The Arylation of Glycosyl Halides by Phenyllithium

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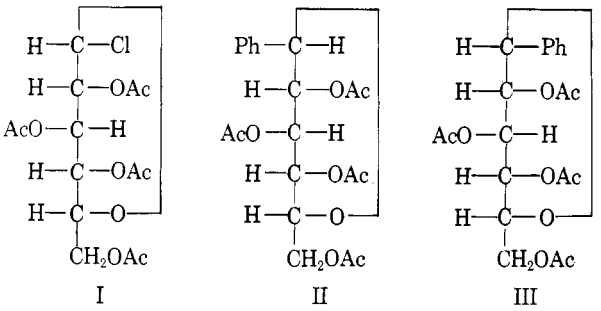
Received April 24, 1964

1β-*C*-Phenyl-1,5-D-anhydroglucitol and presumably the 1α-*C*-anomer are formed by reaction of phenyllithium with tetra-*O*-acetyl-α-D-glucopyranosyl chloride, together with a third isomer whose structure now is established as 2-*C*-phenyl-1,5-D-anhydroglucitol (VII). A reasonable mechanism is presented to account for these three products. Evidence supports the conformation of VII having all equatorial hydroxyls.

In the reaction of phenyllithium with tetra-*O*-acetyl-α-D-glucopyranosyl chloride (I) Hurd and Holysz[1] reported three products: tetra-*O*-acetyl-1-β-*C*-phenyl-1,5-D-anhydroglucitol[2] (II) (after acetylation) in about 10% yield (m.p. 155–156°, $[\alpha]^{20}D$ −18.6°), an uncharacterized crystalline isomer (m.p. 142–143°, $[\alpha]^{24}D$ −2.3°) in about 30% yield, and about 40% yield of



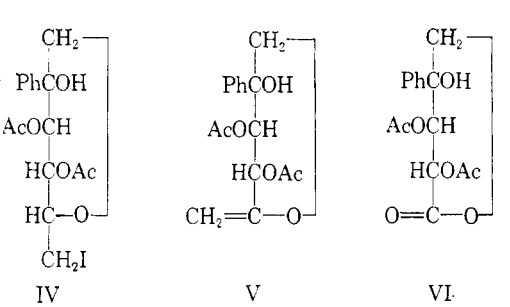
dextrorotatory sirup. Nearly a quantitative yield of 1,1-diphenylethanol accompanied these products. This paper concerns itself with the structure of the above uncharacterized isomer, which will be referred to as Y.

Certain facts about Y were established in the original work: (a) its analysis, $C_{20}H_{24}O_9$; (b) removal of acetyl groups by methanolic sodium methoxide to form a water-soluble sirup, $[\alpha]^{24}D$ 11°; (c) reacetylation of the sirup from b to the original tetraacetate only by use of forcing conditions (Ac_2O, AcONa, 140°); mild conditions (Ac_2O, AcONa, 100°; or Ac_2O, pyridine, 25°) yielded only a triacetate, m.p. 161.5–162°; (d) periodate oxidation of the sirup from b, which consumed $2KIO_4$ and formed 1HCOOH, thus demonstrating the presence of a six-membered ring with one oxygen atom in the ring.

Y cannot be the α-anomer (III) of II since III is known to have different properties. It was obtained[3] by reaction of I with phenylmagnesium bromide, separation of II by crystallization, deacetylation of the sirupy residue, and crystallization: m.p. 187°, $[\alpha]^{26}D$ 90.5°. We deacetylated Y similarly. The product, initially a sirup, became crystalline: m.p. 134.5–135.5°, $[\alpha]^{26}D$ 13.9°. Thus, Y cannot be III. This same evidence tells also that Y cannot be 1α- or 1β-*C*-phenyl-1,5-D-anhydromannitol[4] since both of these compounds are known: the α-compound, m.p. 184–185°, $[\alpha]^{26}D$ 65.2°, and the β-compound, m.p. 206–207°, $[\alpha]^{26}D$ 60.0°. Thus, no simple epimeric transformation at C-2 occurred under conditions of the reaction. Since it would be far less probable for epimeric changes to occur at C-3, -4, or -5 it seems established that the grouping –O–C(Ph)H–CHOH– cannot be considered for C-1 and-2.

The deacetylated Y was not a reducing sugar since it reacted negatively with Benedict's solution and Tollens' reagent. This excludes –O–C(OH)H–CHPh–, a reducing aldose, as a structural possibility. Also it gave no reaction with *p*-nitrophenylhydrazine in the presence of acetic acid, excluding –O–C(OH)Ph–CH_2 which would be a nonreducing ketose. Both of these groupings are excluded also since Y (the tetraacetate) was found to be unreactive in chloroform solution toward titanium tetrachloride. An acylal function such as these would possess, if present, should have changed into a hemiacetal chloride in the same way that titanium tetrachloride[5] converts glucose pentaacetate into I.

The difficulty in preparing Y by reacetylating its deacetylated derivative is strong evidence that the phenyl group is at 2, 3 or 4, giving rise to a tertiary alcohol grouping. A phenyl group at C-5 should not interfere with acetylation, nor should one at C-6 since this would simply be a secondary alcohol. Absence of phenyl at these positions was demonstrated additionally by indirect elimination of the elements of acetic acid, causing formation of a double bond between C-5 and -6. For this to take place, a hydrogen atom, not a phenyl group, must have been at C-5. In this synthesis, Y was deacetylated and then tosylated; thus, $HOCH_2$– at C-6 became $CH_3C_6H_4SO_2OCH_2$–. After acetylation of two of the remaining three hydroxyls, the toluenesulfonate group was replaced by iodide. Treatment of the latter with silver fluoride caused elimination of HI to form the double bond. Structures IV and V show this step. Phenyl is placed at C-2 in these structures for reasons to follow.



(1) C. D. Hurd and R. P. Holysz, *J. Am. Chem. Soc.*, **72**, 1735 (1950).

(2) See W. A. Bonner and C. D. Hurd, *ibid.*, **73**, 4290 (1951), for the stereochemical configuration around C-1. The previously assigned name was tetra-*O*-acetyl-β-D-glucopyranosylbenzene. The two names differ in the choice of principal function, anhydroglucitol *vs.* benzene; clearly, the former portrays the more important function. Another point of nomenclature concerns the position of "D" in the name: should it be -1,5-D-anhydroglucitol or -1,5-anhydro-D-glucitol? Since anhydro is an operational prefix (like cyclo or nor), the root name is anhydroglucitol, not glucitol. Placing "D" in front of the root name emphasizes this fact.

(3) W. A. Bonner and J. Craig, *ibid.*, **72**, 3480 (1950).

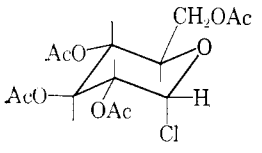
(4) C. D. Hurd and R. P. Holysz, *ibid.*, **72**, 1732 (1950).

(5) E. Pacsu, *Ber.*, **61**, 1508 (1928).

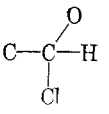
Compound V is 3,4-di-*O*-acetyl-5-methylene-2-*C*-phenyl-1,5-D-anhydroxylitol. It may be thought of as 1-deoxy-5-glucoseen. It was a sirup. From an ozonolysis reaction run on the sirup we were unable to isolate the desired lactone but did obtain instead a small yield of pure V, remaining after incomplete reaction.

Since the phenyl group in Y must be on C-2, -3 or -4, mechanistic considerations strongly indicate that it is on C-2 with retention of D-*gluco* configuration, formed by way of D-1-glucoseen as an intermediate step. This is the only position at which E2 dehydrohalogenation could occur. The C-2 hydrogen in I is certainly more acidic than the hydrogens at C-3 or C-4 since it is next to the aldehydic carbon (C-1). A sufficiently strong base should be capable of abstracting this hydrogen, and phenyllithium appears to be a base of requisite strength. In common with phenylmagnesium bromide (a weaker base), phenyllithium also abstracts chlorine from C-1 to yield II and presumably III in the dextrorotatory sirup (see ref. 3). These competing mechanistic steps seem reasonable.

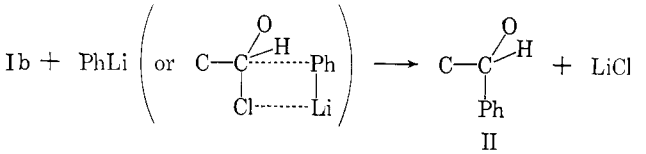
Production of II.—A four-center transition state at C-1, results in replacement of Cl by Ph with no change of configuration. In the conformational structure Ia of compound I, the detail at C-1 is Ib.



Ia

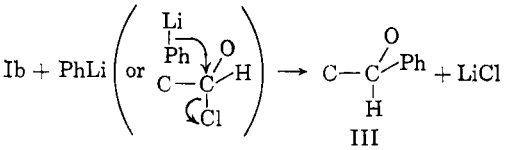


Ib



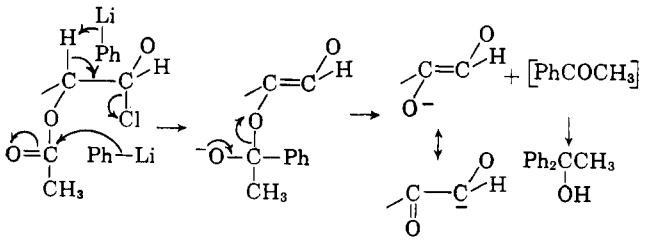
II

Production of III.—Nucleophilic attack on C-1 results in replacement of Cl by Ph, with inversion.

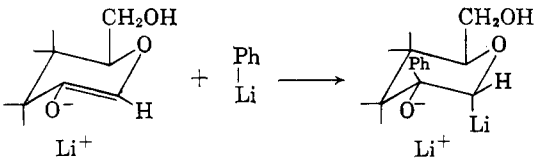


III

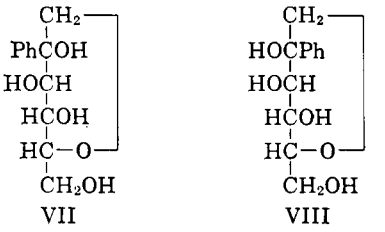
Production of Y.—Displacement of "acidic" hydrogen on C-2 by the strong base, together with removal of acetyl group, results in D-1-glucoseen.



In the anion form, C-1 of the double bond of 1-glucoseen obviously is more negative than C-2. Addition of PhLi to the glucoseen will, therefore, place phenyl at the more positive C-2.

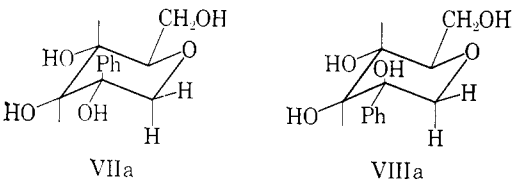


The *gluco* configuration for this product is VII, the *manno* configuration is VIII. If the reasonable assumption holds that these compounds have the same



VII VIII

conformations[6] as glucose and mannose, they are represented by VIIa and VIIIa, respectively. From these structures, it is apparent that the number 2 axial hydroxyl of VIIIa is well suited for *trans* elimination with



VIIa VIIIa

the axial hydrogen at C-1 (180°), whereas the equatorial hydroxyl of VIIIa is not *trans* coplanar with any neighboring C–H bond. The nondehydration under forcing conditions of acetylation supports VIIa as the structure. 1-Phenylcyclohexanol, for example, is converted into 1-phenylcyclohexene on heating with acetic anhydride.[7]

Although the manno conformation which is alternate to VIIIa would not be capable of elimination, the improbability of its presence is evident since it would have one CH_2OH, one phenyl, and two OH groups in axial orientations. The unlikely gluco conformation which is alternate to VIIa would possess one axial CH_2OH and three axial OH groups. It would be capable of elimination. The failure of elimination thus demonstrates both the gluco configuration and its ring conformation as well.

To test the idea of D-1-glucoseen as an intermediate, the compound was synthesized (as its tetraacetate) and treated with phenyllithium. The reaction product failed to crystallize but strong evidence that VII was produced was the fact that from the reaction mixture a spot was found on paper chromatography that moved with the same R_f as our previous product in two solvent systems. Acetylation of the new product under conditions yielding the tetraacetate gave some material having the same retention time on gas chromatography as the original tetraacetate. The sum of all the evidence thus strongly supports 2-*C*-phenyl-1,5-D-anhydroglucitol (VII) as the structure in question.

The general glycosylation reaction, namely, the reaction of esterified glycosyl halides with organic

(6) C. D. Hurd and H. T. Miles, *Anal. Chem.*, **36**, 1375 (1964).
(7) P. Sabatier and A. Mailhe, *Compt. rend.*, **138**, 1322 (1904).

magnesium reagents,[8] organic cadmium reagents,[9] or organic lithium reagents[1] has recently been applied[10] (using a lithium reagent) to the synthesis in low yield of the interesting nucleoside pseudouridine (5-D-ribofuranosyluracil), which occurs as a constituent of soluble ribonucleic acid. It appears likely that an important factor contributing to the low yield is a competing dehydrohalogenating reaction analogous to the one we have observed in the present study. If so, the use of a Grignard reagent rather than the lithium reagent should lead to reduction of this competing reaction and possibly to a higher yield of nucleoside.

Experimental

2-*C*-Phenyl-1,5-D-anhydroglucitol Tetraacetate.—Erratic results were encountered in several attempts to duplicate the original procedure.[1] Yields were generally 5–10%, not 24%, and usually the triacetate was obtained instead of the tetraacetate. Consistent yields of 16–21% were realized with the procedure given below.

Phenyllithium was prepared in the usual way in a flame-dried apparatus from 19.1 g. of lithium shot (low sodium grade, obtained from Metalloy Corporation, Minneapolis, Minn.), 146 ml. of bromobenzene, and 450 ml. of dry ether. Stirring was maintained until amost no lithium remained undissolved. Then a solution of 40 g. of I, m.p. 67–70°, in 450 ml. of absolute ether was added during 3 hr. The mixture was stirred under a slow stream of dry nitrogen overnight, then was refluxed for 4 hr. Hydrolysis was carried out at 0–5° by dropwise addition of 400 ml. of water. The mixture was neutralized with about 80 ml. of acetic acid. The ether layer was extracted once with 200 ml. of water and the water layer with 200 ml. of ether. The ether layer was set aside for later recovery of 1,1-diphenylethanol.[1]

The water layer was concentrated under reduced pressure at 100° to a thick sirup, then was dried to a solid cake by azeotropic distillation with benzene. To the solid was added 300 ml. of acetic anhydride and 10 g. of anhydrous sodium acetate. After 2 hr. at 100° another 150 ml. of acetic anhydride was added and the remaining solid was disintegrated. The mixture was stirred and heated for 1 hr. at 100° and for 25 min. at 130–135°, then was held at 15–20° as water (700 ml.) was added dropwise with stirring. The mixture was repeatedly ether extracted (1200 ml. total) and the ether solution was freed of acetic acid by extraction with water and sodium bicarbonate solution. Then the ether solution was shaken with both Norit and calcium chloride and was filtered through the following layers on a Büchner funnel: calcium chloride (top), Norit, anhydrous magnesium sulfate, Celite. Drying of the resulting light yellow filtrate was completed with magnesium sulfate. Slow evaporation of the solution in an unstoppered flask yielded prismatic crystals. These were collected and washed with ether–pentane to give 8.04 g. (16%) of white crystals of m.p. 140–142°. The filtrate later deposited 1.7 g., m.p. 120–140°, which probably contained more of the same substance.

2-*C*-Phenyl-1,5-D-anhydroglucitol (VI).—A solution of 0.43 g. of the triacetate[1] of this compound, m.p. 162–163°, in 10 ml. of absolute methanol containing 1% of dry hydrogen chloride was refluxed for 15 hr., then was shaken for 8 hr. with 6 g. of silver carbonate, filtered, treated with carbon, filtered through Celite, and evaporated. The crystalline residue was recrystallized from ethanol, yielding 79 mg., m.p. 134.5–135.5°, $[\alpha]^{26}D$ 13.9° (*c* 1.58, ethanol).

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 60.00; H, 6.67. Found: C, 60.30; H, 7.08.[11]

Deacetylation of the acetyl derivative by the Zemplén method (CH_3OH + trace CH_3ONa) gave this substance as an oily product which usually crystallized, however, on standing overnight.

2-*C*-Phenyl-1,5-D-anhydroglucitol 3,4-Diacetate 6-*p*-Toluenesulfonate.—To a solution of 4.1 g. of VI (m.p. 133–136°) in 45 ml. of dry pyridine was added 3.5 g. of *p*-toluenesulfonyl chloride, the solution being kept at 0° for 2 hr. and at 20° for 2 days. Acetylation was then carried out by adding 35 ml. of acetic anhydride to the chilled solution and then keeping the flask again at 0° for 2 hr. and at 20° for 2 days. The solution was poured into 80 ml. of ice-water while shaking the flask in an ice bath to dissipate the heat of reaction. After standing for 1 hr. the mixture was extracted with chloroform (300 ml. total). The extract was washed in turn with dilute sulfuric acid, water, sodium bicarbonate solution, and water, then was dried ($CaCl_2$), concentrated to a solid, and dissolved in boiling ethanol (200 ml.). On cooling, the separated white crystals weighed 5.0 g. (60%), m.p. 175–177° dec. After recrystallization from ethanol the melting point was 166–168° dec. A third crystallization from methanol changed the melting point to 164–165° dec.; $[\alpha]^{30}D$ 58.8° (*c* 7.24, chloroform).

Anal. Calcd. for $C_{23}H_{25}O_9S$: C, 57.74; H, 5.23. Found: C, 57.74; H, 5.49.

Acetic Esters of 6-Iodo-2-*C*-phenyl-6-D-deoxy-1,5-anhydroglucitol. The 3,4-Diacetate.—A mixture of 0.7 g. of the above toluenesulfonate (m.p. 162–163° dec.), 7 ml. of acetic anhydride, and 0.6 g. of sodium iodide was heated at 100° for 2 hr. and then cooled and poured into 12 ml. of ice–water. The oil which formed crystallized on standing overnight. The crystals were separated, washed with water, sodium bicarbonate solution, again with water, and dried, yielding 0.38 g. (58%), m.p. 177–178°. Qualitative tests for the presence of iodine were positive; $[\alpha]^{28}D$ 48.6° (*c* 3.64, chloroform).

Anal. Calcd. for $C_{16}H_{18}IO_6$: C, 44.37; H, 4.19. Found: C, 44.34; H, 4.42.

The 2,3,4-Triacetate.—The same relative amounts of reagents were taken as before but instead of holding the temperature at 100° it was held at reflux (140°) for 75 min. Processing was the same as for the diacetate. From 1.8 g. of the toluenesulfonate, 0.9 g. of crude crystalline triacetate was obtained. Two recrystallizations from ethanol gave 0.50 g. (28%) of pure triacetate, m.p. 175–176°. A third crystallization brought the melting point to 176.5–177.5°; $[\alpha]^{28}D$ 21.7° (*c* 3.96, chloroform). A mixture of the di- and triacetates sintered about 145° and melted between 150–167°. Iodine was present as tested by fusion with sodium.

Anal. Calcd. for $C_{18}H_{20}IO_7$: C, 45.50; H, 4.24. Found: C, 45.55; H, 4.40.

In a comparable run that differed by being refluxed for 50 min. instead of 75, probably both the di- and triacetates were formed, but the diacetate was the only pure compound obtainable (24% yield) on working up the reaction products.

5-Methylene-2-*C*-phenyl-1,5-D-anhydroxylitol 3,4-Diacetate (V).—The above 6-iodo diacetate (1.0 g.) was mixed with 10 ml. of anhydrous pyridine and 1.2 g. of silver fluoride. The procedure was adapted from that of Helferich and Himmen[12] for making methyl 2,3,4-*O*-triacetyl-α-D-5-glucoseenide.

The stoppered flask was covered with aluminum foil to exclude light and was shaken for 35 hr. The mixture was extracted with nine 15-ml. portions of dry ether. Each portion was filtered through Celite on sintered glass. Concentration of the ether to 50 ml., refiltration, and then evaporation of a steam bath left a sirupy residue and some silver. The sirup was dissolved in methanol and filtered. Evaporation left 0.63 g. including some sirup, but no crystals. The material gave a strong test for unsaturation with a 1% solution of bromine in carbon tetrachloride. It refused to crystallize.

It was dissolved in 25 ml. of acetic acid, filtered through sintered glass to remove silver, and a stream of ozone was passed through it for 52 min. Then 60 ml. of dry ether and 24 g. of zinc powder were added. After several hours the mixture was filtered, extracted with water, sodium bicarbonate solution, and water, then was dried ($MgSO_4$). The solvent was evaporated, leaving a small quantity of needle-shaped crystals and some sirup. The crystals were separated and crystallized twice from ethanol and twice more from 2-propanol: m.p. 118–120°. Less than 10 mg. remained, but analysis demonstrated that it was V. The lactone VI, expected by ozonolysis of V, was excluded by analysis (Calcd. for $C_{15}H_{16}O_7$: C, 58.44; H, 4.91.). It may have resisted extraction by ether from the aqueous acetic acid solution. Search for VI was not continued.

Anal. Calcd. for $C_{16}H_{18}O_6$: C, 62.74; H, 5.92. Found: C, 62.93; H, 5.82.

Reaction between Phenyllithium and D-1-Glucoseen Tetraacetate.—A solution of 4.5 g. of D-1-glucoseen tetraacetate (0.014

(8) C. D. Hurd and W. A. Bonner, *J. Am. Chem. Soc.*, **67**, 1972 (1945).
(9) C. D. Hurd and R. P. Holysz, *ibid.*, **72**, 2005 (1950).
(10) R. Shapiro and R. Chambers, *ibid.*, **83**, 3920 (1961).
(11) All analyses in this paper were by Miss H. Beck.
(12) B. Helferich and E. Himmen, *Ber.*, **61**, 1825 (1928).

mole, m.p. 61–63°)[13] in 100 ml. of ether was added dropwise with stirring to 0.15 mole of phenylithium in 130 ml. of ether during 0.5 hr., and was stirred for an additional 2.5 hr., then was refluxed for 3 hr. It was treated with 100 ml. of water, neutralized with acetic acid, and extracted with ether (discard ether layer). Most of the water was evaporated under aspirator vacuum with heating and the remainder at 300 μ at 50°. Final drying was over phosphorus pentoxide under vacuum.

The reaction mixture was acetylated with acetic anhydride and sodium acetate at 100°, poured into ice–water, and extracted with chloroform. The chloroform solution was extracted with sodium bicarbonate solution and then with water before being dried with magnesium sulfate and treated with charcoal. Filtration and evaporation left a brown oil which could not be induced to crystallize.

Part of the oil was deacetylated with potassium methoxide in absolute methanol and aliquots chromatographed on paper in two solvent systems (A, triethylamine–*t*-butyl alcohol–water, 2:10:3, and B, pyridine–*n*-butyl alcohol–water, 4:6:3). The R_f values of the principal component of the reaction mixture, of pure VII, and of glucose were 0.77, 0.77, and 0.31 in A and 0.81, 0.83, and 0.44 in B, respectively.

Part of the material which had been acetylated at 100° was subjected to vigorous acetylation conditions (refluxing acetic anhydride in the presence of sodium acetate), producing another noncrystalline reaction mixture. Gas chromatography of this material showed a principal peak at 10.1 min. (6-ft. column, QF-1 on Gas-Chrom P, 20 p.s.i.), identical with that of the pure tetra-*O*-acetate of VII (m.p. 142–143°). Both materials showed subsidiary peaks, presumably the result of impurities in the first instance and of partial pyrolysis on both experiments.

(13) K. Maurer, *Ber.*, **62**, 332 (1929).

Spectra.—Infrared spectra were taken on several of the compounds, with results given below. Alcohol-free chloroform was taken as solvent and 7% solutions were used unless otherwise noted. A 0.03-mm. cell was used. The spectra for the tetraacetates of VI and II followed each other closely, but significant differences appeared at 8.50, 9.4–9.8, and 10.4–10.9 μ. The tri- and tetraacetates of VI also were close, differing from each other primarily at 2.8, 8.5, 8.7, 9.8, and 10.5–10.9 μ. These assignments are applicable: hydroxyl 2.8, phenyl 3.3 and 6.7, carbonyl (ester) 5.7, C-methyl (of acetyl) 7.3, acetic ester 8.0–8.1, sulfonic ester 8.40 and 8.47, and cyclic ether 9.0–9.1 μ.

VI triacetate, m.p. 162–163°: weak at 2.8, 6.6, 6.8, 10.4, 10.55, and 10.9; medium at 3.3, 7.3, 9.0, 9.36 and 9.53; strong at 5.7 and 8.1 μ.

VI tetraacetate, m.p. 142–143°: weak at 3.3, 6.6, 6.8, 8.5, 8.7, 10.4, and 10.7; medium at 7.3, 9.0, 9.36, 9.53, and 9.8; strong at 5.7 and 8.1 μ.

II tetraacetate, m.p. 155–156°: weak at 3.3, 6.6, 6.8, and 10.9; medium at 7.3, 9.0, and 9.44–9.64; strong at 5.7 and 8.1 μ.

1β-*C*-Phenyl-1,5-D-anhydroxylitol triacetate,[14] m.p. 170°, 16% solution: weak at 3.5, 6.69, 10.7, 11.0, and 11.4; medium at 3.3, 6.87, 7.03, and 10.2; strong at 5.71, 7.30, 8.00–8.12, 9.2, 9.4, and 9.7 μ.

2-*C*-Phenyl-1,5-D-anhydroglucitol 3,4-diacetate 6-*p*-toluenesulfonate, m.p. 164–165° dec.: weak at 2.84, 3.5, 6.25, 6.70, and 11.0; medium at 3.35, 6.94, 8.40, 9.1, 9.4, 9.6, 10.2, and 10.6; strong at 5.71, 7.30, 8.07, and 8.47 μ. The anomalous hydroxyl band at 2.85 μ was weak, but definite.

IV diacetate, m.p. 177–178°: weak at 2.82, 3.35, 6.70, 6.92, 7.07, 8.84, 10.0, 10.4, 10.6, and 11.1; medium at 7.30, 8.34, 9.03, 9.40, and 9.57; strong at 5.70 and 8.07 μ.

(14) C. D. Hurd and W. A. Bonner, *J. Am. Chem. Soc.*, **67**, 1759 (1945)

Catalytic Isomerization of Polyhydric Alcohols.[1] II. The Isomerization of Isosorbide to Isomannide and Isoidide

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Received March 9, 1964

At 220–240° and 150 atm. of hydrogen pressure the reversible interconversion of the 1,4;3,6 dianhydrohexitols of D-glucitol, D-mannitol, and L-iditol reaches a steady state after 2–6 hr. in the presence of nickel–kieselguhr catalyst. At this time the approximate concentrations are 57%, 1,4;3,6-dianhydro-L-iditol; 36%, 1,4;3,6-dianhydro-D-glucitol; and 7%, 1,4;3,6-dianhydro-D-mannitol. These figures are shown to be consistent with probability considerations; *i.e.*, the relative amounts of the dianhydrohexitols are related to the probability of a given hydroxyl group being either *exo* or *endo*. Taking the steady-state mole fraction of 1,4;3,6-dianhydro-L-iditol as 0.57, it is calculated that the probability of a hydroxyl being *exo* is three times the probability of its being *endo*. Calculation of the mole fraction of the other two anhydrohexitols on the basis of these relative probabilities yields values in close agreement with those found experimentally. The isomerization is strongly accelerated by increasing alkalinity of the catalyst–dianhydrohexitol slurry.

Recently[1] we reported on the existence of isomerization equilibrium between the hexitols, D-glucitol, D-mannitol, and L-iditol, established at 170° in the presence of nickel–kieselguhr catalyst and 100 atm. of hydrogen. Our interest in polyhydric alcohols prompted us to reinvestigate the isomerization behavior of the dianhydrohexitols.[2] The analytical problems were simplified by application of gas–liquid chromatography to the analysis of the reaction products.

Fletcher and Goepp[2] had previously shown that 1,4;3,6-dianhydro-L-iditol could be isolated from the reaction products obtained by treating the dianhydride of either D-glucitol or D-mannitol with Raney nickel at 200° and 250 atm. of hydrogen. The present paper extends this work and demonstrates that isomerization equilibrium is established between the three dianhydrohexitols of D-glucitol, D-mannitol, and L-iditol at 220–240°. The isomerization reaction constitutes a good method for the preparation of 1,4;3,6-dianhydro-L-iditol,[3] recoverable yields of 52% being achieved in this work.

Results and Discussion

In the Experimental part of this paper, a description is given of the isolation and identification by gas–liquid chromatography of isomannide and isoidide as the isomerization products of isosorbide. In order to obtain information that would lead to a better understanding of the isomerization reaction, a study was made of the effect of temperature on the isomerization of isosorbide. The results are given in Table I. The data show that

(1) For the first paper of this series, see L. Wright and L. Hartmann, *J. Org. Chem.*, **26**, 1588 (1961).

(2) H. G. Fletcher, Jr., and R. M. Goepp, Jr., *J. Am. Chem. Soc.*, **68**, 938 (1946).

(3) L. W. Wright and J. D. Brandner, U. S. Patent 3,023,223 (Feb. 27, 1962), assigned to Atlas Chemical Industries, Inc.