708. *Aspects of Stereochemistry. Part VII.* The Structure of Some Cyclic Acetals of* D-glycero-D-gluco-*Heptitol* (β-*Sedoheptitol*).

By K. W. Buck, A. B. Foster, N. K. Richtmyer, and E. Zissis.

Graded acetolysis of tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol, followed by saponification, afforded the 2,4-*O*-methylene derivative, the structure of which was proved. Similar treatment of an *O*-methyltri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol yielded the 6-*O*-methyl-2,4-*O*-methylene derivative, thereby showing the precursor to have a 1,3:2,4:5,7-distribution of the acetal groups. The three products of graded acidic hydrolysis of 1,3:2,4:5,6-tri-*O*-benzylidene-D-glucitol were isolated after *p*-phenylazobenzoylation and chromatography on alumina. This method was only partially successful with tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol: 2,4-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol was one product of the graded hydrolysis. Intramolecular hydrogen bonding has been invoked to account for the reaction of D-*glycero*-D-*gluco*-heptitol by only one of the two patterns predicted by the empirical rules.

The reaction pattern [1] of pentitols and higher polyhydric alcohols with aldehydes has been rationalized.[2] In most cases the empirical rules [3] predict formation of a single series of products as acetalation of a polyhydric alcohol proceeds. However, there are instances where two, alternative, series of products are predicted but the rationalizations do not permit a final selection. For example, the formation of a 1,3- or a 3,5-*O*-benzylidene derivative from L-arabinitol is predicted since (in Barker and Bourne's terminology [3]) both these compounds would contain β-rings and βC-rings cannot be formed. Apparently, only the 1,3-*O*-benzylidene derivative is formed experimentally.[4] The suggestion has been made [5] that the 1,3-*O*-benzylidene derivative (I) is preferred because more extensive intramolecular hydrogen bonding is possible than in the 3,5-*O*-benzylidene derivative (II). Possibilities of intramolecular hydrogen bonding, involving the side-chain hydroxyl groups, are similar for both structures (I) and (II), but the former has the remaining hydroxyl group axial to the 1,3-dioxan ring, an arrangement particularly suitable [5,6] for intramolecular hydrogen bonding to the ring oxygen atoms (as shown). The corresponding hydroxyl group in 3,5-*O*-benzylidene-L-arabinitol (II) would be equatorial and hence in a relatively unfavourable position [7] for such bonding. Similarly, D-*glycero*-D-*gluco*-heptitol (β-sedoheptitol) should [3] form either a 1,3:2,4:5,7- or a 1,3:4,6:5,7-tri-*O*-alkylidene derivative (*e.g.*, III or IV), each of which contains one βC and two β-rings. As acetalation of the heptitol proceeds the first preference should [1,3] be for a βC-ring and the two possible structures, 2,4- (V) and 4,6-*O*-alkylidene-D-*glycero*-D-*gluco*-heptitol (VI), are analogous to

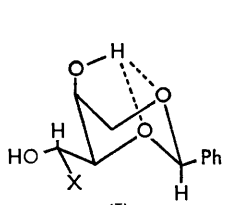
* Part VI, *J.*, 1961, 2338.

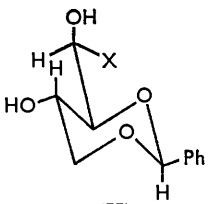
[1] Barker and Bourne, *Adv. Carbohydrate Chem.*, 1952, **7**, 137.
[2] Barker, Bourne, and Whiffen, *J.*, 1952, 3865; Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[3] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1909; Barker and Bourne, *J.*, 1952, 905.
[4] Haskins, Hann, and Hudson, *J. Amer. Chem. Soc.*, 1943, **65**, 1663; Zissis and Richtmyer, *ibid.*, 1954, **76**, 5515.
[5] Brimacombe, Foster, and Stacey, *Chem. and Ind.*, 1958, 1228.
[6] Baggett, Brimacombe, Foster, Stacey, and Whiffen, *J.*, 1960, 2574.
[7] Part VI, *J.*, 1961, 2338.

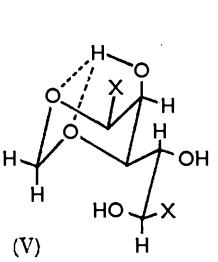
the L-arabinitol derivatives (I) and (II) in possessing similar side chains but differing in the orientation of the hydroxyl group attached to the 1,3-dioxan ring. Since the 2,4-*O*-alkylideneheptitol derivative has an axial hydroxyl group it should be preferred to the alternative structure and should result in a 1,3:2,4:5,7-distribution of the acetal groups in the fully substituted heptitol. The structures of the alkylidene derivatives of D-*glycero*-D-*gluco*-heptitol were unknown when this prediction was made and structural investigation was therefore undertaken. We now report proof that the βC-ring in the tri-*O*-methylene derivative spans the 2,4-positions and evidence that the same structural feature is present in the tri-*O*-benzylidene derivative.

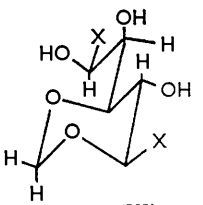
Treatment of D-*glycero*-D-*gluco*-heptitol (for which an improved preparative procedure is described) with aqueous formaldehyde and concentrated hydrochloric acid at 55° gave in excellent yield a crystalline tri-*O*-methylene derivative, further characterized as the *O*-acetyl and *O*-toluene-*p*-sulphonyl derivatives. The last compound did not undergo ester exchange during 6 hr. in boiling butan-2-one containing sodium iodide, thereby suggesting [8] the presence of a secondary toluene-*p*-sulphonyloxy-residue.

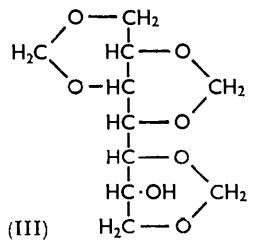
Acetolysis of the tri-*O*-methyleneheptitol, under conditions that would be expected [1] to cleave β-rings but leave βC-rings intact, gave a syrup which was deacetylated to yield crystalline 2,4-*O*-methylene-D-*glycero*-D-*gluco*-heptitol (VII), further characterized as the penta-*O*-acetate. The mono-*O*-methylene derivative consumed 2·04—2·07 mol. of periodate, releasing 0·79—0·89 mol. of formic acid and 1·03 mol. of formaldehyde, and hence contained the ·CH(OH)·CH(OH)·CH_2·OH grouping. Reduction of the resultant pentose derivative (presumably 2,4-*O*-methylene-L-xylose) with sodium borohydride afforded the known 2,4-*O*-methylenexylitol.[9] Therefore the methylene group in the parent compound must span the 2,4-positions. The alternative structure, 4,6-*O*-methylene-D-*glycero*-D-*gluco*-heptitol would have yielded 2,4-*O*-methyleneribitol.[10]

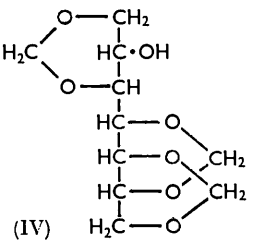


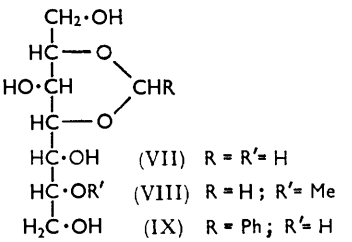












Tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol gave a crystalline mono-*O*-methyl derivative. On acetolysis and then deacetylation the *O*-methyl ether gave a crystalline *O*-methyl-2,4-*O*-methylene-D-*glycero*-D-*gluco*-heptitol (VIII) which did not react with periodate. Hence the methyl group must have been located at position 6, since any other

[8] Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 107.
[9] Hann, Ness, and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 670.
[10] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 1906.

O-methyl-2,4-*O*-methylene derivative should consume one or two mol. of periodate. Thus, the original tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol must have a free 6-hydroxyl group and, since the βC-ring has been shown to span the 2,4-positions, the rules [3] may be confidently invoked to allocate a 1,3:2,4:5,7-distribution of the methylene groups (III).

Tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol was first described by LaForge and Hudson.[11] Graded acetolysis cannot be applied to this compound since both β- and βC-rings would be cleaved.[1] Graded acidic hydrolysis of the tri-*O*-benzylidene derivative, followed by *p*-phenylazobenzoylation [12] of the mixed product and fractionation on alumina,[13] was therefore examined because of the encouraging results obtained with a model compound 1,3:2,4:5,6-tri-*O*-benzylidene-D-glucitol. Thus, D-glucitol and its 2,4-*O*- and 1,3:2,4-di-*O*-benzylidene derivatives gave crystalline *p*-phenylazobenzoates and an artificial mixture of the esters could be fractionated on alumina with recovery of *ca.* 60% of each component. Graded acidic hydrolysis of 1,3:2,4:5,6-tri-*O*-benzylidene-D-glucitol in dioxan–hydrochloric acid at 50° proceeded smoothly under homogeneous conditions. *p*-Phenylazobenzoylation of the mixed product and fractionation then gave the three esters in proportions dependent on the duration of hydrolysis. *p*-Phenylazobenzoylations in pyridine were performed at 95—100° with a significant excess of acid chloride in order to avoid partial esterification. At 0° *p*-phenylazobenzoylation of 2,4-*O*-benzylidene-D-glucitol with 4·4 mol. of acid chloride gave, in addition to the tetra-*O*-*p*-phenylazobenzoate (12·0%), two tri-*O*-*p*-phenylazobenzoates (41·1% and 13·7%) and a di-*O*-*p*-phenylazobenzoate (14·3%). A mono-*O*-*p*-phenylazobenzoate was also detected but not isolated. The location of the ester residues in the partially substituted derivatives was not determined. Attempted methylation by methyl iodide–silver oxide–dimethylformamide gave methyl *p*-phenylazobenzoate. The use of pure dioxan was also mandatory in order to avoid contamination of the products with the mono- and di-*O*-*p*-phenylazobenzoates of ethane-1,2-diol. Authentic 2-*O*-*p*-phenylazobenzoyloxyethanol, hitherto unknown, was readily obtained by partial esterification of ethane-1,2-diol.

When tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol was partially hydrolysed in boiling dioxan–hydrochloric acid and the products were *p*-phenylazobenzoylated, a variety of coloured compounds was formed but none was isolated crystalline. When tri-*O*-benzylidene-*O*-*p*-phenylazobenzoyl-D-*glycero*-D-*gluco*-heptitol was partially hydrolysed and the products were fractionated without further *p*-phenylazobenzoylation, unchanged starting material (20·2%) and a di-*O*-benzylidene-*O*-*p*-phenylazobenzoyl-D-*glycero*-D-*gluco*-heptitol (15·9%), of undetermined structure, were the only crystalline products isolated. Paper chromatography of the graded hydrolysate of tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol (detection with silver nitrate [14]) revealed ten products, considerably more than expected. Chromatography on a cellulose column gave D-*glycero*-D-*gluco*-heptitol (34·5%), its tri-*O*-benzylidene derivative (1·8%), and a small amount (0·7%) of an unidentified di-*O*-benzylidene derivative as the only crystalline products. When the content of fractions which were believed to contain the mono-*O*-benzylidene derivative were oxidised with periodate and then hydrolysed with acid, xylose was formed (identified by paper chromatography and ionophoresis); ribose could not be detected. Thus 2,4-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol (IX) was almost certainly a product of partial hydrolysis and the parent tri-*O*-benzylidene derivative most probably has the same, *i.e.*, 1,3:2,4:5,7-distribution of the acetal groups as has the tri-*O*-methylene compound, provided that acetal migrations do not occur during the graded acidic hydrolysis.

Treatment of D-*glycero*-D-*gluco*-heptitol with acid under the partial-hydrolysis conditions gave small amounts of unidentified products (detected by paper chromatography), possibly

[11] LaForge and Hudson, *J. Biol. Chem.*, 1917, **30**, 61.
[12] Baggett, Foster, Haines, and Stacey, *J.*, 1960, 3528.
[13] Cf. Coleman, Farnham, and Miller, *J. Amer. Chem. Soc.*, 1942, **64**, 1501; Coleman, Rees, Sundberg, and McCloskey, *ibid.*, 1945, **67**, 381; Mertzweiller, Carney, and Farley, *ibid.*, 1943, **65**, 2367; Boissonnas, *Helv. Chim. Acta*, 1947, **30**, 1689, 1703; Umberger and Curtis, *J. Biol. Chem.*, 1949, **178**, 265.
[14] Trevelyan, Proctor, and Harrison, *Nature*, 1950, **166**, 444.

anhydrides, so that similar products are likely in the hydrolysis of the tri-*O*-benzylidene derivative. Under similar acid conditions D-glucitol was unaffected.

Experimental

Methylene Compounds [Mr. E. Zissis]

D-glycero-D-gluco-*Heptitol* (β-*Sedoheptitol*) *from* 2,7-*Anhydro*-β-D-altro*heptulopyranose* (*Sedoheptulosan*).—The earlier directions [15] for the preparation of hexa-*O*-acetyl-α-D-*altro*-heptulopyranose were modified as follows. Powdered sedoheptulosan hydrate (50 g.) was added portion-wise (to moderate the exothermic reaction) to acetic anhydride (200 ml.) and fused sodium acetate (12·5 g.) on the steam-bath, and heating was continued for an additional 2 hr. The mixture was poured on ice (1 kg.) and left overnight at 0—5°, and the product extracted with dichloromethane (2 × 0·8 l.). The combined and dried (Na_2SO_4) extracts were concentrated *in vacuo* to a syrup that contained a small amount of acetic acid. A solution of the syrupy sedoheptulosan tetra-acetate in acetic anhydride (250 ml.) was cooled to 5° and treated with a freshly prepared mixture of 60% perchloric acid (0·5 ml.) and ice-cold acetic anhydride (320 ml.), and then left at 5° for 5 days. The dark solution was poured on ice (1·5 kg.) and, when most of the ice had melted, solid sodium hydrogen carbonate (400—600 g.) was added, with stirring, until the syrupy product became granular and floated to the surface. The mixture was stored at 5° overnight, then filtered and the product was washed with water (*ca.* 1 l.). The crude, air-dried product (75 g.) was dissolved in hot ethanol (150 ml.), charcoal (60 g.; Darco G-60) was added, and the mixture was filtered through carbon (120 g.) which was then washed with hot ethanol (300 ml.). The filtrate was concentrated slowly until crystallization seemed to be complete, but not to a point where a syrupy phase appeared. The filtered crystals were immediately washed with cold ethanol, yielding slightly yellow sedoheptulose hexa-acetate, m. p. 97—99° (30—50 g.), which after recrystallization had m. p. 98—99·5° and $[\alpha]_D^{20}$ +59·0° (*c* 1·2 in $CHCl_3$).

To an ice-cold solution of the once recrystallized sedoheptulose hexa-acetate (60 g.) in methanol (750 ml.) was added a cold 0·5% solution (50 ml.) of sodium methoxide in methanol. The mixture was kept at 5° for 3 days, the excess of sodium methoxide was destroyed by carbon dioxide, and the solution was then filtered together with a small amount of carbon and concentrated. A solution of the syrup in water (100 ml.) was added during 1 hr. to a stirred solution of sodium borohydride (10 g.) in water (100 ml.); the mixture was stirred for an additional 0·5 hr. and left at 5° overnight. The excess of reagent was destroyed with glacial acetic acid, and the solution was decationized with Amberlite IR-120 (H^+ form). The eluate was concentrated to a syrup and freed from boric acid by alternate dissolution in, and evaporation of, methanol (250 ml.), this process being carried out twice more. A solution of the final syrup in warm methanol (150 ml.) deposited volemitol (15 g.) when seeded. The mother-liquor was concentrated to 50 ml., seeded, and left at 5° for 2 weeks; D-*glycero*-D-*gluco*-heptitol (β-sedoheptitol) (7·2 g.) was obtained, having m. p. 128—130° after one recrystallization from aqueous ethanol. A third crop (1·3 g.) was a mixture of the two heptitols.

1,3:2,4:5,7-*Tri*-O-*methylene*-D-glycero-D-gluco-*heptitol*.—A solution of D-*glycero*-D-*gluco*-heptitol (5·2 g.) in concentrated hydrochloric acid (15 ml.) and 37% aqueous formaldehyde (20 ml.) was heated for 2 hr. at 55° and then allowed to concentrate over sodium hydroxide and concentrated sulphuric acid in an evacuated desiccator at room temperature. The crude crystalline product (6 g.) was collected, washed with cold water, and twice recrystallized from 50 parts of hot water, to yield prismatic needles of tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol, m. p. 276—278° (decomp.; sealed capilliary) after sublimation at 130°, $[\alpha]_D^{20}$ −23·3° (*c* 0·4 in $CHCl_3$) (Found: C, 48·6; H, 6·4. $C_{10}H_{16}O_7$ requires C, 48·4; H, 6·5%).

Treatment of the tri-*O*-methyleneheptitol with acetic anhydride and sodium acetate in the usual way gave an O-*acetate*, m. p. 207—209°, $[\alpha]_D^{20}$ −16·9° (*c* 1 in $CHCl_3$) (Found: C, 49·9; H, 6·5; Ac, 14·55. $C_{12}H_{18}O_8$ requires C, 49·65; H, 6·25; Ac, 14·8%); with toluene-*p*-sulphonyl chloride and pyridine it gave a *toluene*-p-*sulphonate* as needles (from 60 parts of 95% ethanol), m. p. 184—185° (decomp.), $[\alpha]_D^{20}$ −31·5° (*c* 1 in $CHCl_3$) (Found: C, 50·5; H, 5·6; S, 8·2. $C_{17}H_{22}O_9S$ requires C, 50·7; H, 5·5; S, 8·0%).

A solution of the toluene-*p*-sulphonate and dry sodium iodide in butan-2-one was boiled

[15] Richtmyer and Pratt, *J. Amer. Chem. Soc.*, 1956, **78**, 4717.

under reflux for 6 hr.; no sodium toluene-*p*-sulphonate separated on cooling, and 80% of the starting material was recovered.

2,4-O-*Methylene*-D-glycero-D-gluco-*heptitol*.—Tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol (3 g.) was dissolved by heat in a mixture of acetic anhydride (280 ml.) and glacial acetic acid (120 ml.); the solution was cooled rapidly to 5° and concentrated sulphuric acid (8 ml.) was added in small portions at such a rate that the temperature of the mixture did not exceed 8° and yet none of the starting material crystallized. After 1 hr. at 5° the solution was poured on ice and left at 5° overnight. The clear solution was partially neutralized by sodium hydrogen carbonate (700 g.) and then extracted with dichloromethane. The extract was washed with aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), filtered with carbon, and concentrated to a syrup that failed to crystallize. This product was deacetylated with sodium methoxide in the usual manner, and the product (1·2 g., 44%) recrystallized from aqueous acetone to furnish prismatic needles (0·8 g.) of 2,4-O-*methylene*-D-glycero-D-gluco-*heptitol hemihydrate* that began to melt at 76° and melted completely at 128—130° (Found: C, 41·4; H, 7·5. $C_8H_{16}O_7,\frac{1}{2}H_2O$ requires C, 41·2; H, 7·35%). A solvent-free *product* was obtained by drying at 60° for 48 hr. or by recrystallization from absolute ethanol as fine needles, m. p. 129—130°, $[\alpha]_D^{20}$ −13·1° (*c* 1 in H_2O) (Found: C, 42·6; H, 7·3. $C_8H_{16}O_7$ requires C, 42·85; H, 7·2%).

When the acetolysis of tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol was carried out for 20 hr. at 5° a syrup was obtained, and this upon deacetylation gave a D-*glycero*-D-*gluco*-heptitol (36%) and only a small amount of its 2,4-*O*-methylene derivative.

Acetylation of the 2,4-*O*-methylene derivative with acetic anhydride and sodium acetate gave a product, which, after three recrystallizations from aqueous acetone, afforded prisms of the *penta*-O-*acetate* (0·5 g., 54%), m. p. 91—92°, $[\alpha]_D^{20}$ +9·8° (*c* 1 in $CHCl_3$) (Found: C, 49·55; H, 6·1; Ac, 49·4. $C_{18}H_{26}O_{12}$ requires C, 49·8; H, 6·0; Ac, 49·5%).

Oxidation of 2,4-O-*Methylene*-D-glycero-D-gluco-*heptitol with Periodate to* 2,4-O-*Methylene*-L-*xylose and Reduction of the Latter to* 2,4-O-*Methylenexylitol*.—2,4-O-Methylene-D-*glycero*-D-*gluco*-heptitol consumed 2·04 and 2·07 mol. of sodium metaperiodate and liberated 0·79 and 0·89 mol. of formic acid at the end of 24 and 120 hr. respectively. The amount of liberated formaldehyde, as determined by the method described by Reeves,[16] was 1·03 mol. The hydrated 2,4-O-methylene-D-*glycero*-D-*gluco*-heptitol (0·5 g.) was oxidized with an excess of sodium metaperiodate for 24 hr., the mixture was deionized and concentrated to 15 ml., and sodium borohydride (0·2 g.) in water (10 ml.) was added dropwise to the stirred solution. After an additional 45 min. at room temperature the mixture was kept overnight at 5° and then acidified with a few drops of acetic acid. Cations were removed with Amberlite IR-120 (H^+ form), and the aqueous solution was concentrated to a residue that was freed from boric acid by several evaporations with methanol. The resulting crystals, when filtered and washed with acetone, gave a product (0·30 g., 85%) which, after one recrystallization from ethanol, had m. p. 109—111° and was identified as 2,4-*O*-methylenexylitol by a mixed m. p. and by similar comparisons of its tri-*O*-acetyl and tri-*O*-toluene-*p*-sulphonyl derivatives with authentic specimens.[9]

6-O-*Methyl*-1,3:2,4:5,7-*tri*-O-*methylene*-D-glycero-D-gluco-*heptitol*.—A mixture of tri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol (3·5 g.), silver oxide (6 g.), Drierite (6 g.), methyl iodide (100 ml.), and a few crystals of iodine was boiled under reflux for 24 hr. Additional amounts of methyl iodide (50 ml.) and silver oxide (5 g.) were added and boiling was continued for another 24 hr. The warm methyl iodide solution was decanted, filtered, and concentrated, to yield the *O*-methyl compound (0·6 g.). The silver oxide residue was extracted repeatedly with warm dichloromethane, and the extract was concentrated to give a mixture (2·7 g.) of the *O*-methyl compound and starting material. This mixture, on further methylation, afforded a further amount (0·8 g.) of *O*-methyl compound and a mixture (1·4 g.); the latter, on remethylation, furnished more *O*-methyl compound (1·1 g.; total yield 2·5 g., 68%). The combined product was recrystallized from hot ethanol and then from hot water, furnishing needles of the O-*methyl ether* m. p. 232—234° (capillary tube, with partial sublimation), $[\alpha]_D^{20}$ −28·9° (*c* 0·25 in $CHCl_3$) (Found: C, 50·5; H, 7·2; OMe, 11·8. $C_{11}H_{18}O_7$ requires C, 50·4; H, 6·9; OMe, 11·8%).

6-O-*Methyl*-2,4-O-*methylene*-D-glycero-D-gluco-*heptitol*.—*O*-Methyltri-*O*-methylene-D-*glycero*-D-*gluco*-heptitol (1·4 g.) was dissolved in cold acetolyzing solution prepared from acetic anhydride (35 ml.), glacial acetic acid, (15 ml.) and concentrated sulphuric acid (1 ml.), left in an ice-bath for 30 min., and then poured on ice. The mixture was kept cold overnight before being neutralized with solid sodium hydrogen carbonate and extracted with dichloromethane

[16] Reeves, *J. Amer. Chem. Soc.*, 1941, **63**, 1476.

(800 ml.). The extract was washed with 5% aqueous sodium hydrogen carbonate and water, dried (Na_2SO_4), filtered with carbon, and concentrated. The resulting syrup (1·7 g., 68%) was deacetylated with sodium methoxide in the usual manner and yielded O-*methyl*-O-*methylene-heptitol* (0·78 g., 90%), which, after recrystallization from aqueous acetone, had m. p. 151—153°, $[\alpha]_D^{20}$ +11·8° (*c* 0·25 in water) (Found: C, 45·1; H, 7·8; OMe, 13·0. $C_9H_{18}O_7$ requires C, 45·4; H, 7·6; OMe, 13·0%). This was not oxidized by sodium metaperiodate in 68 hr.

Benzylidene Compounds [Mr. K. Buck]

Identifications were made on the basis of mixed m. p.s and comparison of infrared spectra. Paper and cellulose-column chromatography was performed with the organic phase of butanol–ethanol–water (4 : 1 : 5). Alumina of activity [6] Brockmann III was used.

Preparation of p-*Phenylazobenzoates.*[12]—A mixture of 1,3:2,4-di-*O*-benzylidene-D-glucitol (0·72 g.), *p*-phenylazobenzoyl chloride (1·5 g., 3 mols.) and pyridine (30 ml.) was boiled under reflux for 6 hr. Water (5 ml.) was then added to the mixture which, after 30 min., was cooled and poured into ice-water (500 ml.). The product was collected, dissolved in chloroform, and washed successively with water, 10% aqueous cadmium chloride (twice), water, and aqueous sodium hydrogen carbonate. The dried (Na_2CO_3) solution was passed through alumina to remove *p*-phenylazobenzoic acid, then evaporated and the residue was recrystallized from benzene–light petroleum to yield 1,3:2,4-*di*-O-*benzylidene* 5,6-*di*-O-p-*phenylazobenzoyl*-D-*glucitol* (1·1 g.), m. p. 263—265° after preliminary melting and resolidification at 230—240°. Resolidification of the product, m. p. 263—265°, gave a compound of m. p. 260—262·5° which on recrystallization afforded a product with the original melting characteristics. These modifications are probably dimorphs since they gave indistinguishable infrared spectra (Nujol mulls).

The esters in the Table were thus prepared and, with the above exception, they showed normal m. p. characteristics.

Analytical and other data for some p-*phenylazobenzoates.*

No. 1: Hexa-*p*-phenylazobenzoyl-D-glucitol.
No. 2: 2,4-*O*-Benzylidene-1,3,5,6-tetra-*O*-*p*-phenylazobenzoyl-D-glucitol.
No. 3: 1,3 : 2,4-Di-*O*-benzylidene-5,6-di-*O*-*p*-phenylazobenzoyl-D-glucitol.
No. 4: 1,3 : 2,4 : 5,7-Tri-*O*-benzylidene-6-O-*p*-phenylazobenzoyl-D-*glycero*-D-*gluco*-heptitol.
No. 5: Hepta-*p*-phenylazobenzoyl-D-*glycero*-D-*gluco*-heptitol.

				Found (%)			Required (%)		
No.	Yield (%)	M. p.	Formula	C	H	N	C	H	N
1	55 [a]	157·5—159°	$C_{84}H_{62}N_{12}O_{12}$	70·1	4·6	11·5	70·5	4·4	11·7
2	90	192—193	$C_{65}H_{50}N_8O_{10}$	70·8	4·3	10·1	70·8	4·6	10·15
3	72	263—265	$C_{48}H_{36}N_4O_8$	71·2	5·2	7·15	71·3	4·9	7·2
4	60 [a]	219—220	$C_{41}H_{36}N_2O_8$	72·0	6·0	3·9	71·9	5·3	4·1
5	68	188—189	$C_{98}H_{72}N_{14}O_{14}$	70·3	4·45	12·0	70·5	4·4	11·7

[a] Prepared at room temperature.

Attempts to perform *p*-phenylazobenzoylations at 0° resulted in partial esterification. Thus, for example, a solution of 2,4-*O*-benzylidene-D-glucitol (1·1 g.) and *p*-phenylazobenzoyl chloride (4·2 g., 4·4 mols.) in pyridine was stored at 0° for 2 days and then worked up as described above. The product was partly soluble in benzene. The insoluble portion, which appeared to be homogeneous on chromatography on alumina and required chloroform for elution, was recrystallized from pyridine–ethanol, yielding a 2,4-O-*benzylidenedi*-O-p-*phenylazobenzoyl*-D-*glucitol* (0·4 g., 14·3%), m. p. 249—250° (Found: C, 68·6; H, 5·3; N, 8·2. $C_{39}H_{34}N_4O_8$ requires C, 68·2; H, 5·0; N, 8·2%).

The benzene-soluble product was fractionated on alumina. Elution with benzene gave 2,4-*O*-benzylidene-1,3,5,6-tetra-*O*-*p*-phenylazobenzoyl-D-glucitol (0·54 g., 12·0%), m. p. 191—192·5° (from pyridine–ethanol). Subsequent elution with ether–benzene (1 : 4 v/v) and fractional crystallization of the product from benzene–light petroleum gave, as the less soluble fraction, a 2,4-O-*benzylidenetri*-O-p-*phenylazobenzoyl*-D-*glucitol* (0·5 g., 13·7%), m. p. 252—254° after recrystallization (Found: C, 69·6; H, 4·7; N, 9·7. $C_{52}H_{42}N_6O_9$ requires C, 69·8; H, 4·7; N, 9·4%), and as the more soluble fraction and after further chromatography on alumina a second *tri*-O-p-*phenylazobenzoate* (1·5 g., 41·1%), m. p. 210—213° (Found: C, 69·9; H, 4·85;

N, 9·2%). The infrared spectra (Nujol mulls) of the two tri-*O*-*p*-phenylazobenzoates differed particularly in the region 700—1100 cm.$^{-1}$, indicating that they are probably positional isomers. Evidence was obtained for the presence of a mono-*O*-*p*-phenylazobenzoate in the reaction mixture.

Fractionation of Mixtures of p-*Phenylazobenzoates.*—(*a*) A solution of hexa-*O*-*p*-phenylazobenzoyl-D-glucitol (*A*; 50 mg.), 2,4-*O*-benzylidene-1,3,5,6-tetra-*O*-*p*-phenylazobenzoyl-D-glucitol (*B*; 50 mg.) and 1,3:2,4-di-*O*-benzylidene-5,6-di-*O*-*p*-phenylazobenzoyl-D-glucitol (*C*; 50 mg.) in benzene was introduced on to alumina held in a tapered column (4 × 0·75 in.; Scientific Glass Co., New Jersey). The column was washed in the dark with benzene, yielding two zones. Extrusion of the column and extraction of the upper zone gave, after recrystallization, material *A* (63·8%), m. p. 157—158°. The extracted lower zone on further chromatography on alumina by development initially with benzene–ether (99 : 1 v/v) and subsequently with light petroleum (b. p. 60—80°) gave an upper zone from which material *B* (63% after recrystallization), m. p. 189—190°, was recovered and a lower zone which afforded material *C* (60% after recrystallization), m. p. 262—264°.

(*b*) A solution of 1,3:2,4:5,6-tri-*O*-benzylidene-D-glucitol (0·125 g.) in dioxan (11·25 ml.) and 0·5N-hydrochloric acid (1·25 ml.) was kept at 50° for 1·5 hr. Aqueous ammonia (*d* 0·88; 0·5 ml.) was then added, the solution was evaporated, and the residue was dried at 120° for 2 hr. and extracted with dry pyridine (*ca.* 40 ml.). The extract was evaporated and the residue esterified with pyridine (25 ml.) and *p*-phenylazobenzoyl chloride (0·75 g.). The product was fractionated on alumina as in (*a*), yielding *A* 43·8%, *B* 13·5%, and *C* 12·1%.

If the graded hydrolysis was continued for only 30 min. the proportions of products were: *A* 6·2%, *B* 21·3%, and *C* 47·4%.

Aqueous dimethyl sulphoxide and aqueous tetrahydrofuran were also suitable solvents for graded hydrolysis. It was important to use purified dioxan [17] in order to avoid contamination of the products with the mono- and di-*O*-*p*-phenylazobenzoates of ethane-1,2-diol. Complete removal of ammonium chloride and the excess of ammonia was also necessary in order to prevent subsequent formation of *p*-phenylazobenzamide [18] (m. p. 225—226°) and *p*-phenylazobenzonitrile [19] (m. p. 119—120°).

p-*Phenylazobenzoates of Ethane*-1,2-*diol.*—A mixture of *p*-phenylazobenzoyl chloride (0·243 g.), ethane-1,2-diol (62 mg.), and pyridine (5 ml.) was heated at 100° for 12 hr. The product, isolated by the usual procedure, was fractionated on alumina. Elution with benzene–ether (24 : 1 v/v) gave 1,2-di-*p*-phenylazobenzoyloxyethane [12] (0·125 g.), m. p. 216—217° (from benzene–light petroleum); subsequent elution with ethanol gave 2-*hydroxyethyl* p-*phenylazobenzoate* (0·025 g.), m. p. 131—132° (from benzene–light petroleum or aqueous ethanol) (Found: C, 66·6; H, 5·1; N, 10·2. $C_{15}H_{14}N_2O_3$ requires C, 66·7; H, 5·2; N, 10·4%).

Graded Acidic Hydrolysis of Derivatives of D-glycero-D-gluco-*Heptitol.*—(*a*) 0·05N-Hydrochloric acid (0·375 ml.) was added to a boiling solution of tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol (0·125 g.) in dioxan (12·5 ml.) and boiling was continued for 30 min. The solution was neutralized with concentrated aqueous ammonia and evaporated to dryness, and the residue was extracted with boiling water, leaving unchanged starting material (19·8 mg., 15·8%), m. p. 267—271°. The aqueous extract was evaporated and the residue was esterified with pyridine (25 ml.) and *p*-phenylazobenzoyl chloride (0·7 g.). Chromatography on alumina of the mixed product isolated by the usual procedure revealed several components, none of them crystalline. No suitable solvent system could be found for paper chromatography of the *p*-phenylazobenzoates.

(*b*) Tri-*O*-benzylidene-*O*-*p*-phenylazobenzoyl-D-*glycero*-D-*gluco*-heptitol (95·8 mg.) in dioxan (10 ml.) and 0·1N-sulphuric acid (1 ml.) was boiled under reflux for 1 hr., then cooled and poured into ice-water. The mixture was extracted with chloroform and the combined and dried ($MgSO_4$) extracts were evaporated. The residue was chromatographed on alumina. Elution with benzene gave unchanged starting material (19·4 mg., 20·2%), m. p. 200—205°. Subsequent elution with ether yielded a *di*-O-*benzylidene*-O-p-*phenylazobenzoyl*-D-glycero-D-gluco-*heptitol* (13·3 mg., 15·9%), m. p. 226—227° (from aqueous methanol) (Found: C, 68·8; H, 5·7; N, 4·8. $C_{34}H_{32}N_2O_8$ requires C, 68·5; H, 5·4; N, 4·7%). Further coloured components were eluted with methanol and aqueous methanol, but none was obtained crystalline.

[17] Vogel, " Textbook of Practical Organic Chemistry," Longmans, Green & Co., London, 1956, p. 177.
[18] Jacobson and Steinbrenk, *Annalen*, 1898, **303**, 385.
[19] Freundler, *Compt. rend.*, 1906, **142**, 1153.

(*c*) A solution of tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol (50 mg.) in boiling dioxan (5 ml.) was treated with 0·05N-sulphuric acid (0·15 ml.). At intervals of 10 min. during 110 min. samples were withdrawn, neutralized with concentrated aqueous ammonia, and analyzed by paper chromatography. Sodium metaperiodate–starch iodide [20] and 2,4-dinitrophenylhydrazine–sulphuric acid were used for detection. The accumulation of D-*glycero*-D-*gluco*-heptitol (R_F 0·10) and disappearance of the di-*O*-benzylidene derivative (R_F 0·90) was clearly revealed; in addition, components with R_F 0·15, 0·70, and 0·90 severally were seen. Detection with silver nitrate [14] revealed other components.

Tri-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol (1·5 g.) was hydrolyzed as above for 1 hr. and the neutralized solution was evaporated. Extraction of the residue with boiling water left unchanged starting material (27·4 mg., 1·8%), m. p. 240—250°. The aqueous solution was extracted with ether (50 ml.) to remove benzoic acid and benzaldehyde, and then examined by paper chromatography. Products with R_F 0·10, 0·29, 0·35, 0·40, 0·68, 0·70, 0·75, and 0·9 severally were detected with silver nitrate.[14] The last three compounds were also detected with 2,4-dinitrophenylhydrazine. Exhaustive extraction of the aqueous solution with ether removed the component of R_F 0·9 and partially removed those with R_F 0·10, 0·70, and 0·75. The product from an unextracted aqueous solution was dissolved in the chromatographic organic phase (10 ml.), and storage of this solution gave crystals (200 mg.), m. p. 130—132°, which comprised mainly D-*glycero*-D-*gluco*-heptitol. The mother-liquor was fractionated (25 ml. fractions) on a column of cellulose powder (48 × 4 cm.):

Fractions 1—12 yielded a syrup (12·5 mg.) containing a product with R_F 0·90.

Fractions 13—18 gave a product (75·4 mg.) which contained components of R_F 0·55, 0·70, 0·75, 0·90. Fractional crystallization from methanol gave a compound (8·0 mg.), m. p. 209—210°, R_F 0·9 (Found: C, 66·05; H, 7·0. Calc. for $C_{21}H_{24}O_7$: C, 65·0; H, 6·2%), which was probably an impure di-*O*-benzylidene-D-*glycero*-D-*gluco*-heptitol.

Fractions 19—20 afforded a syrup (44·7 mg.) which contained components with R_F 0·55, 0·70, and 0·75. A solution of the syrup in water (5 ml.) containing sodium metaperiodate (0·3 g.) and sodium hydrogen carbonate (0·1 g.) was stored overnight at room temperature and then extracted with chloroform. The extract was evaporated and the residue was treated with ~N-hydrochloric acid at 100° for 15 min. The residue obtained by evaporation of the neutralized hydrolysate was subjected to paper chromatography and paper ionophoresis [21] in a borate buffer (pH 10) which revealed (aniline hydrogen phthalate) a pentose with mobility (R_G 1·49, M_G 0·96) identical with that of D-xylose and different from that of D-ribose (R_G 1·74, M_G 0·80).

Fractions 21—34 yielded a syrup (0·209 g.) which contained components with R_F 0·16, 0·19, 0·29, 0·34, 0·42, 0·55, and 0·70.

Fractions 35—44 gave D-*glycero*-D-*gluco*-heptitol (*ca.* 50 mg.), R_F 0·1.

When D-*glycero*-D-*gluco*-heptitol was treated with dioxan–hydrochloric acid, as for the tri-*O*-benzylidene derivative, traces of compounds with R_F 0·16, 0·19, and 0·30 were formed. No products resulted from similar treatment of D-glucitol.

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