NEIGHBORING-GROUP PARTICIPATION IN CARBOHYDRATE CHEMISTRY

PART I. NEIGHBORING-GROUP PARTICIPATION OF THE 6-*O*-BENZOYL GROUP IN A NUCLEOPHILIC DISPLACEMENT OF A 5-*p*-TOLUENESULFONATE*

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ABSTRACT

The reaction of 6-*O*-benzoyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranose with potassium acetate in *N*,*N*-dimethylformamide proceeds both by direct displacement to yield the corresponding 5-*O*-acetyl derivative **3**, and by neighboring-group participation of the benzoyl group to yield the 6-*O*-acetyl-5-*O*-benzoyl product **4**. Under the reaction conditions employed, both **3** and **4** react further by elimination of the 3-*O*-*p*-tolylsulfonyloxy group and the formation of the corresponding olefinic sugars, 5-*O*-acetyl-6-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose (**5**) and 6-*O*-acetyl-5-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose (**6**). An additional reaction resulted in the production of 6-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose (**7**). The structures of **5**, **6**, and **7** were confirmed by independent synthesis of **3** and **4** by unequivocal routes. 1,2-*O*-Isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose **13**, was selectively benzoylated to yield the 6-benzoyl derivative **14**, which was converted into **3**. Tritylation and subsequent acetylation of **13** gave the 5-*O*-acetyl derivative **16**, which was detritylated into 6-*O*-acetyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**18**), as a result of acyl migration; benzoylation of **18** yielded **4**. In addition, **18** was prepared by the treatment of 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose with potassium acetate in *N*,*N*-dimethylformamide.

INTRODUCTION

The neighboring-group participation of a 6-acyloxy group in the displacement of a carbohydrate 5-*p*-toluenesulfonate group, *e.g.* 3-*O*-acetyl-6-*O*-benzoyl-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (**1**)[1] has been reported to be unfavorable[2] although the reason for this was not obvious**. We wish to report that

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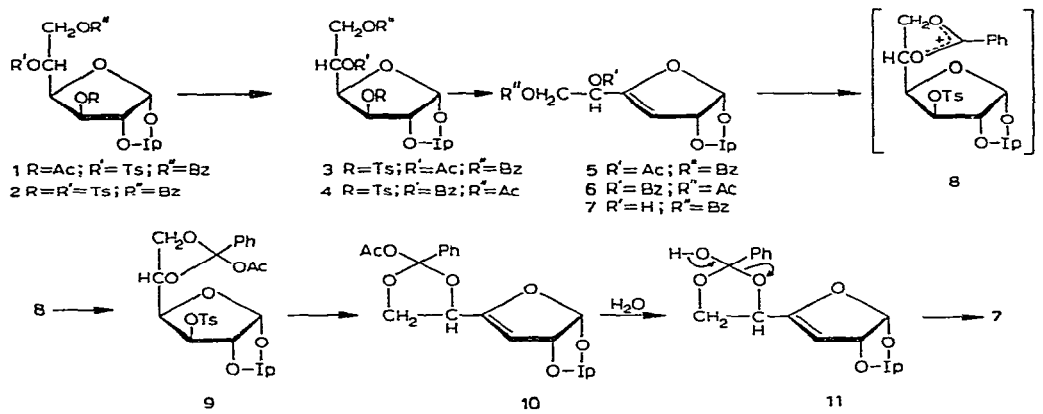
**After preparation of this manuscript a preliminary communication dealing with similar neighboring-group participations appeared[3].

this view is erroneous, since we have found that the participation of a 6-*O*-benzoyl group in the nucleophilic displacement of a carbohydrate 5-*p*-toluenesulfonate can be a major reaction pathway depending on the conditions employed.

RESULTS AND DISCUSSION

The nucleophilic displacement of the 5-*p*-toluenesulfonate group of 6-*O*-benzoyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (**2**)[4] by anhydrous potassium acetate in *N*,*N*-dimethylformamide under reflux was examined. The starting material was consumed after 4–5 h, at which time the composition of the reaction mixture was examined by chromatography on silica gel.

The first fraction obtained was an oil which appeared homogenous by t.l.c. but, based on the n.m.r. spectrum, was a mixture of at least two components. There were two singlets in the approximate ratio 5:1 at δ 2.10 and 2.03 p.p.m., probably due to the presence of two magnetically nonequivalent acetoxy groups. The *p*-tolylsulfonyl group was absent and the presence of a trisubstituted double bond was indicated by the i.r. spectrum [1670 (C=C stretch) and 820 cm^{-1} (CH wag.)]. This observation suggested the possibility that, in addition to direct nucleophilic displacement of the 5-*O*-*p*-tolylsulfonyloxy group and subsequent elimination of the 3-*O*-*p*-tolylsulfonyloxy group to yield 5-*O*-acetyl-6-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose **5**, the reaction could proceed via neighboring-group participation



Scheme 1

of the 6-*O*-benzoyl group. This latter course would result in the formation of 6-*O*-acetyl-5-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose **6**. The cyclic benzoxonium ion **8** obtained by the nucleophilic attack of the carbonyl oxygen of the C-6 benzoyloxy group at C-5, would be opened by reaction with an acetate anion exclusively at C-6. Thus, **6** would be formed as a result of the neighboring-group participation of the C-6 benzoyloxy group. The crystalline product that was isolated from this mixture showed an n.m.r. peak for the acetate methyl protons at δ 2.11 p.p.m., suggesting that the material was the direct displacement product **5**, since in this case the acetate group would be allylic and the small but finite

lower field shift would be expected for the methyl protons (an acetate methyl group bound to an aliphatic carbon has a chemical shift at δ 2.01, whereas binding to an allylic carbon causes a slight shift towards a lower field[5]). This interpretation was confirmed by synthesizing the crystalline olefinic sugar **5**, by treating 5-*O*-acetyl-6-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**3**) with potassium acetate in *N*,*N*-dimethylformamide under reflux. The olefinic sugar **6** was similarly synthesized from 6-*O*-acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**4**) and found to be identical with the second component of the mixture.

The second major fraction was a mixture of several compounds and was further resolved by rechromatography on silica gel. The first product obtained, although apparently homogenous on t.l.c. and containing *p*-toluenesulfonate, benzoate, and acetate groups (i.r. data), was nevertheless considered a mixture, on the basis of the n.m.r. spectrum, and at least two components were assumed to be present: the direct displacement product, 5-*O*-acetyl-6-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**3**), and the product of neighboring-group participation of the C-6 benzoyloxy group, 6-*O*-acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**4**). The latter compound was isolated in crystalline form from the mixture and its assumed structure confirmed. The former compound was identified as having the structure assigned by comparison with material synthesized by an independent route.

A subsequent chromatographic fraction contained a third olefinic sugar **7**, well resolved from the two L-idose derivatives. The structure assigned to this compound was based, in part, on the i.r. spectrum which indicated the presence of a hydroxyl group, a benzoyl group, and a trisubstituted double bond but no acetate. Based on the results of Goodman and associates[6] that the attack of a nucleophile on an acyloxonium ion can occur at the carbonyl carbon atom of the acyl group as well, the following explanation can be postulated for the formation of this third olefinic sugar. If the acetate anion attacks the carbonyl carbon atom of the intermediate **8**, the product would be an ortho ester derivative **9** which, after the elimination of the 3-*O*-*p*-tolylsulfonyloxy group to give **10**, would rapidly react with water to give the intermediate **11** which, in turn, would be converted into the ordinary ester **7**. The formation of only one product suggests that this is a thermodynamically controlled reaction with one product strongly favored over the other. If this assumption is correct, then the acetylation of this olefinic sugar should give either **5** or **6** as a product. Indeed, the acetylation of the olefinic sugar **7** yielded **5**, showing that **7** was 6-*O*-benzoyl-3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-hex-3-enofuranose. Treatment of **5** under the reaction conditions does not give rise to **7**, so that simple hydrolysis of **5** is not the mechanism for the formation of **7**.

It should be noted that, at the present time, it is not known whether the S_N2 substitution at C-5 or E2 elimination of the 3-*O*-*p*-tolylsulfonyloxy group is the initial step for the formation of the olefinic sugars. In the just described mechanism, it is assumed that displacement by a nucleophile, either external by acetate anion or

internal by the C-6 benzoyloxy groups, is the primary process in the reaction. An equally likely alternative is the prior elimination of the 3-*O*-*p*-tolylsulfonyloxy group of **2** to give **12** from which the olefinic sugars **5**, **6**, and **7** can be formed.

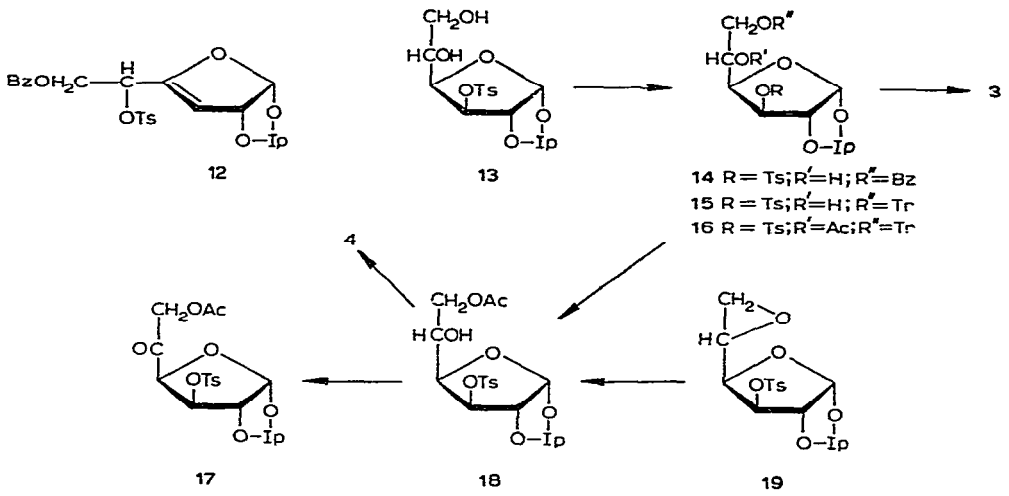
It is interesting to note that the anomeric proton of the unsaturated sugars **5**, **6**, and **7** does not appear as a pure doublet, but shows an additional splitting with J very small compared to $J_{1,2}$, probably due to virtual coupling[7] with the olefinic proton at C-3.

The previously reported findings[3], as well as the present results, suggest that the extent of neighboring-group participation of C-6 acyloxy group in the nucleophilic displacement of a 5-*p*-toluenesulfonate is strongly solvent dependent. In *N*,*N*-dimethylformamide, direct displacement is predominant, whereas in acetic anhydride and Dowex 1(X-10, AcO^-) as a nucleophile and in acetonitrile and potassium acetate as a nucleophile, neighboring-group participation is the exclusive reaction route. This can be readily explained if one assumes that these reactions are kinetically controlled and are, therefore, dependent on the concentration of acetate anion in the solvent employed, since the "concentration" of the neighboring C-6 acyloxy group is constant in all cases. Potassium acetate is readily soluble in *N*,*N*-dimethylformamide, but practically insoluble in acetonitrile. However, it cannot be excluded that the polarity of the solvent might have some influence on the direction of the reaction. The reaction of the intermediate acyloxonium ion with a nucleophile (acetate) is very solvent dependent. In *N*,*N*-dimethylformamide, the acetate ion attacks predominantly at C-6 to give the corresponding C-6 acetoxy derivative **4**, whereas in acetonitrile, the acetate ion attacks exclusively at the carbonyl carbon atom of the acyloxonium transition complex to give the corresponding *ortho*-ester derivative **9**.

The formation of the unsaturated sugars **5**, **6**, and **7** is clearly an E2 elimination, probably as a consequence of the high basicity of potassium acetate in *N*,*N*-dimethylformamide and of the favorable *trans*-configuration of the H-4 and 3-*O*-*p*-tolylsulfonyloxy group. The fact that the unsaturated sugars were not formed, when acetonitrile was used as a solvent, indicates that this elimination reaction is temperature and solvent dependent.

The structures of compounds **3** and **4**, and therefore the structures of the olefinic sugars **5**, **6**, and **7**, were proved by independent synthesis. Partial hydrolysis of the L-idose derivative, that was obtained by the action of Dowex 1(X-10, AcO^-) on 6-*O*-benzoyl-1,2-*O*-isopropylidene-3,5-di-*O*-*p*-tolylsulfonyl-α-D-glucofuranose (**2**) in acetic anhydride under reflux, gave 1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**13**). This compound, upon selective benzoylation with benzoyl chloride in pyridine, gave the corresponding 6-*O*-benzoyl derivative **14**. Acetylation of **14** with acetic acid and pyridine at room temperature gave **3**. The possible acyl migration in this last reaction was excluded on the basis that compound **14** was quantitatively recovered when treated with pyridine under the experimental conditions of acetylation; in addition, **3** does not give rise to **14** when treated with potassium acetate in *N*,*N*-dimethylformamide at reflux.

Tritylation of **13** gave the 6-*O*-trityl derivative **15** which upon acetylation



Scheme 2

afforded **16**. Detritylation of **16** unexpectedly gave the 6-*O*-acetyl derivative **18**, indicating very facile migration of the acetyl group from C-5 to C-6. Benzoylation of **18** yielded **4** which was identical with the previously isolated product[8]. The structure of **18** was confirmed by oxidation with ruthenium tetroxide into the ketone **17**, and by independent synthesis from 5,6-anhydro-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**19**)[9] treated with potassium acetate in refluxing *N*,*N*-dimethylformamide.

EXPERIMENTAL

General. — Silica gel used for all column chromatography was E. Merck (Darmstadt, Germany) silica gel, grain size <0.08 mm. M.p. are uncorrected. Optical rotations were determined with a Cary-60 spectropolarimeter in a 1.0-cm cell. I.r. spectra were recorded with a Perkin–Elmer infrared spectrophotometer Model 337, and n.m.r. spectra with a Varian T-60 spectrometer with tetramethylsilane as the internal standard. Chemical shifts (δ) are expressed in p.p.m.

Treatment of 6-O-benzoyl-1,2-O-isopropylidene-3,5-di-O-p-tolylsulfonyl-α-D-glucofuranose (**2**) *with potassium acetate in refluxing* N,N-*dimethylformamide.* — A solution of *N*,*N*-dimethylformamide (80 ml) containing **2** (5.00 g, 8 mmoles) and anhydrous potassium acetate (60 mmoles, 5.00 g) was heated for 5 h under reflux. The reaction mixture was cooled to room temperature, diluted with water (80 ml), and extracted with two 250-ml portions of ether. The combined ether extracts were successively washed with saturated aqueous sodium hydrogen carbonate and water, dried with magnesium sulfate, and evaporated *in vacuo*. The oily residue (2.10 g) was chromatographed on silica gel (130 g), and elution with 3:1 hexane–acetone gave two fractions. The first fraction (1.16 g, 42%) was a mixture of the two unsaturated sugars **5** and **6**, and the second fraction (800 mg) was a mixture of the two L-idose derivatives **3** and **4** and a third unsaturated sugar **7**. Trituration of Fraction 1 with 1:1 hexane–petroleum

ether (b.p. 30–60°) and recrystallization of the crystalline product from the same solvent system afforded 500 mg (18%) of pure **5**. The olefinic sugar **6** could not be isolated in pure form from the above reaction mixture, but its presence was indicated by the i.r. and n.m.r. spectra of the mixture. The olefinic sugar **6** was, however, synthesized by an independent route.

Fraction 2 was chromatographed on silica gel (70 g), and elution with 95:5 benzene–2-propanol gave three fractions: The first was an amorphous mixture of compounds **3** and **4** (480 mg, 12%). Trituration of this fraction with ethanol afforded a crystalline substance which, after recrystallization from abs. ethanol, exhibited i.r. and n.m.r. spectra identical with those of an authentic sample of 6-*O*-acetyl-5-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**4**)[8]; m.p. and mixed m.p. 125.5–126.5°. The second amorphous fraction (200 mg) consisted of **7**, and the third fraction (115 mg) contained **7** together with some more polar impurities. Rechromatography of the latter fraction on silica gel and elution with 1:1 benzene–ether afforded an additional 80 mg of pure **7** (overall yield 280 mg, 12%). The unsaturated sugar **7** was not crystalline and had $[\alpha]_D^{27}$ −3.3° (*c* 1.0, chloroform); i.r. data: $\nu_{max}^{CHCl_3}$ 3580 (OH), 3010 (aromatic CH), 1720 (benzoate C=O), 1660 (olefinic C=C stretch), 1600 (aromatic C=C), and 1280 cm^{-1} (benzoate C–O); n.m.r. in chloroform-*d*: δ 8.18–7.30 (5-proton multiplet, Ph), 6.08 (1-proton doublet, $J_{1,2}$ 6.0 Hz, H-1), 5.31 (1-proton doublet, $J_{1,2}$ 6.0 Hz, H-2), 5.33 (1-proton singlet, H-3), 4.50 (3-proton, slightly broadened singlet, H-5, H-6, and H′-6), 3.00 (1-proton broad singlet, OH), and 1.43 (6-proton singlet, Me of Ip).

Anal. Calc. for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.72; H, 6.01.

5-O-Acetyl-6-O-benzoyl-3-deoxy-1,2-O-isopropylidene-β-L-threo-hex-3-enofuranose (**5**). — 5-*O*-Acetyl-6-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**3**) (140 mg, 0.27 mmole) was dissolved in *N*,*N*-dimethylformamide (10 ml), and after the addition of anh. potassium acetate (140 mg, 1.42 mmoles) the solution was heated for 5 h under reflux. The reaction mixture was cooled to room temperature, water was added (10 ml), and the solution extracted twice with 100-ml portions of ether. The ether extracts were washed with sat. sodium hydrogen carbonate and then water, dried with magnesium sulfate, and evaporated. The residue (93 mg) was chromatographed on silica gel (20 g) and elution with 3:1 hexane–acetone afforded 51 mg (56%) of pure **5**, m.p. 95–97°, $[\alpha]_D^{27}$ −12.5° (*c* 1.0, chloroform); i.r. data (chloroform): 1665 (olefinic C=C stretch) and 1600 cm^{-1} (aromatic C=C); n.m.r. in chloroform-*d*: δ 8.2–7.3 (5-proton multiplet, Ph), 6.11 (1-proton doublet, $J_{1,2}$ 6.0 Hz, H-1), 5.78 (1-proton quartet, $J_{5,6}$ 4.0 Hz and $J_{5,6}$ 6.0 Hz, H-5), 5.55–5.33 (2-proton multiplet, H-2 and H-3), 4.56 (two 2-protons doublets, $J_{5,6}$ 4.0 Hz and $J_{5,6'}$ 6.0 Hz, H-6 and H′-6), 2.10 (3-proton singlet, Me of Ac), and 1.40 (6-proton singlet, Me of Ip).

Anal. Calc. for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 62.08; H, 5.80.

6-O-Acetyl-5-O-benzoyl-3-deoxy-1,2-O-isopropylidene-β-L-threo-hex-3-enofuranose (**6**). — A solution of **4** (600 mg; 1.15 mmoles) and anhydrous potassium acetate (600 mg) in *N*,*N*-dimethylformamide (15 ml) was heated for 5 h under reflux. The

solution was cooled to room temperature, water was added (15 ml), and the reaction mixture was extracted with two 150-ml portions of ether. The ethereal solution was washed with saturated sodium hydrogen carbonate solution, water, and dried with magnesium sulfate. The ether was evaporated *in vacuo*, and the crystallized starting material was removed after trituration of the crude product (500 mg) with ethanol. The residual oil (274 mg) was chromatographed on silica gel (80 g). Elution with 3:1 hexane–acetone afforded 187 mg (48%) of pure **6**, oil; $[\alpha]_D^{27}$ +11.0° (*c* 1.0, choroform); i.r. data (chloroform): 1670 (olefinic C=C stretch), 1600 (aromatic C=C), and 822 cm^{-1} (olefinic CH wag.); n.m.r. in chloroform-*d*: δ 8.20–7.37 (5-proton multiplet, Ph), 6.10 (1-proton doublet, $J_{1,2}$ 6.0 Hz, H-1), 5.67 (1-proton triplet, $J_{5,6}$ 6.0 Hz, H-5), 5.40–5.23 (2-proton multiplet, H-3 and H-4), 4.47 (2-proton doublet, $J_{5,6}$ 6.0 Hz, H-6 and H'-6), 2.03 (3-proton singlet, Me of Ac), 1.47 and 1.43 (two 6-proton singlets, Me of Ip).

Anal. Calc. for $C_{18}H_{20}O_7$: C, 62.06; H, 5.79. Found: C, 62.20; H, 5.96.

1,2-O-Isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**13**). — Compound **4** (5.00 g; 0.96 mmole) was dissolved in abs. ethanol (250 ml). Sodium hydroxide (1.3 g; 32.4 mmoles) was added to the resulting solution and, after being kept for 3 h at room temperature, the reaction mixture was neutralized to pH 7 with 10% acetic acid. The solvent was removed *in vacuo*, and the dry residue extracted with chloroform (300 ml). The chloroform extract was washed two times with water, dried with magnesium sulfate and, after removal of solvent, the residue was chromatographed on silica gel. Elution with 19:1 and 1:1 benzene–methanol afforded pure **13** (3.27 g, 91%) which was crystallized from petroleum–ether (b.p. 30–60°), m.p. 92–93°, $[\alpha]_D^{27}$ −38.3° (*c* 1.0, chloroform); n.m.r. in chloroform-*d*: δ 7.96–7.26 (4-proton multiplet, C_6H_4), 5.77 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 4.90 (1-proton doublet, $J_{3,4}$ 3.2 Hz, H-3), 4.70 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2), 4.33 (1-proton quartet, $J_{3,4}$ 3.2 Hz and $J_{4,5}$ 7.6 Hz, H-4), 4.10–3.60 (1-proton multiplet, H-5), 3.56–3.36 (2-proton multiplet, H-6 and H'-6), 2.63 (2-proton singlet, 2 OH), 2.46 (3-proton singlet, Me of Ts), 1.46 and 1.28 (two 6-proton singlets, Me of Ip).

Anal. Calc. for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92; S, 8.56. Found: C, 51.53; H, 6.02; S, 8.34.

6-O-Benzoyl-1,2-O-isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**14**). — Compound **13** (340 mg, 0.9 mmole) was dissolved in abs. pyridine (10 ml), benzoyl chloride (124 mg, 1.0 mmole) was added, and the resulting solution was heated for 70 h at 40°. An additional portion of benzoyl chloride (62 mg) was added after 24 h and again after 48 h. The excess benzoyl chloride was destroyed by adding methanol to the reaction mixture, the methyl benzoate and solvents were removed *in vacuo*, and the residue (660 mg) was chromatographed on silica gel (100 g). Elution with 97:3 benzene–2-propanol afforded 180 mg (41%) of **14**, and 246 mg (46%) of 5,6-di-*O*-benzoyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-β-L-idofuranose, m.p. 145–147°, $[\alpha]_D^{27}$ −8.5° (*c* 1.0, chloroform).

Anal. Calc. for $C_{30}H_{30}O_{10}S$: C, 61.85; H, 5.19; S, 5.50. Found: C, 61.99; H, 5.31; S, 5.62.

After recrystallization from petroleum ether, **14** had m.p. 136°, $[\alpha]_D^{27}$ −51.0° (*c* 1.0, chloroform); n.m.r. in chloroform-*d*: δ 8.20–7.34 (9-proton multiplet, Ph and Ts), 6.00 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 4.93 (1-proton doublet, $J_{3,4}$ 3.4 Hz, H-3), 4.80 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2), 4.50–4.06 (4-proton multiplet, H-4, H-5, H-6, and H′-6), 2.66 (1-proton, broad peak, OH), 2.40 (3-proton singlet, Me of Ts), 1.46 and 1.30 (two 6-proton singlets, Me of Ip).

Anal. Calc. for $C_{23}H_{26}O_9S$: C, 57.74; H, 5.48; S, 6.70. Found: C, 57.49; H, 5.50; S, 6.66.

5-O-Acetyl-6-O-benzoyl-1,2-O-isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**3**). — Acetic anhydride (3.0 ml) was added to a solution of **14** (400 mg, 0.84 mmole) in abs. pyridine (10 ml), and the reaction mixture allowed to stand for 2 h at room temperature. The excess acetic anhydride was destroyed by addition of methanol at 0°, the solvents were evaporated *in vacuo*, and the oily residue was chromatographed on silica gel. Elution with 2:1 hexane–acetone afforded pure **5** (400 mg, 92%), which is an oil at room temperature but can be crystallized from ethanol at −20°; $[\alpha]_D^{27}$ −4.0° (*c* 1.0, chloroform); n.m.r. in chloroform-*d*: δ 8.13–7.23 (9-proton multiplet, Ph and Ts), 6.00 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 5.63–5.26 (1-proton multiplet, H-5), 4.96 (1-proton doublet, $J_{3,4}$ 3.6 Hz, H-3), 4.83 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2), 4.53 (1-proton quartet, $J_{3,4}$ 3.6 Hz and $J_{4,5}$ 8.0 Hz, H-4), 4.52–3.93 (2-proton multiplet, H-6 and H′-6), 2.43 (3-proton singlet, Me of Ts), 2.03 (3-proton singlet, Me of Ac), 1.50 and 1.31 (two 3-proton singlets, Me of Ip).

Anal. Calc. for $C_{25}H_{28}O_{10}S$: C, 57.68; H, 5.42; S, 6.16. Found: C, 57.80; H, 5.35; S, 6.28.

1,2-O-Isopropylidene-3-O-p-tolylsulfonyl-6-O-trityl-β-L-idofuranose (**15**). — Compound **13** (1.300 g, 3.47 mmoles) was dissolved in anh. pyridine (50 ml) and chlorotriphenylmethane (4.00 g, 14.35 mmoles) was added to the solution which was kept for 7 days at room temperature. Ice–water (1,000 ml) was added and the mixture stirred for 1 h. The resulting precipitate was filtered off and dissolved in chloroform. The chloroform solution was washed with a 10% solution of acetic acid and then with water. After being dried with magnesium sulfate, the chloroform was evaporated *in vacuo*, and the residue chromatographed on silica gel (120 g). Elution with 98:2 benzene–2-propanol gave 1.500 g (66%) of pure **15**, which was recrystallized from benzene–hexane, m.p. 84–86°, $[\alpha]_D^{27}$ −32.5° (*c* 1.0, chloroform); n.m.r. in chloroform-*d*: δ 7.73–7.10 (19-proton multiplet, aromatic protons of Tr and Ts), 5.90 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 4.76 (1-proton doublet, $J_{3,4}$ 3.4 Hz, H-3), 4.66 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2), 4.53 (1-proton triplet, $J_{3,4}$ 3.6 Hz and $J_{4,5}$ 3.4 Hz, H-4), 3.86 (1-proton, broad triplet, $J_{5,6}$ 5.2 Hz, H-5), *ca.* 3.16 (2-proton octet, $J_{5,6}$ 5.2 Hz, $J_{6,6'}$ 9.0 Hz, H-6, and H′-6), 2.40 (3-proton singlet, Me of Ts), 1.50 and 1.26 (two 6-proton singlets, Me of Ip).

Anal. Calc. for $C_{35}H_{36}O_8S$: C, 68.17; H, 5.88; S, 5.20. Found: C, 68.45; H, 6.04; S, 5.07.

6-O-Acetyl-1,2-O-isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**18**). — Acetic anhydride (10 ml) was added to a pyridine solution (50 ml) of **15** (1. 0 g;

1.62 mmoles). The solution was kept for 20 h at room temperature, methanol was added at 0° to destroy the excess acetic anhydride, and the solvent was evaporated *in vacuo* to yield 928 mg (87%) of a white amorphous product, **16**, $[\alpha]_D^{27}$ −5.5° (*c* 1.0, chloroform); this product was not further purified but directly detritylated. Compound **16** (1.400 g, 2.12 mmoles) was dissolved in glacial acetic acid (10 ml), and a 40% solution of hydrogen bromide in acetic acid (0.5 ml) was added to the solution. After 2 min, the precipitated bromotriphenylmethane was filtered off, the filtrate was poured into 1,000 ml of ice–water and the solution extracted with chloroform. The chloroform extract was washed four times with ice–water, dried with magnesium sulfate, evaporated *in vacuo*, and the crude product (600 mg, 68%) chromatographed on silica gel (70 g). Elution with 2:1 hexane–acetone afforded 200 mg (23%) of pure **18** as an oil, $[\alpha]_D^{27}$ −24.5° (*c* 1.0, chloroform); n.m.r. in chloroform-*d*: δ 8.00–7.30 (4-proton multiplet, Ts), 5.96 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-1), 4.90 (1-proton doublet, $J_{3,4}$ 3.2 Hz, H-3), 4.73 (1-proton doublet, $J_{1,2}$ 4.0 Hz, H-2), 4.36–3.90 (4-proton multiplet, H-4, H-5, H-6, and H′-6), 2.06 (3-proton singlet, Me of Ac), 1.46 and 1.30 (two 3-proton singlets, Me of Ip).

Anal. Calc. for $C_{18}H_{24}O_9S$: C, 51.92; H, 5.81. Found: C, 51.86; H, 5.69.

6-O-Acetyl-5-O-benzoyl-1,2-O-isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**4**). — A pyridine solution (1.0 ml) containing 52 mg of **18** and 0.1 ml of benzoylchloride was kept at room temperature for 1 h, and after removal of the solvent, the solid residue was recrystallized from ethanol to yield **4**, m.p. 124–125°.

Oxidation of compound **18** *with ruthenium tetroxide–sodium periodate.* — A suspension of ruthenium tetroxide (obtained from 500 mg of ruthenium dioxide and 6 g of sodium periodate) was added at 0° to a solution of **18** (500 mg, 1.20 mmoles), in carbon tetrachloride (100 ml), covered with water (30 ml). After being stirred for 1 h, the reaction mixture was allowed to warm to room temperature and was stirred for an additional 2 h. The excess of ruthenium tetroxide was destroyed by the addition of 2-propanol (5 ml) in carbon tetrachloride (50 ml), and the precipitate of ruthenium dioxide was filtered off, and washed with water (30 ml) and with carbon tetrachloride (50 ml). The combined filtrates were washed with sat. sodium hydrogen carbonate solution (100 ml) and water, and the organic extract was dried with magnesium sulfate. After removal of the solvent, the residue was chromatographed on silica gel (50 g). Elution with 19:1 benzene–methanol afforded pure 6-*O*-acetyl-1,2-*O*-isopropylidene-3-*O*-*p*-tolylsulfonyl-α-D-glucofuran-5-ulose (**17**) (300 mg, 60%) which, after recrystallization from ether, had m.p. 125–125.5°; i.r. data: $\nu_{max}^{CHCl_3}$ 3010 (aromatic CH), 1750 (ketone C=O), 1740 (AcO C=O), 1600 (aromatic C=C), 1235 (AcO C–O), 1193 and 1181 cm^{-1} (Ts, sym. SO_2 stretch); n.m.r. in chloroform-*d*:δ 7.86–7.23 (4-proton multiplet, Ts), 6.10 (1-proton doublet, $J_{1,2}$ 3.8 Hz, H-1), 5.03–4.83 (4-proton multiplet, H-3, H-4, H-6, and H′-6), 4.70 (1-proton doublet, $J_{1,2}$ 3.8 Hz, H-2), 2.46 (3-proton singlet, Me of Ts), 2.13 (3-proton singlet, Me of Ac), 1.43 and 1.33 (two 6-proton singlets, Me of Ip)

Anal. Calc. for $C_{18}H_{22}O_9S$: C, 52.17; H, 5.35; S, 7.74. Found: C, 52.14; H, 5.29; S, 7.68.

Treatment of 5,6-anhydro-1,2-O-isopropylidene-3-O-p-tolylsulfonyl-β-L-idofuranose (**19**) *with potassium acetate in* N,N-*dimethylformamide at reflux.* — Compound **19** (500 mg, 1.40 mmoles) was treated with anh. potassium acetate (500 mg) in *N,N*-dimethylformamide (10 ml) for 15 min at reflux. The reaction mixture was diluted with water (10 ml) and extracted with two 100-ml portions of ether. The ether extract was washed with saturated sodium hydrogen carbonate and water, and dried with magnesium sulfate. After removal of the solvent *in vacuo*, the residue (480 mg) was chromatographed on silica gel (35 g). Elution with 19:1 benzene–methanol afforded the starting material **19** (360 mg) and a mixture of products (52 mg) which was rechromatographed on silica gel (10 g). Elution with 19:1 benzene–2-propanol afforded pure **18** (15 mg, 3%), which was identical with the product obtained by detritylation of **16**.

Treatment of compound **2** *with potassium acetate in acetonitrile under refluxing.* — A solution of **2** (5.000 g; 9.60 mmoles) and potassium acetate (8.00 g) in acetonitrile (150 ml) was heated for 47 days at reflux. The suspension was filtered and, after removal of the solvent, the residue was chromatographed on silica gel (160 g). Elution with 97:3 benzene–2-propanol afforded 1.600 g of starting material **2** and 2.000 g (54%) of pure **14**, which after recrystallization from acetone–petroleum ether (b.p. 30–60°) had m.p. 136°, and was identical with the product obtained by partial benzoylation of **13**.

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