetals obtained from D-glucitol (36.4 g) as in the preparation of **12** was dissolved in pyridine (250 mL) and treated with tosyl chloride (70 g). The mixture was kept overnight at room temperature, and then water (10 mL) was added below 10°; after 1 h at room temperature, it was processed in the usual way. Treatment of the residue (from evaporation of the chloroform solution) with methanol (150 mL) afforded pure **14** (25 g, 24%), m.p. 136–138°, $[\alpha]_D^{20}$ +6.8°; R_F 0.80 (*C*), 0.65 (*D*).

Anal. Calc. for $C_{26}H_{34}O_{10}S_2$: C, 54.72; H, 6.01; S, 11.24. Found: C, 54.58; H, 5.98; S, 11.07.

1-Deoxy-1-iodo-2,3:5,6-di-O-isopropylidene-4-O-(methylsulfonyl)-D-glucitol (**15**). — A solution of the dimesylate **13** (4.2 g) and sodium iodide (2 g) in *N,N*-dimethylformamide (42 mL) was heated on a steam bath for 20 h. The solution was evaporated and the residue was partitioned between chloroform and water; the organic solution was washed with water, dried, and evaporated. The residue was purified by column chromatography, using solvent *C* for elution. The fractions having R_F 0.60 were

evaporated, and the residue was filtered with the aid of light petroleum, to give pure **15** (2.95 g, 64.5%), m.p. 106–108°, $[\alpha]_D^{20}$ +19.6°.

Anal. Calc. for $C_{13}H_{23}IO_7S$: C, 34.67; H, 5.15; I, 28.19; S, 7.12. Found: C, 34.55; H, 5.20; I, 28.32; S, 7.10.

*1-Deoxy-2,3:5,6-di-*O*-isopropylidene-4-*O*-(methylsulfonyl)-*D*-glucitol* (**16**). — A solution of the iodide **15** (2.25 g) in methanol (50 mL) was hydrogenated in the presence of Raney nickel (3 g) and triethylamine (3 mL). After the theoretical amount of hydrogen had been consumed (2 h), chloroform was added, and the catalyst was filtered off. The filtrate was evaporated, and the residue dissolved in chloroform; the solution was washed with water, dried, and evaporated. The residue was passed, with the aid of ether, through a short column, to give, after evaporation of the eluate, and recrystallization of the residue from light petroleum at −70°, pure **16** (1.15 g, 71%), m.p. 42–43°, $[\alpha]_D^{20}$ +19.4°; R_F 0.50 (*C*).

Anal. Calc. for $C_{13}H_{24}O_7S$: C, 48.13; H, 7.46; S. 9.89. Found: C, 48.21; H, 7.55; S, 9.70.

*1-Deoxy-2,3:5,6-di-*O*-isopropylidene-*D*-glucitol* (**17**). — A suspension of compound **19** (4 g) and sodium amalgam (4%, 60 g) in a mixture of methanol (80 mL) and water (20 mL) was stirred for 20 h at room temperature. The clear solution was decanted from the mercury, made neutral with carbon dioxide, and evaporated. The residue was extracted with ethanol, and the salts were filtered off. The filtrate was evaporated, and the residue extracted with light petroleum, to give, after filtration and evaporation, compound **17** as a colorless syrup (1.8 g, 73%), $[\alpha]_D^{20}$ −12.8°; R_F 0.35 (*D*).

Anal. Calc. for $C_{12}H_{22}O_5$: C, 58.51; H, 9.00. Found: C, 58.86; H, 9.31.

Tosylation of compound **17** (0.6 g) in pyridine (5 mL) with tosyl chloride (0.6 g) during 3 days at room temperature gave, after the usual processing, tosylate **19** (0.66 g, 67.5%), identical with that already described.

*1-Deoxy-1-iodo-2,3:5,6-di-*O*-isopropylidene-4-*O*-p-tolylsulfonyl-*D*-glucitol* (**18**). — A solution of the ditosylate **14** (22.8 g) and sodium iodide (23 g) in *N*,*N*-dimethylformamide (230 mL) was heated on a steam bath for 1 h. The solution was processed as described for compound **15**, to give, after recrystallization from ethanol–water, pure **18** (17.5 g, 83%), m.p. 82–83°, $[\alpha]_D^{20}$ 0°; R_F 0.80 (*D*).

Anal. Calc. for $C_{19}H_{27}IO_7S$: C, 43.35; H, 5.17; I, 6.09; S, 24.11. Found: C, 43.28; H, 5.32; I, 5.98; S, 23.87.

*1-Deoxy-2,3:5,6-di-*O*-isopropylidene-4-*O*-p-tolylsulfonyl-*D*-glucitol* (**19**). — A solution of the iodide **18** (6.8 g) in methanol (130 mL) was hydrogenated in the presence of Raney nickel (6 g) and triethylamine (6 mL). The mixture was processed as described for compound **16**, to give, after recrystallization from methanol, pure **19** (4.2 g, 81.5%), m.p. 116–118°, $[\alpha]_D^{20}$ +19.2°; R_F 0.70 (*D*).

Anal. Calc. for $C_{19}H_{28}O_7S$: C, 56.98; H, 7.04; S, 8.00. Found: C, 56.75; H, 7.12; S, 7.86.

*1-Deoxy-*D*-glucitol* (**20**). — Compound **17** (1 g) was boiled with 0.01M aqueous hydrochloric acid (20 mL) for 1 h. The cooled solution was made neutral with an

anion-exchange resin, to give, after filtration and evaporation, a syrup which was dried by evaporation with ethanol. The solid residue gave, on recrystallization from ethanol (5 mL), pure **20** (0.57 g, 84.8%), m.p. 134–135°, $[\alpha]_D^{20}$ +3° (*c* 1.7, H_2O); R_F 0.50 (*E*); lit.[5] m.p. 131–132°, $[\alpha]_D^{27}$ +4° (*c* 4, H_2O); lit.[6] m.p. 130–131°, $[\alpha]_D^{27}$ +5° (*c* 1.7, H_2O); lit.[7] m.p. 131–133°, $[\alpha]_D^{20}$ +4° (*c* 4, H_2O).

Acetylation of **20** (0.55 g) with acetic anhydride (3 mL) in pyridine (5 mL) gave, after the usual processing, the pentaacetate **21** (0.8 g, 72.5%), m.p. 105–107°, $[\alpha]_D^{20}$ +18.5° (*c* 1.6, MeOH); R_F 0.55 (*C*); lit.[6] m.p. 105–106°, $[\alpha]_D^{27}$ +22° (*c* 1.6, MeOH); lit.[8] m.p. 105–106°, $[\alpha]_D^{21}$ +20.6 ±2° (*c* 1.8, MeOH); lit.[9] m.p. 105.5–107°.

*4,5-Anhydro-2,3-*O*-isopropylidene-1-*O*-(methylsulfonyl)-*D*-galactitol* (**23**). — A stirred slurry of the dimesylate **13** (8.4 g) in a mixture of acetic acid (64 mL) and water (16 mL) was heated on a steam bath. A clear solution was obtained in 5 min. After being heated for a further 5 min, the solution was evaporated below 30°, and two portions of water were added to, and evaporated from, the residue. The remaining slurry was filtered with the aid of water, to yield 0.6 g of unchanged starting-material **13**. The filtrate, containing mainly the mono-isopropylidene derivative **22** [R_F 0.70 (*A*) and 0.15 (*B*)] was evaporated to dryness, and chloroform (3 × 30 mL) was added to, and evaporated from, the residue, which was dissolved in a mixture of chloroform (50 mL) and methanol (10 mL), and treated at room temperature with 5M methanolic sodium methoxide (5 mL). After 10 min, the mixture was washed with water, dried, and evaporated. The solid residue was filtered with the aid of ether, to give **23** (2.7 g, 47.9%), m.p. 78–80°, $[\alpha]_D^{20}$ +12.6°; R_F 0.75 (*A*).

Anal. Calc. for $C_{10}H_{18}O_7S$: C, 42.54; H, 6.43; S, 11.36. Found: C, 42.45; H, 6.27; S, 11.65.

*4,5-Anhydro-2,3-*O*-isopropylidene-1,6-*di*-O-(methylsulfonyl)-*D*-galactitol* (**24**). — A solution of the epoxide **23** (2.8 g) in pyridine (15 mL) was treated at 0° with mesyl chloride (1.5 mL). After the mixture had been kept for 2 h at room temperature, it was poured into water. The precipitate was filtered off, dried, and recrystallized from methanol (20 mL), to give pure **24** (2.8 g, 77.5%), m.p. 97–99°, $[\alpha]_D^{20}$ +14.2°; R_F 0.40 (*B*).

Anal. Calc. for $C_{11}H_{20}O_9S_2$: C, 36.66; H, 5.59; S, 17.79. Found: C, 36.98; H, 5.93; S, 17.71.

*1-Deoxy-2,3:5,6-di-*O*-isopropylidene-4-*O*-methyl-*D*-glucitol* (**27**). — To a solution of **17** (4 g) in *N*,*N*-dimethylformamide (24 mL) were added silver oxide (4 g) and methyl iodide (4 mL), and the mixture was stirred for 8 h at room temperature; then the silver salts were filtered off, and the filtrate was evaporated. The residue was dissolved in chloroform, the solution washed with water, dried, and evaporated, and the residue distilled, to yield pure **27**, $b.p._{0.01}$ 65–67°, $[\alpha]_D^{20}$ +15.3°; mass-spectral data: peaks at *m/e* 260 ($[M^+]$, 0.5% of base peak at *m/e* 115), 245 (23), 187 (17), 101 (70), 95 (17), 71 (19), 59 (26), and 43 (20).

G.l.c. investigation of the acetalation reaction. — D-Glucitol was treated with acetone–zinc chloride as described for the preparation of compound **12**, but the reaction was processed after 2 h. The resulting, syrupy mixture of acetals was ace-

tylated with acetic anhydride–pyridine, and the acetates analyzed by g.l.c. The following components (with retention times relative to that of 1,2:3,4:5,6-tri-*O*-isopropylidene-D-glucitol as unity) were obtained: **a** 1.3 (3%), **b** 3.8 (1%), **c** 3.9 (1%), **d** 4.1 (23%), **e** 4.5 (26%), **f** 5 (6%), **g** 7.2 (7%), **h** 7.8 (1%), **i** 8.1 (2%), **j** 8.25 (23%), **k** 8.7 (20%), and **l** 11.6 (3%). Peak **d** refers to the acetate of compound **12**, and peak **l** to hexa-*O*-acetyl-D-glucitol.

ACKNOWLEDGMENTS

The authors are indebted to Gy. Horváth for determining and evaluating the mass spectra, and to Mrs. L. Tomori for the g.l.c. investigations.

REFERENCES

1 J. KUSZMANN, *Carbohydr. Res.*, 71 (1979) 123–133.
2 B. C. PRESSMAN, L. ANDERSON, AND H. A. LARDY, *J. Am. Chem. Soc.*, 72 (1950) 2404–2406.
3 E. J. BOURNE, G. P. MCSWEENEY, M. STACEY, AND L. F. WIGGINS, *J. Chem. Soc.*, (1952) 1408–1414.
4 T. G. BONNER, E. J. BOURNE, R. F. J. COLE, AND D. LEWIS, *Carbohydr. Res.*, 21 (1972) 29–35.
5 H. MÜLLER AND T. REICHSTEIN, *Helv. Chim. Acta*, 21 (1938) 251–272.
6 M. L. WOLFROM, B. W. LEW, AND R. M. GOEPP, JR., *J. Am. Chem. Soc.*, 68 (1946) 1443–1448.
7 H. KAUFMANN AND T. REICHSTEIN, *Helv. Chim. Acta*, 50 (1967) 2280–2286.
8 K. GÄTZI AND T. REICHSTEIN, *Helv. Chim. Acta*, 21 (1938) 914–925.
9 J. K. N. JONES AND D. L. MITCHELL, *Can. J. Chem.*, 36 (1958) 206–211.
10 G. N. BOLLENBACK AND L. A. UNDERKOFLER, *J. Am. Chem. Soc.*, 72 (1950) 741–745.
11 F. VOTOČEK AND J. MIKŠIČ, *Bull. Soc. Chim. Fr.*, 43 (1928) 220–224.
12 S. J. ANGYAL AND K. JAMES, *Aust. J. Chem.*, 24 (1971) 1219–1227.