PREPARATION OF UNSATURATED CARBOHYDRATES FROM METHYL 4,6-*O*-BENZYLIDENE-3-CHLORO-3-DEOXY-β-D-ALLOPYRANOSIDE, AND THEIR UTILITY IN THE SYNTHESIS OF SUGARS OF BIOLOGICAL IMPORTANCE*†

E. H. WILLIAMS, W. A. SZAREK, AND J. K. N. JONES
Department of Chemistry, Queen's University, Kingston, Ontario (Canada)
(Received December 28th, 1970; accepted February 8th, 1971)

ABSTRACT

Methyl 4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**2**) is readily obtained from methyl 4,6-*O*-benzylidene-3-chloro-3-deoxy-β-D-allopyranoside (**1**). Treatment of compound **2** or its 2-*O*-acetyl derivative (**3**) with dilute hydrochloric acid in acetone affords the α,β-unsaturated ketone **4** in high yield. Examples of the synthetic utility of compound **4** are provided by its ready conversion into methyl 2,3,6-trideoxy-β-D-*threo*-hexopyranoside (methyl β-D-rhodinoside, **8**) and the D-*erythro* isomer (methyl β-D-amicetoside, **13**).

INTRODUCTION

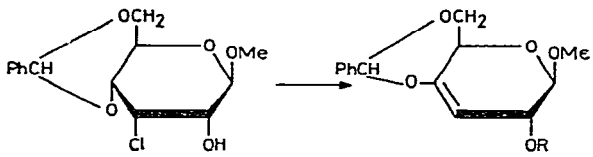
In an earlier publication in this series[1], the reaction of methyl 4,6-*O*-benzylidene-3-chloro-3-deoxy-β-D-allopyranoside (**1**) with sodium azide was described. The reaction was performed in *N,N*-dimethylformamide at 120–130°; a crystalline product was isolated after 1 h, and was shown to consist of two components (t.l.c.). Because, in our hands, a separation of the components could not be achieved by crystallization or by preparative t.l.c., the mixture was treated with acetic anhydride–pyridine to give methyl 2-*O*-acetyl-3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside (60%) and the unsaturated derivative methyl 2-*O*-acetyl-4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**3**). The displacement of the chloro group in compound **1** with azide ion has also been achieved by other investigators[2]; in that work, compound **1** was treated with sodium azide in *N,N*-dimethylformamide at reflux temperature for 4 days. In addition to methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside, another component was present which, on the basis of its t.l.c. behavior, was concluded to be starting material; the formation of an unsaturated derivative was not recorded. This discrepancy has now been investigated, and the results confirm our original findings, just summarized; full details of these studies are given in the Experimental section. The present article also describes an alternative procedure

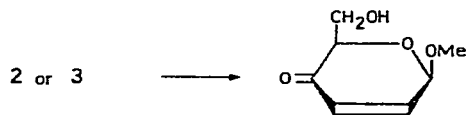
*Dedicated to Dr. Nelson K. Richtmyer in honor of his 70th birthday.
†Part V in the series "Synthesis and Reactions of Chlorodeoxy Sugars".

for the preparation of compound **3** from the readily available[1] chlorodeoxy sugar **1**, and some further transformations leading to the synthesis of sugars of biological importance.

RESULTS AND DISCUSSION

When compound **1** was heated with sodium benzoate in tetrahydrofuran at reflux temperature, elimination occurred to give, in 85% yield, methyl 4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**2**), which could be converted into the 2-*O*-acetyl derivative (**3**) obtained previously[1]. A comparable elimination reaction





has been reported by Horton *et al.*[3]; on treatment with potassium *tert*-butoxide in refluxing xylene, methyl 4,6-*O*-benzylidene-2,3-dibromo-2,3-dideoxy-α-D-altropyranoside undergoes elimination of the elements of hydrogen bromide to give a 90% yield of crystalline methyl 4,6-*O*-benzylidene-2-bromo-2,3-dideoxy-α-D-*threo*-hex-3-enopyranoside.

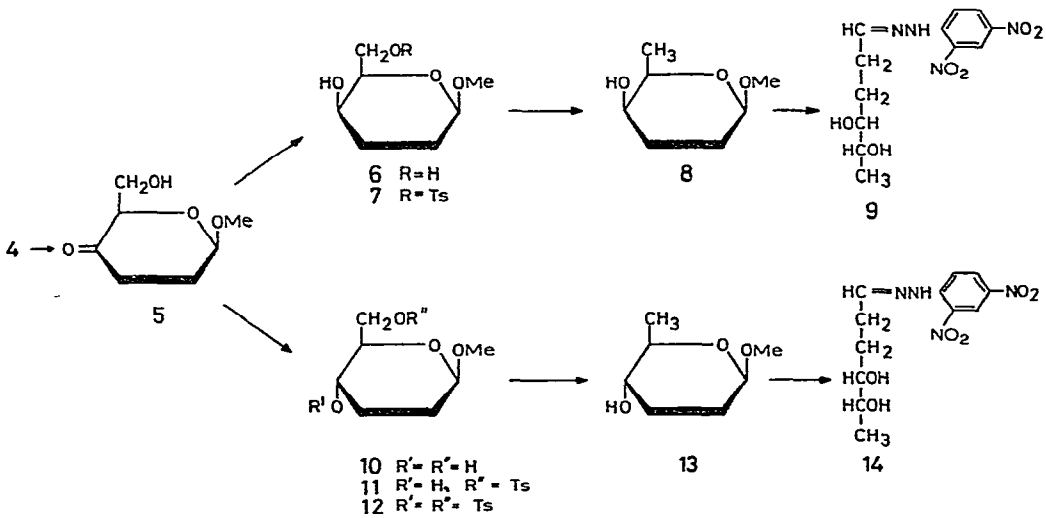
Treatment of compound **2** with dilute hydrochloric acid in acetone at reflux temperature resulted in de-*O*-benzylidenation and elimination of water, to afford, in 71% yield, a hexopyranoside containing an α,β-unsaturated ketone grouping, namely, methyl 2,3-dideoxy-β-D-*glycero*-hex-2-enopyranosid-4-ulose (**4**). A higher yield of compound **4** could be obtained by using the 2-*O*-acetyl derivative (**3**) in the acid-catalyzed reaction. Very recently, the synthesis of some other alkyl 2,3-dideoxy-2-enopyranosid-4-uloses has been reported[4]. There is considerable interest in such compounds because of their potential utility as intermediates in the synthesis of other sugar derivatives, such as deoxy, branched-chain, and aminodeoxy sugars of biological significance.

The structure assigned to compound **4** is completely in accord with the ultraviolet (u.v.) and nuclear magnetic resonance (n.m.r.) spectra obtained for it. The n.m.r. spectrum is very similar to that reported[4b] for ethyl 2,3-dideoxy-α-D-*erythro*-hex-2-enopyranosid-4-ulose. In the spectrum of that compound, however, the signal for H-1 appears as a doublet devoid of any secondary splitting, whereas, in the

spectrum of compound **4**, H-1 shows splittings of 2.2 and 1.8 Hz with H-2 and H-3, respectively; these values are consistent with a *quasi*-axial orientation of H-1 in compound **4** in the *H1* conformation[5].

Two examples of the synthetic utility of compound **4** are provided by its facile conversion into methyl 2,3,6-trideoxy-β-D-*threo*-hexopyranoside (methyl β-D-rhodinoside, **8**) and methyl 2,3,6-trideoxy-β-D-*erythro*-hexopyranoside (methyl β-D-amicetoside, **13**). The L enantiomer of the parent sugar of **8**, rhodinose, has been found in the antibiotics rhodomycin[6] and streptolydigin[7]; a synthesis of the D enantiomer, which substantiated the assignment of the *threo* configuration, has been reported[8]. The parent sugar of **13**, namely, amicetose, is a constituent of the antibiotic amicetin[9]; syntheses of this trideoxyhexose have also been reported[8,10].

Hydrogenation of methyl 2,3-dideoxy-β-D-*glycero*-hex-2-enopyranosid-4-ulose (**4**) over palladium black, in ethanol, gave, after 2 days, mainly methyl 2,3-dideoxy-β-D-*glycero*-hexopyranosid-4-ulose (**5**); the presence of several other components was, however, revealed by t.l.c., and the saturated ketone **5** was isolated in only 45% yield. When a W-4 Raney nickel catalyst was used, compound **5** was obtained after 30 min in 72% yield. Hydrogenation of compound **5** over W-4 Raney nickel catalyst for 3 days resulted in ~50% conversion into an ~9:1 mixture of methyl 2,3-dideoxy-β-D-*threo*-hexopyranoside (**6**) and its D-*erythro* isomer (**10**). The factors controlling the stereoisomeric composition of the products obtained by catalytic hydrogenation of substituted cyclohexanones have been studied[11], and the preponderance of compound **6** is in accord with that work. The structures of compounds **6** and **10** remained equivocal at this stage, but were proved by the further reactions of the compounds.



Treatment of compound **6** with 1.1 molar proportions of *p*-toluenesulfonyl chloride gave mainly the 6-*O*-*p*-tolylsulfonyl derivative **7**, together with a small proportion of a component that migrated faster in t.l.c., presumably the 4,6-di-*O*-*p*-tolylsulfonyl derivative. Desulfonyloxylation of **7** with lithium aluminum hydride in

tetrahydrofuran afforded the desired methyl β-D-rhodinoside (**8**) as a chromatographically homogeneous syrup. Treatment of the glycoside **8** with (2,4-dinitrophenyl)hydrazine in 2M hydrochloric acid gave crystalline 2,3,6-trideoxy-D-*threo*-hexose (2,4-dinitrophenyl)hydrazone (**9**), whose physical constants were in close agreement with literature[8] values.

Reduction of compound **5** with sodium borohydride gave methyl 2,3-dideoxy-β-D-*erythro*-hexopyranoside (**10**) and its D-*threo* isomer (**6**) in the ratio of 2:1. The rest of the route used for the preparation of methyl β-amicetoside (**13**) was the same as that just described for the conversion of compound **6** into methyl β-D-rhodinoside (**8**); treatment of syrupy compound **10** with 1.1 molar proportions of *p*-toluenesulfonyl chloride gave crystalline methyl 2,3-dideoxy-6-*O*-*p*-tolylsulfonyl-β-D-*erythro*-hexopyranoside (**11**) which, on desulfonyloxylation with lithium aluminum hydride in tetrahydrofuran, afforded methyl β-amicetoside (**13**). Compound **13** yielded crystalline 2,3,6-trideoxy-D-*erythro*-hexose (2,4-dinitrophenyl)hydrazone (**14**), whose physical constants were in close agreement with those reported[9,10] previously for this compound.

The synthesis of compounds **8** and **13** is of further interest, as oxidation of either compound to the 4-ketone leads to other naturally occurring sugars or their enantiomers. Very recently, for example, a new sugar called cinerulose A has been isolated from the anthracycline antibiotic cinerubin A, and shown to have the structure of 2,3,6-trideoxy-L-*glycero*-hexopyranos-4-ulose[12]. A 2,3,6-trideoxyhexopyranos-4-ulose has also been isolated from a basic macrolide antibiotic[13]. Albano and Horton[14] have utilized methyl 2,3,6-trideoxy-α-D-*glycero*-hexopyranosid-4-ulose in the synthesis of 2,3,4,6-tetradeoxy-4-(dimethylamino)-D-*erythro*-hexose (forosamine) and its D-*threo* epimer by way of the oxime of the 4-ketone; the D-*threo* isomer has the structure of ossamine, a component of ossamycin[15]. The work of Albano and Horton[14] also includes the preparation of the D-enantiomer of tolyposamine, a component of tolypomycin Y; tolyposamine has been shown to be 4-amino-2,3,4,6-tetradeoxy-L-*erythro*-hexose[16].

EXPERIMENTAL

General. — Melting points were determined on a Fisher–Johns melting-point apparatus and are uncorrected. Optical rotations were measured with a Perkin–Elmer Model 141 automatic polarimeter at 23 ±2°. I.r. spectra were recorded with a Beckman IR5A spectrophotometer. N.m.r. spectra were recorded at 60 MHz in chloroform-*d* with tetramethylsilane as the internal standard. U.v. spectra were recorded with a Unicam SP 800B spectrophotometer. T.l.c. was performed with Silica Gel G as the adsorbent; the developed plates were air-dried, sprayed with 5% ethanolic sulfuric acid, and heated at about 150°. The term "petroleum ether" refers to the fraction of b.p. 60–80°.

Reaction of methyl 4,6-O-benzylidene-3-chloro-3-deoxy-β-D-allopyranoside (**1**) *with sodium azide.* — Compound **1** was treated with sodium azide in dry *N*,*N*-di-

methylformamide at ~130° as described previously[1]. After 1 h, t.l.c. with 2:1 (v/v) ether–petroleum ether showed the presence of only two components, R_F 0.30 and 0.44; the starting material **1** has R_F 0.22 in this solvent. The faster-moving component was shown to be methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside, and the slower-moving, methyl 4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**2**), by the work described next.

The two components were isolated as a crystalline mixture which was treated with acetic anhydride–pyridine; the mixture of products was isolated in the usual way. Fractional recrystallization yielded, as before[1], methyl 2-*O*-acetyl-3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside and methyl 2-*O*-acetyl-4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**3**). The 3-azido-3-deoxy sugar **3** was treated with sodium methoxide in order to hydrolyze the acetate group; t.l.c. then showed the presence of a major component having R_F 0.44 and a trace of a component having R_F 0.30, the same mobilities as observed for the original two components produced by treatment of compound **1** with sodium azide. An authentic sample of methyl 4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**2**) (prepared as described in the following experimental procedure) was found to have R_F 0.30; the component having R_F 0.44 was, therefore, methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside*.

The products of the reaction of compound **1** with sodium azide were also examined by t.l.c. in the solvent used by other investigators[2] for this purpose [20:6:1 (v/v) chloroform–2,2,4-trimethylpentane–methanol]. The presence of two components was again detected; the slower-moving component was methyl 4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**2**), and the faster was methyl 3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside. In this solvent, however, the starting material **1** migrates at essentially the same rate as the unsaturated derivative **2**, a fact that presumably caused these investigators[2] to overlook the presence of the unsaturated derivative and to conclude that the displacement with sodium azide was very slow.

*Improved procedure for preparation of methyl 4,6-*O*-benzylidene-β-*D-erythro-*hex-3-enopyranoside* (**2**) *and its 2-acetate* **3**. — A solution of compound **1** (12.6 g) in dry tetrahydrofuran (500 ml) containing sodium benzoate (12 g) was boiled for 2 h under reflux. The cooled suspension was filtered, and the filtrate was evaporated to dryness. The residue was extracted with chloroform, and the extract was washed with water, dried (magnesium sulfate), and evaporated to dryness. Crystallization of the product from chloroform–petroleum ether gave compound **2**, yield 8.8 g (85%); m.p. 134–135°, $[\alpha]_D$ −43.3° (*c* 1.58, chloroform); λ_{max}^{Nujol} 5.9 μm (C=C); n.m.r. data:

*Evidently, a small amount of elimination, as well as de-*O*-acetylation, occurred during treatment of methyl 2-*O*-acetyl-3-azido-4,6-*O*-benzylidene-3-deoxy-β-D-glucopyranoside with sodium methoxide. The possibility that, during the acetylation of the original mixture produced by treatment of compound **1** with sodium azide, some elimination from this 3-azido-3-deoxy sugar occurred, to give methyl 2-*O*-acetyl-4,6-*O*-benzylidene-β-D-*erythro*-hex-3-enopyranoside (**3**), was investigated by keeping the 3-azido-3-deoxy sugar for the same period of time in pyridine; the presence of compound **3** was not observed by t.l.c. with 1:1 (v/v) ether–petroleum ether.

τ 2.38–2.8 (5 protons, aromatic H), 4.43 (1-proton singlet, benzylidene-methine H), 4.55–4.7 (1-proton multiplet, vinylic H), 5.55 (1-proton doublet, $J_{1,2}$ 6 Hz, H-1), and 6.45 (3-proton singlet, OMe).

Anal. Calc. for $C_{14}H_{16}O_5$: C, 63.6; H, 6.1. Found: C, 63.4; H, 6.1.

A solution of compound **2** (6 g) in pyridine (12 ml) and acetic anhydride (4.9 ml) was kept for 7 h at room temperature. The mixture was poured into water, and the product was isolated in the usual way. Crystallization from chloroform–petroleum ether gave compound **3**, yield 5.6 g (80%), having the physical constants reported previously[1], namely, m.p. 130–131°, $[\alpha]_D$ −164° (*c* 1.05, chloroform).

*Methyl 2,3-dideoxy-β-*D-glycero-*hex-2-enopyranosid-4-ulose* (**4**). — A solution of compound **2** (4 g) in acetone (60 ml) and 0.05M hydrochloric acid (40 ml) was boiled for 30 min under reflux. The solution was cooled, and made neutral with barium carbonate, and the mixture was filtered. The acetone was evaporated, and the resulting aqueous solution was washed with petroleum ether, and then extracted with chloroform; the extracts were washed with a small amount of water (to remove material that did not migrate in t.l.c.), dried (magnesium sulfate), and evaporated, to give compound **4** as a chromatographically homogeneous syrup, yield 1.7 g (71%); R_F 0.67 [1:9 (v/v) methanol–ethyl acetate]; $[\alpha]_D$ −14.3° (*c* 0.84, ethanol); λ_{max}^{water} 215 nm (ε 7,000); n.m.r. data: τ 3.15 (1-proton quartet, $J_{2,3}$ 10 Hz and $J_{1,2}$ 2.2 Hz, H-2), 3.85 (1-proton quartet, $J_{2,3}$ 10 Hz and $J_{1,3}$ 1.8 Hz, H-3), 4.75 (1-proton quartet, $J_{1,2}$ 2.2 Hz and $J_{1,3}$ 1.8 Hz, H-1), 5.73 (1-proton triplet, $J_{5,6}$ 4 Hz, H-5), 6.09 (2-proton doublet, H-6), and 6.41 (3-proton singlet, OMe).

Anal. Calc. for $C_7H_{10}O_4$: C, 53.2; H, 6.3. Found: C, 53.1; H, 6.4.

The foregoing procedure was repeated with methyl 2-*O*-acetyl-4,6-*O*-benzylidene-*β*-D-*erythro*-hex-3-enopyranoside (**3**, 6 g). In this experiment, the formation of only one new component was observed by t.l.c. Compound **4** was isolated as a syrup, yield 5.6 g (80%).

*Methyl 2,3-dideoxy-β-*D-glycero-*hexopyranosid-4-ulose* (**5**). — A mixture of compound **4** (750 mg) and palladium black (100 mg) in ethanol (20 ml) was hydrogenated at a pressure of 40 lb. in.$^{-2}$ for 2 days at room temperature. T.l.c. with 1:9 (v/v) methanol–ethyl acetate showed the presence of one major component and several faster- and slower-moving components; the major component had the same mobility as the starting material **4**, but when the developed t.l.c. plate was sprayed with ethanolic sulfuric acid and heated, it charred faster than **4** and gave a different color. The catalyst was filtered off, and the filtrate was evaporated to a syrup. The major component, namely **5**, was separated by column chromatography on silica gel by elution with the same solvent as used for t.l.c., and isolated as a syrup, yield 340 mg (45%); $[\alpha]_D$ −63.2° (*c* 1.3, chloroform); n.m.r. data: τ 4.99–5.2 (1-proton multiplet, H-1), 5.88 (1-proton triplet, $J_{5,6}$ 4 Hz, H-5), 6.17 (2-proton doublet, H-6), 6.45 (3-proton singlet, OMe), and 7.26–7.96 (4-protons, H-2,2′ and H-3,3′).

Anal. Calc. for $C_7H_{12}O_4$: C, 52.5; H, 7.5. Found: C, 52.6; H, 7.5.

Compound **4** (3 g) was also hydrogenated over W-4 Raney nickel catalyst[17] in ethanol at room temperature and a pressure of 40 lb. in^{-2}; after 30 min, the formation

of only the saturated ketone **5** was revealed by t.l.c. Compound **5** was isolated as a syrup, yield 2.2 g (72%).

*Methyl 2,3-dideoxy-β-*D-threo-*hexopyranoside* (**6**). — A solution of compound **5** (500 mg) in ethanol containing W-4 Raney nickel catalyst was treated with hydrogen at a pressure of 40 lb. in.$^{-2}$. The progress of the reaction was monitored by t.l.c. with 1:19 (v/v) methanol–ethyl acetate; the formation of a new component having R_F 0.31 was revealed first, and, after 3 days, there was ~50% conversion into two components, R_F 0.31 and 0.42, in the ratio of ~9:1. The suspension was filtered free of catalyst, the filtrate was evaporated to a syrup, and the two components were separated by column chromatography on silica gel, with 1:9 (v/v) methanol–ethyl acetate as eluant. Compound **6** was obtained as a syrup, yield 220 mg (44%); $[\alpha]_D$ −115.3° (*c* 0.60, chloroform); R_F 0.31. The component having R_F 0.42 was the D-*erythro* isomer (**10**).

*Methyl 2,3-dideoxy-6-*O-p-*tolylsulfonyl-β-*D-threo-*hexopyranoside* (**7**). — Compound **6** (160 mg) in pyridine (5 ml) was treated with *p*-toluenesulfonyl chloride (300 mg, 1.1 molar proportions) in pyridine (2 ml) below 0°. After the solution had been kept overnight at 5°, t.l.c. with 3:2 (v/v) ethyl acetate–petroleum ether showed the presence of a major component having R_F 0.38 (compound **7**) and a small proportion of a second component having R_F 0.7. The solution was poured into water (25 ml), and the mixture was extracted several times with chloroform. The extracts were combined, washed successively with M sulfuric acid, sodium hydrogen carbonate solution, and water, and evaporated to a syrup; this was chromatographed on silica gel, with 7:3 (v/v) ethyl acetate–petroleum ether as eluant, to yield crystalline compound **7**. Recrystallization from chloroform–petroleum ether gave **7** as needles, yield 220 mg (71%); m.p. 72–74°, $[\alpha]_D$ −59.3° (*c* 0.52, chloroform); n.m.r. data: τ 2.0–2.75 (4 protons, aromatic H), 6.5 (3-proton singlet, OMe), 7.5 (3-proton singlet, aromatic Me), and 7.6–8.5 (4 protons, H-2,2′ and H-3,3′).

Anal. Calc. for $C_{14}H_{20}O_6S$: C, 53.2; H, 6.3. Found: C, 53.4; H, 6.3.

*Methyl 2,3,6-trideoxy-β-*D-threo-*hexopyranoside* (*methyl β-*D-*rhodinoside*, **8**). — The 6-*O-p*-tolylsulfonyl derivative **7** (150 mg) was boiled for 2 h under reflux with lithium aluminum hydride (200 mg) in tetrahydrofuran (10 ml). Compound **8** was isolated in the usual way, to give a chromatographically homogeneous syrup, yield 35 mg (51%)*, $[\alpha]_D$ −40° (*c* 0.35, chloroform); R_F 0.25 [3:2 (v/v) ethyl acetate–petroleum ether].

*2,3,6-Trideoxy-*D-threo-*hexose* (*2,4-dinitrophenyl)hydrazone* (**9**). — To a solution of (2,4-dinitrophenyl)hydrazine (120 mg) in 2M hydrochloric acid (5.0 ml) was added a solution of syrupy **8** in 2M hydrochloric acid (2.5 ml); a crystalline precipitate separated within 10 min. The product was collected, and washed with a little water. Recrystallization from benzene gave pure **9**, m.p. 120–123°, $[\alpha]_D$ +12.9° (*c* 1.0, pyridine); lit.[8] m.p. 121–122°, $[\alpha]_D^{25}$ +13.7° (*c* 0.9, pyridine).

*Methyl 2,3-dideoxy-β-*D-erythro-*hexopyranoside* (**10**). — To a stirred solution of

*The desulfonyloxylated compounds (**8** and **13**) are quite highly volatile, so that some loss of product may occur during the isolation.

5 (500 mg) in methanol (10 ml) was added dropwise a solution of sodium borohydride (250 mg) in methanol (5 ml). After 4 h, t.l.c. [1:19 (v/v) methanol–ethyl acetate] showed the presence of two new components, R_F 0.31 and 0.42. To the mixture was added methanol containing a small proportion of acetic acid; the solution was evaporated to dryness, and the procedure was repeated several times. Chromatography of the resultant syrup on silica gel, with 1:9 (v/v) methanol–ethyl acetate as the eluant, afforded compound **10** as a syrup, yield 300 mg (60%), $[\alpha]_D$ −90.2° (*c* 1.0, chloroform); R_F 0.42. The component having R_F 0.31 was the D-*threo* isomer (**6**); it, too, was obtained as a syrup, yield 130 mg (30%).

*Methyl 2,3-dideoxy-6-*O-p-*tolylsulfonyl-β-*D-erythro-*hexopyranoside* (**11**). — Compound **10** (200 mg) in dry pyridine (5 ml) was treated with *p*-toluenesulfonyl chloride (370 mg, 1.1 molar proportions) in pyridine (2 ml) below 0°. After the solution had been kept overnight at 5°, t.l.c. showed the presence of one new component (compound **11**) and a small amount of starting material. A crystalline product was isolated in the usual way. Recrystallization from chloroform–petroleum ether gave the pure 6-*p*-toluenesulfonate **11**, yield 242 mg (62%); m.p. 95–96°, $[\alpha]_D$ −43.8° (*c* 1.1, chloroform); n.m.r. data: τ 2.08–2.8 (4 protons, aromatic H), 6.6 (3-proton singlet, OMe), 7.59 (3-proton singlet, aromatic Me), and 7.66–8.72 (4 protons, H-2,2′ and H-3,3′).

Anal. Calc. for $C_{14}H_{20}O_6S$: C, 53.2; H, 6.3. Found: C, 53.5; H, 6.2.

Compound **10** was also converted into the 4,6-di-*O*-*p*-tolylsulfonyl derivative **12**, in the following way. Compound **10** (45 mg) in dry pyridine (2 ml) was treated with *p*-toluenesulfonyl chloride in pyridine initially at 0°; more reagent (total 600 mg) was then added in portions during 2 days at room temperature. That the 6-*O*-*p*-tolylsulfonyl derivative **11** was formed first was revealed by t.l.c. with 2:1 (v/v) ethyl acetate–petroleum ether; it had R_F 0.41. This was followed by the formation of compound **12**, having R_F 0.6. Crystalline **12** was isolated in the usual way. Recrystallization from chloroform–petroleum ether gave pure **12**, yield 100 mg (76%); m.p. 136–138°; n.m.r. data: τ 2.1–2.85 (8 protons, aromatic H), 6.69 (3-proton singlet, OMe), 7.55 (6-proton singlet, aromatic Me), and 7.75–8.9 (4 protons, H-2,2′ and H-3,3′).

Anal. Calc. for $C_{21}H_{26}O_8S_2$: C, 54.8; H, 5.6. Found: C, 54.6; H, 5.8.

*Methyl 2,3,6-trideoxy-β-*D-erythro-*hexopyranoside* (*methyl β-*D-*amicetoside*, **13**). — The 6-*O*-*p*-tolylsulfonyl derivative **11** (200 mg) was boiled for 2 h under reflux with lithium aluminum hydride (250 mg) in tetrahydrofuran (10 ml). Compound **13** was isolated in the usual way, giving a chromatographically homogeneous syrup, yield 63 mg (68%)*, $[\alpha]_D$ −21.9° (*c* 0.82, chloroform); R_F 0.32 [3:2 (v/v) ethyl acetate–petroleum ether].

*2,3,6-Trideoxy-*D-erythro-*hexose* (*2,4-dinitrophenyl)hydrazone* (**14**). — To a solution of (2,4-dinitrophenyl)hydrazine (160 mg) in 2M hydrochloric acid (5.0 ml) was added a solution of syrupy **13** in 2M hydrochloric acid (2.5 ml). A crystalline precipitate separated immediately. The mixture was allowed to stand for 30 min at room temperature, and the precipitate was then collected, and washed with a little

water. Recrystallization from benzene gave pure **14**, m.p. 152–153°, $[\alpha]_D$ −9.0° (*c* 0.9, pyridine); lit.[9] m.p. 152–153°, $[\alpha]_D^{25}$ −10.0° (*c* 0.86, pyridine).

ACKNOWLEDGMENTS

The authors thank the National Research Council of Canada for financial support of this work, and Dr. B. T. Lawton for making some preliminary studies.

REFERENCES

1 B. T. LAWTON, W. A. SZAREK, AND J. K. N. JONES, *Chem. Commun.*, (1969) 787; *Carbohyd. Res.*, 15 (1970) 397.
2 S. HANESSIAN AND N. R. PLESSAS, *J. Org. Chem.*, 34 (1969) 1045.
3 E. L. ALBANO, D. HORTON, AND J. H. LAUTERBACH, *Chem. Commun.*, (1968) 357; *Carbohyd. Res.*, 9 (1969) 149.
4 (*a*) B. FRASER-REID, A. MCLEAN, AND E. W. USHERWOOD, *J. Amer. Chem. Soc.*, 91 (1969) 5392; (*b*) B. FRASER-REID, A. MCLEAN, E. W. USHERWOOD, AND M. YUNKER, *Can. J. Chem*, 48 (1970) 2877.
5 E. W. GARBISCH, *J. Amer. Chem. Soc.*, 86 (1964) 5561; R. J. FERRIER AND N. PRASAD, *J. Chem. Soc. (C)*, (1969) 581.
6 H. BROCKMANN AND T. WAEHNELDT, *Naturwissenschaften*, 50 (1963) 43; *Fortschr. Chem. Org. Naturstoffe*, 21 (1963) 121.
7 K. L. RINEHART, JR., AND D. B. BORDERS, *J. Amer. Chem. Soc.*, 85 (1963) 4037.
8 C. L. STEVENS, P. BLUMBERGS, AND D. L. WOOD, *J. Amer. Chem. Soc.*, 86 (1964) 3592.
9 C. L. STEVENS, K. NAGARAJAN, AND T. H. HASKELL, *J. Org. Chem.*, 27 (1962) 2991.
10 E. L. ALBANO AND D. HORTON, *J. Org. Chem.*, 34 (1969) 3519.
11 R. J. WICKER, *J. Chem. Soc.*, (1956) 2165.
12 W. KELLER-SCHIERLEIN AND W. RICHLE, *Chimia*, 24 (1970) 35.
13 T. SUZUKI, *Bull. Chem. Soc. Jap.*, 43 (1970) 292.
14 E. L. ALBANO AND D. HORTON, *Carbohyd. Res.*, 11 (1969) 485.
15 C. L. STEVENS, G. E. GUTOWSKI, C. P. BRYANT, R. P. GLINSKI, O. E. EDWARDS, AND G. M. SHARMA, *Tetrahedron Lett.*, (1969) 1181.
16 T. KISHI, S. HARADA, M. ASAI, M. MUROI, AND K. MIZUNO, *Tetrahedron Lett.*, (1969) 97.
17 A. A. PAVLIC AND H. ADKINS, *J. Amer. Chem. Soc.*, 68 (1946) 1471.