Aminonitrile of 4-methylbenzophenone IX. A solution of the iminium salt V (prepared from 38.0 g. of the corresponding imine) in 180 ml. of acetonitrile was added to a stirred solution of 33.0 g. of potassium cyanide in 300 ml. of water. An oil almost immediately separated from the solution. At the end of 30 min. the oil was taken up in ether and the extract washed with water. The residue obtained when the solvent was removed from the dried extract was distilled at 2.0 mm. to afford 38.6 g. (91% based on imine) of the extremely viscous colorless product, b.p. 158–160°.

A sample was redistilled at the same pressure, b.p. 157–159°. All attempts to crystallize this very pure sample failed.

Anal. Calcd. for $C_{17}H_{16}N_2$: C, 81.56; H, 7.25; N, 11.19. Found: C, 81.31; H, 7.41; N, 10.94.

Reaction of the aminonitrile IX *with acids. (a) d-10-Camphorsulfonic acid.* A solution of 20.0 g. (0.08 mole) of the aminonitrile and 8.5 g. (0.037 mole) of the acid in 30 ml. of ethanol was warmed at reflux for 1 hr. The hot solution was then poured into water and the resulting oil taken into ether. The ethereal solution was washed with water, dried by percolation through sodium sulfate, and evaporated *in vacuo.* The residual oil was fractionally distilled at 2.2 mm. to afford 5.78 g. of 4-methylbenzophenone b.p. 147–150°, 5.06 g. of a middle cut b.p. 150–155°, and 5.03 g. of recovered starting material. The first cut was recrystallized first from ethanol and then from low boiling (30–60°) petroleum ether to afford the ketone of m.p. 54–55°, mixed melting point with an authentic smple, 54–55°.

The infrared spectrum of the high boiling sample was superimposable on one of the starting aminonitrile.

(*b*) *Picric acid.* A small sample of the aminonitrile was dissolved in a saturated ethanolic solution of picric acid. In 2 hr. large crystals slowly formed. The melting point of this picrate (158-160°) was not depressed on admixture with authentic sample of the picrate of dimethylamine.

Reaction of the ternary salt of benzophenone I *with potassio phenylacetonitrile.* A solution of 0.05 mole of potassium amide was prepared from 1.95 g. of the metal in 200 ml. of liquid ammonia. To this there was then added a solution of 5.85 g. (0.05 mole) of phenylacetonitrile in 50 ml. of tetrahydrofuran. An additional 150 ml. of tetrahydrofuran was then added to the green solution and the ammonia allowed to evaporate by bringing the solution to the reflux temperature of tetrahydrofuran. The tetrahydrofuran was allowed to distill over until free of the odor of ammonia. The salt (17.6 g. 0.05 mole) was then added from a flask through a piece of Gooch tubing. A transitory lavender color accompanied the exothermic reaction. At the end of an additional 1 hr. stirring, the solid was removed by filtration and washed with ether. The volume of the filtrate was reduced to about 50 ml. *in vacuo,* and this solution treated with ether. This solution was washed once with water and then extracted with concentrated hydrochloric acid. The acid solution was then made strongly alkaline with potassium hydroxide pellets, and the resulting solid collected by filtration. The crude product (13.5 g.) was recrystallized from hexane to afford 10.6 g. (62%) of colorless crystals of X, m.p. 132–140°. Since this product apparently decomposes on simply heating in ethanol, no picrate was prepared. When a sample was treated with an excess of methyl iodide in acetonitrile for 24 hr. the only isolable product was recovered starting material (53%).

A sample of the β-aminonitrile was recrystallized from cyclohexane to a constant m.p. of 142–144°.

Anal. Calcd. for $C_{23}H_{22}N_2$: C, 84,62; H, 6.79; N, 8.58. Found: C, 84.74, H, 6.75; N, 8.47

Reaction of the ternary salt I *with water.* One gram of the salt prepared from benzophenone was added to a small amount of water covered by ether. Within 20 min. the solid was completely in solution. The ethereal layer was separated, washed with water, and taken to dryness. Upon scratching, the residue afforded 0.45 g. (87%) of benzophenone, m.p. 45–46.5°; mixed melting point with authentic sample, 45–46°.

Reaction of the ternary salt I *with ammonia.* Two grams of the solid was added to 50 ml. of liquid ammonia in a potassium hydroxide drying tube protected flask. A white solid formed which slowly went into solution. The oil which remained when the ammonia had evaporated was washed with ether. The residue from the ether extracts (λ, 2.9μ, 3.0μ and 6.0μ) formed crystals from 10 ml. of dilute hydrochloric acid. Enough water (20 ml.) was added to produce a solution. On further standing, 0.92 g. (89%) of benzophenone, m.p. 45–46°, was deposited from the solution.

DURHAM, N. C.

[CONTRIBUTION FROM THE NATIONAL RESEARCH COUNCIL OF CANADA, PRAIRIE REGIONAL LABORATORY]

Hydrogenolysis of Carbohydrates. VI. Cyclic Ketals and Related Compounds

P. A. J. GORIN

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Some alkylidene-sugar derivatives have been hydrogenolyzed using copper chromite catalyst in dioxane. Carbon-oxygen bonds in the 1,3-dioxolane rings of carbons-5 and -6 of 1,2-5,6-di-*O*-isopropylidene- and 1,2-5,6-di-*O*-cyclohexylidene-D-glucofuranoses being cleaved. *O*-Isopropylidene groups attached to the reducing center of a sugar molecule, however, do not hydrogenolyze to *O*-isopropyl derivatives in a similar manner. The 1,3-dioxolane ring of 1,6-anhydro-D-glucopyranose is split, reductive fission of the carbon-2 hydroxyl group also taking place. The inversion of configuration of hydroxyl groups under hydrogenolysis conditions is considered.

In the course of investigating possible applications of hydrogenolysis reactions to carbohydrate synthesis, various types of sugar derivatives are being investigated as substrates.[1] In a previous publication, 1,2-*O*-isopropylidene-D-glucofuranose was hydrogenated at 180° in dioxane using Adkin's copper chromite catalyst.[2] The main products were 1,2-*O*-isopropylidene-L-idofuranose and a crystalline 3,4-dideoxy-hexitol. In the present paper, the reactions of 1,2,5,6-di-*O*-isopropylidene- and 1,2-5,6-di-*O*-cyclohexylidene-D-glucofuranoses, 1,6-anhydro-D-

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(1) Presented at the 134th meeting of the American Chemical Society, Chicago, September 1958; issued as N.R.C. No. 5013.

(2) P. A. J. Gorin and A. S. Perlin, *Can. J. Chem.*, **36,** 661 (1958).

glucopyranose.1 ,2-*O*-Isopropylidene-D-xylofuranose and 1,2-*O*-isopropylidene-D-fructopyranose under hydrogenolysis conditions are described.

Unlike the monosubstituted derivative, di-*O*-isopropylidene glucose was not affected at 180°, unchanged starting material being completely recovered. At 200°, however, degradation occurred and on acid hydrolysis of a portion of the reaction product, two reducing spots in addition to glucose were detected on a paper chromatogram using the *p*-anisidine hydrochloride spray.[3] Also, at least two other components, nonreducing to the *p*-anisidine spray, were detected on development with ammoniacal silver nitrate[4]; these minor products were not examined further. After crystallization of unchanged di-*O*-isopropylidene glucose the material in the mother liquor was hydrolyzed with acid and the reducing sugars produced were isolated by cellulose column chromatography.[5] The yields obtained were 7.5% (component having R_{Rh} 1.7) and 6.1% (R_{Rh} 2.0).[6]

The compound with R_{Rh} 1.7 was crystalline and a crystalline acetate and phenylosazone were derived. From physical and chemical determinations (see Experimental section) and by comparison with an authentic specimen, the sugar was shown to be 6-*O*-isopropyl-D-glucose. The other aldose, R_{Rh} 2.0, did not crystallize and was reduced with sodium borohydride[7] to the corresponding alcohol which was also a sirup, but gave a crystalline pentaacetate identical with synthetic penta-*O*-acetyl-6-*O*-isopropyl-L-iditol. The hydrogenolysis product was therefore 6-*O*-isopropyl-L-idose which must have been formed *via* inversion of the hydroxyl-group at C-5 (compare Ref. 2). Under more vigorous hydrogenolysis conditions (230–250°), 1,2-5,6-di-*O*-isopropylidene-D-glucofuranose was degraded to a unidentified mobile sirup.

A pattern of hydrogenolysis similar to that of 1,2-5,6-di-*O*-isopropylidene-D-glucofuranose at 200° was exhibited by 1,2-5,6-di-*O*-cyclohexylidene-D-glucofuranose. The products obtained after acid hydrolysis were crystalline 6-*O*-cyclohexyl-D-glucose identical to synthesized material and sirupy 6-*O*-cyclohexyl-L-idose characterized by conversion on sodium borohydride reduction to known 6-*O*-cyclohexyl-L-iditol. The yields of the two aldoses were lower than those of the *O*-isopropyl analogs.

The mode of hydrogenolysis of these 1,2-5,6-di-*O*-alkylidene-D-glucofuranoses appears to be a scission of the alkyl carbon-oxygen bond adjacent to C-5 to afford the 6-*O*-alkyl-1,2-*O*-isopropylidene-D-glucofuranose. The possibility of concomitant formation of 5-*O*-alkyl-derivatives by reductive cleavage of the bond adjacent to C-6 exists since the mixture of products may not have been separated completely. This cleavage of a 1,3-dioxolane ring is, perhaps, not surprising since some types of furan rings can be readily broken under similar hydrogenation conditions.[8] The inversion of configuration of hydroxyl groups on carbon atoms is a common feature of the action of copper chromite[2,9,10] and Raney nickel[11] on carbohydrates under hydrogenation conditions. It is suggested that this inversion is due to dehydrogenation to a ketone followed by reduction to the two possible stereoisomeric alcohols. Dunbar and Arnold[12] have shown that copper chromite dehydrogenates primary and secondary alcohols at 300–325° to aldehydes and ketones, respectively. Presumably, under the present conditions the dehydrogenating action of the catalyst is only lessened and not eliminated completely.

A similar type of reaction occurred when 1,6-anhydro-D-glucopyranose was hydrogenolyzed at 180°, no reaction occurring at 150°. Scission of the 1,3-dioxolane ring afforded 1,2-dihydro-D-glucal (at least 14.2%) and a smaller proportion of 1,2-dihydro-D-altral (5.1%) formed by hydroxyl-group inversion at C-3. The 1,6-*O*-linkage was, therefore, cleaved at the C-1 to oxygen bond with reduction of the hydroxyl group at C-2, no 1,5-anhydro-D-sorbitol being produced in the reaction. Under identical hydrogenation conditions dihydro-D-glucal is isomerized to dihydro-D-altral in 17% yield.[13]

Hydrogenolysis of 1,2-ketals was not detected with 1,2-*O*-isopropylidene- and 1,2-5,6-di-*O*-isopropylidene-D-glucofuranoses. Lack of reactivity was shown further by using 1,2-*O*-isopropylidene-D-fructopyranose (at 180°) and 1,2-*O*-isopropylidene-D-xylofuranose (at 200°) as substrates. In none of these instances were any derived 2-*O*-isopropyl polyols or isopropyl glycosides, formed by C-O bond scission, detected. In the last two cases, however, considerable hydroxyl-group inversion took place, three ketohexoses being detected chromatographically with urea oxalate spray on acid hydrolysis of the reaction product in the case of 1,2-*O*-isopropylidene-D-fructopyranose. 1,2-*O*-Isopropylidene-D-xylofuranose appeared to furnish a mixture of D-xylose (58%) and ribose (42%) on hydrogenation followed by acid hydrolysis. Thus extensive inversion at C-3 took place.

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6-*O*-Isopropyl-D-glucose, 6-*O*-cyclohexyl-D-glucose, penta-*O*-acetyl-6-*O*-isopropyl-L-iditol, and 6-*O*-cyclohexyl-L-iditol were synthesized as crystalline reference compounds in order to identify the hydrogenolysis products from the di-*O*-alkylidene-D-glucofuranoses. The steps used in the synthesis of these materials are outlined in the Experimental section. Dihydro-D-altral was synthesized from D-altrose according to general reaction procedures. The series of reactions, during which none of the intermediates were obtained crystalline, afforded a complex mixture which was fractionated on a cellulose column to give, in poor yield, dihydro-D-altral. The synthetic material was identical with a substance proved to be a 1,2-dihydro-hexital by von Rudloff and Tulloch, who obtained it by hydrogenolysis of α-methyl-D-glucopyranoside.[9] Although the yield of dihydro-D-altral from D-altrose was low the hydroxyl configuration was therefore established.

EXPERIMENTAL

All optical rotations were measured at 27°. Evaporations were carried out under reduced pressure using a bath temperature of 50°. Solvents used were butanol-ethanol-water (40:11:19 v./v.) for paper chromatograms and benzene-ethanol-water (500:50:1 v./v.) for cellulose column fractionations. Sprays used for developing paper chromatograms were *p*-anisidine hydrochloride and ammoniacal silver nitrate.

*Hydrogenolysis of 1,2-5,6-di-O-isopropylidene-*D*-glucofuranose.* Trial hydrogenations of di-*O*-isopropylidene glucose using copper chromite catalyst and dioxane as solvent indicated that under hydrogen pressures of 1000–2000 p.s.i. the substrate was unaffected at 180° and extensively degraded at 230–250°.

Di-*O*-isopropylidene glucose (150 g.) was dissolved in dioxane (2.5 l.) containing copper chromite catalyst (50 g.) and heated with shaking at 200° for 6 hr. under a hydrogen pressure of 1000–1500 p.s.i. The mixture was cooled, filtered, and evaporated to a sirup which crystallized from chloroform-light petroleum (b.p. 30–60°). The uncrystallizable residue (96 g.) obtained on evaporation of the mother liquor was dissolved in 0.1*N* sulfuric acid (500 cc) and the solution heated at 100° for 1 hr. The hydrolyzate was neutralized ($BaCO_3$), filtered, and evaporated to a sirup (55 g.) which afforded, as well as material corresponding to glucose, spots with R_{Rh} 1.7, 2.0, 2.2, and 2.4 on a paper chromatogram, the first two being reducing and the latter two nonreducing. The mixture was fractionated on cellulose columns to yield the material having R_{Rh} 1.7 (9.6 g.) and the compound having R_{Rh} 2.0 (7.8 g.). The nonreducing materials with R_{Rh} 2.2 and 2.4 (1.8 g.) were not further examined.

(*a*) *R_{Rh} 1.7 Fraction.* The fraction crystallized and the material was recrystallized twice from methanol-ether and then from acetone and had m.p. 128–130° undepressed on mixing with authentic 6-*O*-isopropyl-D-glucose and $[\alpha]_D$ $+83° \rightarrow +47°$ (constant value: *c* 1.0, H_2O). Calculated for $C_9H_{18}O_6$: C, 48.6%; H, 8.2%. Found: C, 48.7%; H, 8.3%. The x-ray diffraction patterns of this material and 6-*O*-isopropyl-D-glucose were identical. The aldose had an alkaline iodine equivalent corresponding to a molecular weight of 218[14] and based on this figure and lead tetraacetate consumptions were: 1.62, 1.93, 1.99, and 2.08 moles after 3, 5, 11, and 26 min., respectively, thus indicating 5- or 6-substitution in the molecule.[15] The compound absorbed in the infrared in regions corresponding to isopropyl-substitution[16] and when the sugar was dealkylated[17] by heating for 10 min. in 42% hydrobromic acid at 100° the product, after neutralization (Ag_2CO_3) and evaporation, ran at the same speed as glucose on a paper chromatogram.

The derived phenylosazone of the sugar was prepared by heating the aldose (52 mg.) at 80° for 3 hr. in water (3 cc.) containing phenylhydrazine (0.10 cc.) and acetic acid (0.2 cc.). The yellow precipitate which formed on cooling was filtered off and recrystallized twice from methanol-benzene. It had m.p. 169–170° and $[\alpha]_D$ $-107° \rightarrow -67°$ (constant value: *c*, 0.7, pyridine). The 6-*O*-isopropyl-D-glucose phenylosazone had a molecular weight of 391 measured by the method of Barry, McCormick, and Mitchell.[18] It consumed 2.0 moles of sodium periodate after 15 and 30 min.[19] and produced 1 mole of formic acid when oxidized by lead tetraacetate in 90% acetic acid containing potassium acetate[20] thus proving 6-substitution. Calculated for $C_{21}H_{28}O_4N_4$: C, 63.0%; H, 7.1%. Found: C, 63.0%; H, 7.0%.

6-*O*-Isopropyl-D-glucose (30 mg.) was heated for 1 hr at 100° in acetic anhydride (1 cc.) containing sodium acetate (30 mg.). After adding to an excess of ice water, the mixture was left for 3 hr. and then extracted with benzene. The extract was washed twice with water and evaporated to a sirup which crystallized. Two crystallizations from light petroleum (b.p. 30–60°) afforded fine needles (15 mg.) of 1,2,3,4-tetra-*O*-acetyl-6-*O*-isopropyl-D-glucose with m.p. 124–125° and $[\alpha]_D$ +11° (*c*, 0.5, 2,4-lutidine).

Anal. Calcd. for $C_{17}H_{26}O_{10}$: C, 52.3%; H, 6.7%. Found: C, 52.3%; H, 6.6%.

(*b*) *R_{Rh} 2.0 Fraction.* The sugar had $[\alpha]_D$ −13° (*c*, 2.1, H_2O) and could not be induced to crystallize. The compound (2.60 g.) was reduced in 3 hr. by an aqueous solution of sodium borohydride (1.20 g. in 200 cc.). Excess reagent was destroyed with acetic acid, the solution treated with Amberlite IR120, and evaporated to dryness. Repeated evaporations from the residue with methanol yielded a sirup (2.10 g.) containing 6-*O*-isopropyl-L-iditol.

The polyol (0.97 g.) was acetylated as described previously: the acetate crystallized and was recrystallized 3 times from ether-light petroleum (b.p. 30–60°). The pentaacetate had m.p. 87–88° and $[\alpha]_D$ −7.5° (*c*, 1.0 2,4-lutidine), the melting point was undepressed on mixing with penta-*O*-acetyl-6-*O*-isopropyl-L-iditol.

Anal. Calcd. for $C_{19}H_{30}O_{11}$: C, 52.5%; H, 7.0%. Found: C, 52.3%; H, 6.9%.

The x-ray diffraction pattern of the product was identical with that of an authentic specimen.

*Hydrogenolysis of 1,2-5,6-di-O-cyclohexylidene-*D*-glucofuranose.* Using the same hydrogenolysis and hydrolysis conditions as for the 1,2-5,6-di-*O*-isopropylidene-derivative, the cyclohexylidene-compound (25.0 g.) was converted to glucose and reducing materials of R_f's 0.58 and 0.70 on a paper chromatogram. The mixture was extracted continuously by chloroform from water. After a short time, the chloroform extract (0.90 gm.) contained mainly the compound with R_f 0.70 with a trace of the material with R_f 0.58 as well as some nonreducing material of high R_f. On prolonged extraction, the slower moving compound was obtained (0.53 g.). Fractionation on a cellulose column of

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the initial chloroform extract yielded 0.36 g. of the faster and 71 mg. of slower material. The overall yields corresponded to 2.4% and 1.4%, respectively, for the R_f 0.58 and 0.70 compounds.

(*a*) *R_f 0.58 Fraction.* The fraction crystallized and afforded 6-*O*-cyclohexyl-D-glucose, after two recrystallizations from acetone, which softened at 106° and melted at 115–117° (undepressed with authentic crystals) and had $[\alpha]_D$ +60° → +45° (constant value: *c*, 1.0 H_2O). Calculated for $2C_{12}H_{22}O_6.H_2O$: C, 53.1%; H, 8.5%. Found: C, 52.9%, H, 8.5%. Its x-ray diffraction pattern was identical to that of the known material.

(*b*) *R_f 0.70 Fraction.* The sirupy product did not crystallize and a portion (144 mg.) was dissolved in water (10 cc.) containing sodium borohydride (30 mg.). After 3 hr. the mixture was worked up as the earlier sodium borohydride reduction. The sirup (122 mg.), thus formed, deposited crystals from acetone and these were recrystallized twice from acetone. The melting point of the product was 78–80° not lowered on mixing with 6-*O*-*cyclo*hexyl-L-iditol, and had $[\alpha]_D$ −5° (*c*, 1.1 sat. borax).

Anal. Calcd. for $C_{12}H_{24}O_6$: C, 54.5%; H, 9.2%. Found: C, 54.7%; H, 9.4%.

6-O-Cyclohexyl-L-iditol, obtained by hydrogenolysis and borohydride reduction, gave an x-ray diffraction pattern identical with that of the authentic compound.

Hydrogenolysis of 1,6-anhydro-D-glucopyranose. 1,6-Anhydro-D-glucopyranose (3.0 g.) was hydrogenated for 6 hr. at 180° in dioxane (150 cc.) containing copper chromite (1.0 g.) using a pressure of 1000–1500 p.s.i. After filtration and evaporation the resulting sirup (2.62 g.) was examined on a paper chromatogram using ammoniacal silver nitrate as spray. The main spot had R_{Rh} 1.3 with smaller amounts at R_{Rh} 1.4, 1.8 and the starting material (R_{Rh} 1.1).

The mixture was fractionated on a cellulose column and the component having R_{Rh} 1.4 (0.14 gm.) crystallized and was recrystallized three times from ethyl acetate to give a substance having m.p. 105–106° (undepressed on admixture with dihydro-D-altral) and $[\alpha]_D$ +73° (*c*, 0.8 H_2O).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.6%; H, 8.2%. Found: C, 48.4%; H, 8.2%.

Its x-ray diffraction pattern was identical with that of dihydro-D-altral.

The next fraction having R_{Rh} 1.3 (0.39 g.) gave crystals with m.p. 87–88° after three recrystallizations from ethyl acetate and had $[\alpha]_D$ +19° (*c*, 1.0 H_2O).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.6%; H, 8.2%. Found: C, 48.3%; H, 8.2%.

The melting point was not depressed on mixing with dihydro-D-glucal, which gave an x-ray diffraction pattern identical with the hydrogenolysis product. A further fraction (0.55 gm.) was obtained from the column and contained a mixture of the compounds having R_{Rh}'s 1.1 and 1.3. No 1:5-anhydro-D-sorbitol was detectable in any fraction.

Hydrogenation of 1,2-O-isopropylidene-D-fructopyranose. 1,2-*O*-isopropylidene-D-fructopyranose (14.0 g.) was dissolved in dioxane (250 cc.) containing copper chromite (3.0 g.) and hydrogenated at 1500–2000 p.s.i. for 6 hr. at 180°. The solution was filtered and evaporated to a sirup (12.7 g.) which was hydrolyzed in 0.1*N* sulfuric acid (30 cc.) at 100° for 30 min. Neutralization ($BaCO_3$) followed by filtration and evaporation yielded a sirup which was shown to contain fructose and two other ketohexoses, moving faster than fructose on a paper chromatogram which gave blue colors with the urea oxalate spray.[21] A visual estimate of the proportion of the new sugars was about 15% of the whole ketose fraction. Also, a pink spot of R_{Rh} 1.0 was detected (brown on development with *p*-anisidine hydrochloride). When a chromatogram was sprayed with ammoniacal silver nitrate polyols of $R_{Rh} > 1.0$ were observed and these (0.62 g.) were fractionated on a cellulose column. However, these were shown to contain no isopropyl groups on examination with an infrared absorptionmeter. No material behaving as an isopropyl-ketoside was observed (on a paper chromatogram) since on acid hydrolysis of the hydrogenation product the spots did not disappear.

Hydrogenation of 1,2-O-isopropylidene-D-xylofuranose. The isopropylidene xylose (5.1 g.) was hydrogenated at 200° using the same procedure as above and the sirupy product (3.7 g.) was examined on a paper chromatogram using the *p*-anisidine hydrochloride and ammoniacal silver nitrate sprays. A small amount of nonreducing material (R_{Rh} 1.2) was detected before and after acid hydrolysis (in 0.1*N* H_2SO_4 for 1 hr. at 100°) and was shown to be present as 7.4% of the total by chromatography on cellulose. The remainder appeared to consist of a mixture of xylose and ribose (paper chromatographic examination) which contained 42% of the latter as shown by the orcinol–ferric chloride[22] method after the two components were separated by chromatography on filter paper strips.

The polyol fraction described did not give infrared absorption in the isopropyl region.

6-O-Isopropyl-D-glucose. 3-*O*-Benzyl-6-*O*-toluenesulfonyl-1,2-*O*-isopropylidene-D-glucofuranose[23] (3.83 g.) was heated under reflux in isopropanol (40 cc.) in which sodium (0.79 g.) had been dissolved. After 18 hr., benzene was added and the solution washed three times with water. Removal of solvent yielded a brown sirup (2.32 g.) with $[\alpha]_D$ −16° (*c*, 1.4 EtOH) which contained 3-*O*-benzyl-6-*O*-isopropyl-1,2-*O*-isopropylidene-D-glucofuranose.

A portion of the product (1.16 g.) was debenzylated by dissolving in methanol (50 cc.) containing Raney Nickel[23] and heating for 4 hr. at 70° under 1500 p.s.i. hydrogen pressure. The mixture was filtered and evaporated to a colorless sirup (0.67 g.) having $[\alpha]_D$ −14° (*c*, 1.9 EtOH).

The 6-*O*-isopropyl-1,2-*O*-isopropylidene-D-glucofuranose (0.48 g.) was hydrolyzed at 100° for 30 min. in 0.1*N* hydrochloric acid. The solution was neutralized (Ag_2CO_3), filtered, and evaporated to a sirup (0.35 g.) which was shown on a paper chromatogram to contain the required 6-*O*-isopropyl-D-glucose with R_{Rh} 1.7 contaminated with a little glucose. The glucose was removed by dissolution of the mixture in acetone and addition of a large excess of boiling ether. The liquid was decanted and evaporated to a small volume from which crystals (0.15 g.) were deposited. These were twice recrystallized from acetone to give material having m.p. 126–128° and $[\alpha]_D$ +90° → +50° (constant value; *c*, 0.5 H_2O).

Anal. Calcd. for $C_9H_{18}O_6$: C, 48.6%; H, 8.2%. Found: C, 48.8%; H, 8.2%.

6-O-Cyclohexyl-D-glucose. 3-*O*-benzyl-6-*O*-*p*-toluenesulfonyl-1,2-*O*-isopropylidene-D-glucofuranose (2.42 g.) was heated at 100° for 18 hr. in 50% cyclohexanol in dioxane (40 cc.) in which potassium (0.80 g.) had been dissolved. Benzene was added and the solution was extracted 3 times with water to remove salts. Evaporation yielded 3-*O*-benzyl-6-*O*-cyclohexyl-1,2-*O*-isopropylidene-D-glucofuranose (1.61 g.) as a brown sirup having $[\alpha]_D$ −18° (*c*, 1.4 MeOH).

The product (0.82 gm.) was hydrogenated, as with the isopropyl analog, to give sirupy colorless 6-*O*-cyclohexyl-1,2-*O*-isopropylidene-D-glucofuranose (0.52 gm.) with $[\alpha]_D$ −23° (*c*, 2.2 EtOH). Acid hydrolysis of the product followed by purification of the 6-*O*-cyclohexyl-D-glucose by ether extraction as in the preparation of 6-*O*-isopropyl-D-glucose furnished a solid (0.18 g.) which was recrystallized twice from acetone. The product softened at 105° and had m.p. 116–117° and $[\alpha]_D$ +66° → +37° (constant value; *c*, 0.7 H_2O).

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Anal. Calcd. for $2C_{12}H_{22}O_6.H_2O$: C, 53.1%; H, 8.5%. Found: C, 53.0%; H, 8.7%.

*Penta-O-acetyl 6-O-isopropyl-*L*-iditol.* 1,2–3,4-Di-*O*-isopropylidene-L-iditol[24] (2.60 g.) was dissolved in pyridine (6 cc.) and *p*-toluenesulfonyl chloride (1.90 g.) in benzene (6 cc.) added.[25] After 3 hr., water (0.1 cc.) was added, followed by benzene and the reaction mixture was washed successively with dilute sulfuric acid, aqueous sodium bicarbonate, and then water. Evaporation of the benzene solution yielded 1,2–3,4-di-*O*-isopropylidene-6-*O*-*p*-toluenesulfonyl-L-iditol as a sirup (3.74 gm.) with $[\alpha]_D$ +1° (*c*, 2.2 EtOH).

The tosyl compound (0.94 g.) was heated for 18 hr. in refluxing isopropanol (30 cc.) in which sodium (0.20 g.) had been dissolved. Benzene was added and the solution was washed three times with water and then evaporated to a sirup (0.49 g.) with $[\alpha]_D$ +12° (*c*, 2.4 EtOH). Acid hydrolysis (30 min. at 100° in 5 cc. of $0.1N$ sulfuric acid) of the material which contained 6-*O*-isopropyl 1,2–3,4-di-*O*-isopropylidene-L-iditol yielded, after neutralization ($BaCO_3$), filtration, and evaporation, a complex mixture (0.32 g.). On a paper chromatogram, the main product had R_{Rh} 1.7 and components which moved at the speeds of rhamnose, ribose, and glucose.

The mixture (92 mg.) was acetylated in a manner identical to that used previously in the synthesis of tetra-*O*-acetyl-6-*O*-isopropyl-D-glucose. The sirupy product crystallized from ether-light petroleum (b.p. 30–60°) and two recrystallizations from the same solvent followed by one recrystallization from aqueous methanol yielded a product (49 mg.) with m.p. 87–88° and $[\alpha]_D$ −5° (*c*, 1.0 2,4-lutidine). Deacetylation yielded a polyol having R_{Rh} 1.7.

Anal. Calcd. for $C_{19}H_{30}O_{11}$: C, 52.5%; H, 7.0%. Found: C, 52.1%; H, 7.2%.

*6-O-Cyclohexyl-*L*-iditol.* 1,2–3,4-Di-*O*-isopropyl-6-*O*-*p*-toluenesulfonyl-L-iditol (8.0 g.) was mixed with a solution of dioxane (100 cc.) and cyclohexanol (100 cc.) in which potassium (3.0 g.) was dissolved. This was heated at 100° for 18 hr. and then evaporated as fully as possible. The solution was brought to neutrality with $6N$ hydrochloric acid and then acidified with 100 cc. of $0.1N$ hydrochloric acid in ethanol (200 cc.). The isopropylidene groups were removed from the 6-O-cyclohexyl-1,2–3,4-di-*O*-isopropylidene-L-iditol derivative by heating the solution under reflux for 2 hr. It was then neutralized (Ag_2CO_3), filtered, and evaporated to a mobile sirup to which water was added. Cyclohexanol was removed by shaking the liquid with light petroleum (b.p. 30–60°) and the remaining aqueous layer was evaporated to dryness. Extraction with hot acetone afforded a sirup (1.82 g.) which crystallized and was recrystallized twice from acetone-ether and then once from acetone. The product gave the properties expected of 6-*O*-cyclohexyl-L-iditol having m.p. 80–81°, $[\alpha]_D$ −7.5° (*c*, 1.0 sat. borax) and −2.5° (*c*, 1.0 H_2O), and consumed 4.1 moles/mole of sodium periodate with concomitant release of 2.9 moles/mole of formic acid.

Anal. Calcd. for $C_{12}H_{24}O_6$: C, 54.5%; H, 9.2%. Found: C, 54.5%; H, 9.0%.

*Dihydro-*D*-altral from* D*-altrose.* D-Altrose (22 g.) was converted to its pentaacetate by heating at 100° for 1 hr. in acetic anhydride (100 cc.) containing sodium acetate (10 g.). The reaction mixture was added, with stirring, to excess ice water and after 3 hr. the solution was extracted with benzene, which was washed 3 times with water, and evaporated to a sirup (27 g.).

The pentaacetate was dissolved in chloroform (250 cc.) and acetic acid saturated with hydrobromic acid (250 cc.) added. After 6 hr. at room temperature it was added with stirring to ice water and the chloroform layer was washed 4 times with water, dried ($MgSO_4$), filtered, and evaporated to a sirupy product (26 g.) which contained 2,3,4,6-tetra-*O*-acetyl-1-bromo-D-altrose.

The product was dissolved in acetic acid (60 cc.) and added to zinc dust (28 g.) contained in a vigorously stirred mixture of acetic acid (60 cc.) and water (120 cc.) cooled to −5°. The solution was allowed to warm to room temperature and after stirring overnight it was extracted with benzene, which was washed 3 times with water and evaporated to a sirup (4.1 g.).

Reduction of the 3,4,6-tri-*O*-acetyl-D-altral in methanol (25 cc.) containing platinic oxide (100 mg.) for 3 hr. at ambient pressure afforded a mixture to which sodium (100 mg.) was added in order to promote deacetylation. After 2 hr. the product was evaporated to a sirup (1.96 g.) which was fractionated on a cellulose column. A material (80 mg.) was obtained which, after two crystallizations from ethyl acetate, gave dihydro-D-altral, m.p. 105–106° and $[\alpha]_D$ +72° (*c*, 0.9 H_2O).

Anal. Calcd. for $C_6H_{12}O_4$: C, 48.6%; H, 8.2%. Found: C, 48.9%; 8.3%.

The material was identical, by its x-ray diffraction pattern and undepressed mixed melting point, with a dihydro hexital synthesized by von Rudloff and Tulloch.[9]

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