TWO SYNTHESES OF 1,5:3,6-DIANHYDRO-2,4-*O*-METHYLENE-D-GLUCITOL: STABILITY OF THE METHYLENE ACETAL BRIDGE TOWARD AQUEOUS ACID[1]

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ABSTRACT

1,5:3,6-Dianhydro-2,4-*O*-methylene-D-glucitol has been synthesized by two wholly independent routes. The methylene acetal bridge was found to be stable in hot water and dilute aqueous acid and thus differs from the methylene bridges in 1,4:3,6-dianhydro-2,5-*O*-methylene-D-mannitol and in the D-iditol analogue of the latter compound. It is suggested that this difference may be due to the ease of folding of the glucitol derivative as compared to the rigidity of the mannitol and iditol structures.

A previous (1) publication has indicated that extreme molecular rigidity occurs in cyclic compounds such as 1,4:3,6-dianhydro-2,5-*O*-methylene-D-mannitol (I) and 1,4:3,6-dianhydro-2,5-*O*-methylene-D-iditol (II) so that the strain within the bonds of I and II cannot be dissipated by folding or twisting of these bonds. It follows that these substances should be unstable and cleavage of the most highly strained group within the molecules I and II would occur. It was shown (1) that the methylene acetal groups in I and II were extremely unstable and hydrolytic cleavage occurred with great facility.

It was suggested (1) that the substance 2,5-*O*-methylene-D-mannitol (III), being capable of folding and twisting to overcome internal strain, should be stable to the hydrolytic conditions used for I and II. This was found to be the case.

Further work was undertaken to investigate the feasibility of the hypothesis and a dianhydro-*O*-methylene hexitol was synthesized that would not possess great molecular rigidity. This substance, 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol (IV), was found to be very stable toward hot water and 0.01 *N* hydrochloric acid. This stability was expected on the basis of the views postulated previously (1), as examination of a model of IV shows that the tricyclic structure may fold or twist to overcome internal strain within the molecule and the methylene acetal group should then be stable.

Vargha (2) showed that 2,4-*O*-benzylidene-1,6-di-*O*-*p*-tolylsulphonyl-D-glucitol (V), on treatment with one molecular equivalent of sodium methoxide, lost one *p*-tolylsulphonyl group with the formation of the ethylene oxide derivative, 5,6-anhydro-2,4-*O*-benzylidene-1-*O*-*p*-tolylsulphonyl-D-glucitol (VI). Application of Vargha's method to 2,4-*O*-methylene-1,6-di-*O*-*p*-tolylsulphonyl-D-glucitol (VII) yielded 5,6-anhydro-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (VIII). The ethylene oxide ring was very easily cleaved by dilute hydrochloric and sulphuric acids to yield 6-chloro-6-deoxy-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (IX) and 2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (X) respectively. The 6-chloro derivative (IX) on treatment with

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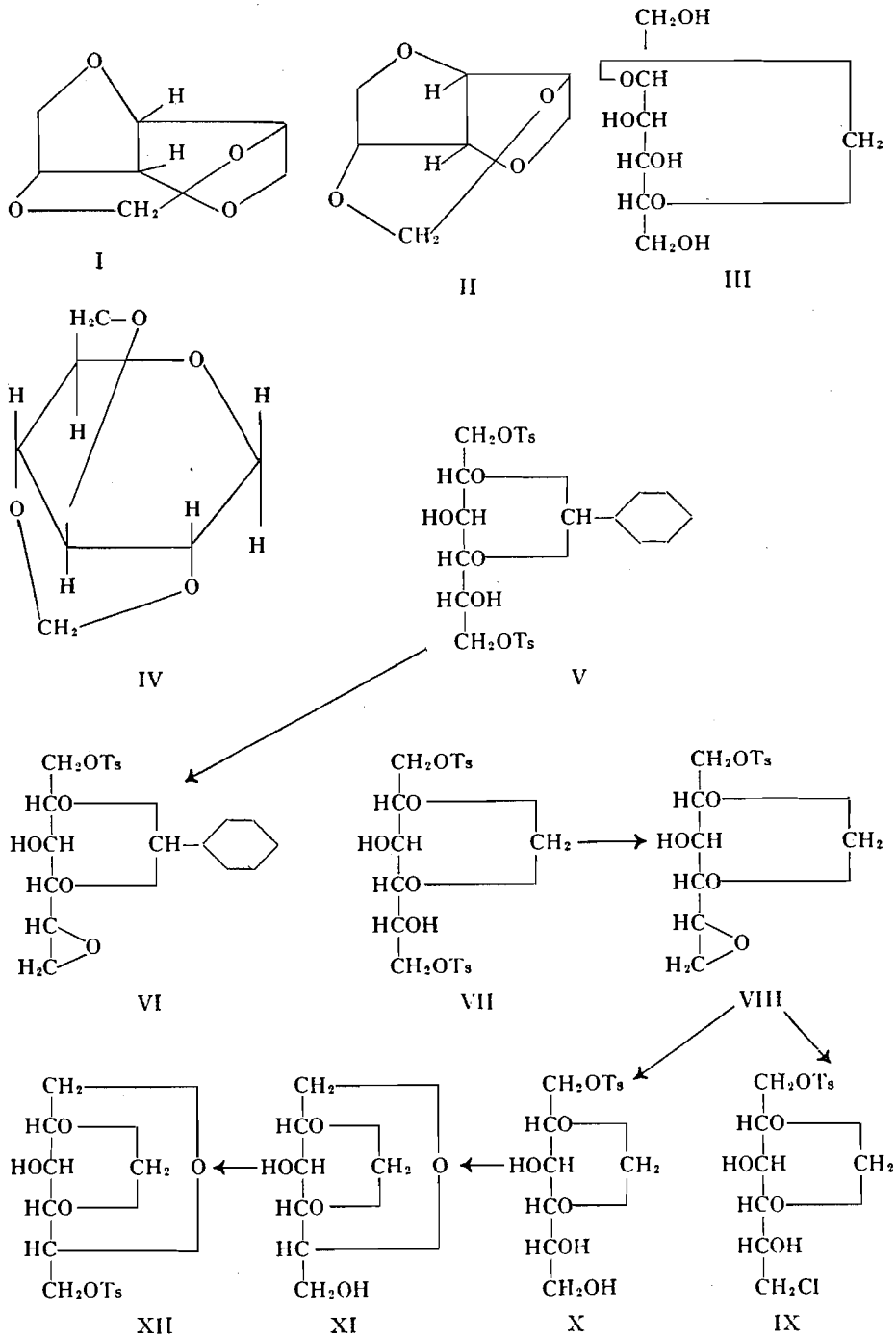
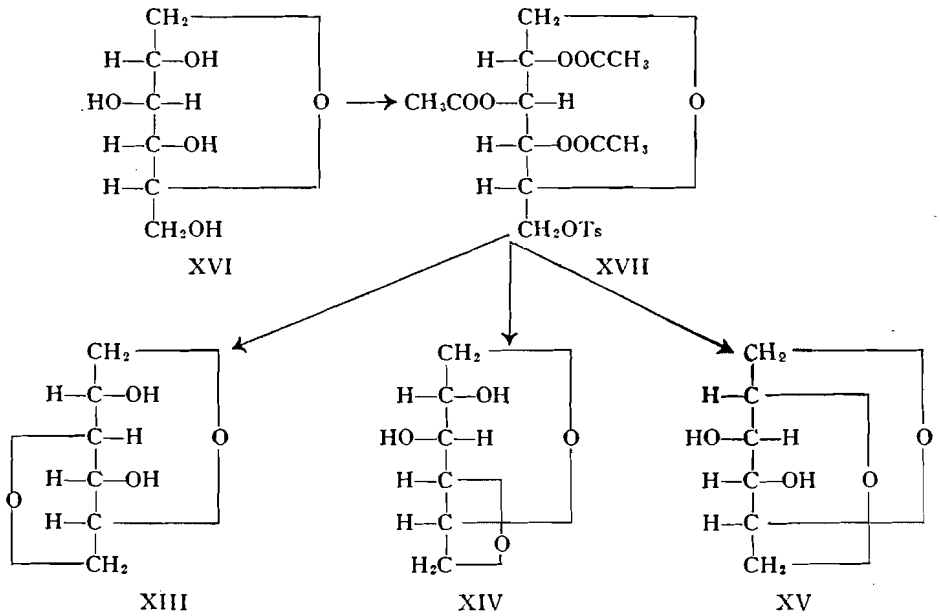


one molecular equivalent of sodium methoxide yielded VIII. This showed that the chlorine atom was situated either on the terminal carbon atom or on C-5, but most probably on the terminal position since otherwise an L-iditol derivative would be obtained. Additional proof of the absence of an hydroxyl group on C-6 was obtained when tritylation of the chloro derivative IX did not occur.

The substance (X) reduced a glacial acetic acid solution of lead tetraacetate to the extent of one mole per mole oxidant thus showing the presence of vicinal hydroxyl groups in X. Monotosylation of X with tosyl chloride in pyridine yielded 2,4-*O*-methylene-1,6-di-*O*-*p*-tolylsulphonyl-D-glucitol (VII). Therefore X was a glucitol derivative, which was expected since cleavage of an anhydro ring which is on a terminal carbon atom occurs without Walden inversion. Saponification of X with aqueous sodium hydroxide yielded an anhydro derivative (XI) that reacted readily with trityl chloride in pyridine. Lead tetraacetate was not reduced, thereby indicating the absence of vicinal hydroxyl groups. Thus the anhydro ring could not be either 1,6 or 1,3. The latter ring would be unlikely on steric grounds. Therefore the substance had to be 1,5-anhydro-2,4-*O*-methylene-D-glucitol (XI). Treatment of XI with tosyl chloride in pyridine yielded the monotosylate XII, 1,5-anhydro-2,4-*O*-



methylene-6-*O*-*p*-tolylsulphonyl-D-glucitol, which on saponification with sodium methoxide yielded 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol or 2,4-*O*-methylene-*neo*glucide* (IV). This latter substance on treatment with hot water or 0.01 *N* hydrochloric acid was recovered unchanged. Hydrolysis of

*The prefix "neo" is used here to indicate analogous ring structure with neo-mannide, which is 1,5:3,6-dianhydro-D-mannitol.

the methylene group occurred only on prolonged heating in 1 *N* hydrochloric acid. The tricyclic ring structure of IV is therefore relatively stable.

Synthesis of 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol (IV) by a different route served to confirm its structure. The D-glucitol derivative D-*neo*-glucide* (XIII) was synthesized by a route that made possible one of three structures (XIII, XIV, XV). 1,5-Anhydro-D-glucitol (polygalitol) (XVI), whose structure is known with certainty, was condensed with one molecular equivalent of tosyl chloride in pyridine and then acetylated with acetic anhydride. Isolation of the reaction product yielded a crystalline derivative that had three acetyl groups. Saponification of the latter, 2,3,4-tri-*O*-acetyl-1,5-anhydro-6-*O*-*p*-tolylsulphonyl-D-glucitol (XVII), with sodium methoxide yielded a product that could be XIII, XIV, or XV. The compounds XIV and XV having 1,2-glycol groups should be oxidized by lead tetraacetate. However, since this substance was stable to the action of this oxidant, it is very probably XIII. The product of the reactions described above,1,5:3,6-dianhydro-D-glucitol (XIII), was treated with formaldehyde solution and hydrochloric acid and the isolated product proved to be identical with 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol (IV), prepared earlier.

EXPERIMENTAL

5,6-Anhydro-2,4-O-methylene-1-O-p-tolylsulphonyl-D-glucitol (VIII)

2,4-*O*-Methylene-1,6-di-*O*-*p*-tolylsulphonyl-D-glucitol (VII) (47.4 gm.) was dissolved in chloroform (500 cc.). Methanol (75 cc.) in which sodium (2.2 gm.) had been dissolved was added to the cold (0°) chloroform solution. A gel formed immediately and the mixture was allowed to stand overnight at 5°. The small excess of sodium methoxide was converted to carbonate, and water (100 cc.) was added to dissolve the sodium salts. The chloroform layer was separated, dried over anhydrous sodium sulphate, and concentrated *in vacuo* to a thick sirup which was then dissolved in a small volume of 99% ethanol. The solution was kept at −15° overnight and the crystalline mass, thus obtained, was washed with a little cold 99% ethanol and finally dried. The yield was 24 gm. (80%) and melting point was 94–95.5°. This substance was pure enough for subsequent work.

A sample was dissolved in a hot mixture of ethyl acetate–isopropyl ether (1:3) and, after cooling slowly to 20°, crystallization occurred in the form of clusters of rosettes. The melting point was 95–95.5°; $(\alpha)_D^{24°}$ −4.4° ($CHCl_3$; *c*, 5.6724). Anal.: Calc. for $C_{14}H_{18}SO_7$: C, 50.91; H, 5.45; S, 9.69. Found: C, 50.80; H, 5.86; S, 9.6.

Effect of Hydrochloric Acid on 5,6-Anhydro-2,4-O-methylene-1-O-p-tolylsulphonyl-D-glucitol (VIII)

The compound above (5 gm.) was heated to boiling for about one minute with 8% hydrochloric acid (120 cc.). The starting material melted, dissolved, and precipitation occurred. The precipitate was filtered, washed with water to remove all traces of acidity, and then air-dried. The yield was 4.1 gm. (74.5%). The crude product was recrystallized from ethyl acetate and the

melting point was 162–162.5° and rotation $(\alpha)_D^{25°}$ –21.2° (pyridine; *c*, 2.9048). Anal.: Calc. for $C_{14}H_{19}SClO_7$: C, 45.75; H, 5.17; S, 8.7. Found: C, 45.68; H, 5.22; S, 8.7.

A sample (1 gm.) of the above, 6-chloro-6-deoxy-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (IX), was suspended in chloroform (100 cc.) and 0.3 *M* sodium methoxide in methanol (10 cc.) was added. The solid dissolved and precipitation of sodium chloride occurred. The reaction mixture was allowed to stand overnight at 5°, the small excess sodium methoxide converted to carbonate, and the mixture washed once with a small volume of water to remove sodium salts. The chloroform solution was dried over anhydrous sodium sulphate, the solvent removed *in vacuo*, and the resulting sirup dissolved in a little 95% ethanol and the solution cooled to −15°. Precipitation occurred and water was added so that most of the product separated as a crystalline mass. The air-dried substance melted broadly at 82–92° and was recrystallized from 250 cc. of boiling isopropyl ether in a yield of 0.7 gm. (77%). Alone or in admixture with 5,6-anhydro-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol it melted at 95–96°.

*Nonreaction of Trityl Chloride with 6-Chloro-6-deoxy-2,4-O-methylene-1-O-p-tolylsulphonyl-*D*-glucitol (IX)*

A sample (0.3 gm.) of the above substance was dissolved in anhydrous pyridine (5 cc.) and trityl chloride (0.23 gm., 1 mol. equiv.) was added. The mixture was allowed to stand for three days at 24° and was then added to cold water. The crystalline substance that separated was removed by filtration and washed well with water to remove most of the pyridine. After drying in air, the solid was extracted for one hour in boiling isopropyl ether (50 cc.) and filtered. The insoluble fraction (0.24 gm.) melted at 160–162° when mixed with the starting material. The isopropyl ether filtrate was concentrated to dryness and the solid was found to be slightly impure tritanol by a mixed melting point determination with authentic tritanol. This experiment proved that the terminal carbon atom did not have an hydroxyl group and the starting material was thus 6-chloro-6-deoxy-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (IX).

*2,4-O-Methylene-1-O-p-tolylsulphonyl-*D*-glucitol (X)*

5,6-Anhydro-2,4-*O*-methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (52 gm.) was added to boiling water (1500 cc.). Concentrated sulphuric acid (15 cc.) dissolved in water (60 cc.) was added and the molten glucitol derivative (X), dissolved in about 10 min. The clear solution was quickly neutralized with barium carbonate and the barium sulphate and carbonate were removed by filtration through a thin layer of decolorizing charcoal. The clear filtrate was then concentrated *in vacuo* to a thick sirup and the latter was dissolved in hot 95% ethanol and a slight turbidity removed by filtration through a layer of charcoal. The alcoholic filtrate was then concentrated to dryness and traces of water were removed by codistillation with 99% ethanol. The colorless sirup was dissolved in 99% ethanol, petroleum ether (30–60°) was added to turbidity, and the solution cooled at −15°. Soft, feathery crystals melting at 113–

114.5° separated. The crude product was recrystallized from the same solvent mixture with practically no loss and then melted at 115–115.5°. It was soluble in acetone, ethanol, methanol, chloroform, and hot water. It was insoluble in ether and petroleum ether. It rotated $(\alpha)_D^{24°}$ –0.24° (acetone; *c*, 2.2876). Anal.: Calc. for $C_{14}H_{20}SO_8$: C, 48.27; H, 5.75; S, 9.2. Found: C, 48.15; H, 5.91; S, 9.1.

*Conversion of 2,4-O-Methylene-1-O-p-tolylsulphonyl-*D*-glucitol (VIII) into 2,4-O-Methylene-1,6-di-O-p-tolylsulphonyl-*D*-glucitol (VII)*

2,4-*O*-Methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (1 gm.) was dissolved in anhydrous pyridine (10 cc.). The solution was cooled to −5° and tosyl chloride (0.55 gm.) was added. The solution was allowed to stand for three hours after warming up to room temperature (24°) and it was then added to cold water. The crystalline product that separated was removed by filtration, washed with water on the filter, dried, and then recrystallized from 95% ethanol. It melted at 129–130° and the mixed melting point with authentic 2,4-*O*-methylene-1,6-di-*O*-*p*-tolylsulphonyl-D-glucitol was 128–130°.

*Lead Tetraacetate Oxidation of 2,4-O-Methylene-1-O-p-tolylsulphonyl-*D*-glucitol*

A sample of the compound above (0.2727 gm.)was dissolved in 0.0329 *M* lead tetraacetate in glacial acetic acid in a 100.0 ml. volumetric flask and made up to volume with the tetraacetate solution. After 1, 2, and 24 hr. 0.94, 0.99, and 1.06 mol. equiv. of lead tetraacetate were consumed.

*1,5-Anhydro-2,4-O-methylene-*D*-glucitol (2,4-O-Methylene-polygalitol)*

2,4-*O*-Methylene-1-*O*-*p*-tolylsulphonyl-D-glucitol (10 gm.) was dissolved in freshly boiled water (200 cc.). Sodium hydroxide (1.1 gm.) was added and the solution heated on the steam bath in the absence of carbon dioxide. A few drops of 1% phenolphthalein was added and after two hours the reaction mixture became neutral. The solution was then concentrated *in vacuo* and traces of water were removed by codistillation with 99% ethanol. The white crystalline residue was heated with chloroform (400 cc.) and filtered to remove the insoluble sodium *p*-toluenesulphonate. The chloroform filtrate was concentrated to about 200 cc. and petroleum ether (30–60°) was added until a faint turbidity was formed. Crystallization occurred almost immediately and the mixture was cooled to −15° overnight to assure complete crystallization. The product was found to be pure, as an additional recrystallization did not change the melting point of 135–135.5°. It rotated $(\alpha)_D^{19°}$ –24.2° (H_2O; *c*, 2.0632). Anal.: Calc. for $C_7H_{12}O_5$: C, 47.72; H, 6.82. Found: C, 47.50; H, 6.93.

*1,5-Anhydro-2,4-O-methylene-6-O-trityl-*D*-glucitol*

1,5-Anhydro-2,4-*O*-methylene-D-glucitol (3 gm.) and trityl chloride (4.7 gm.) were dissolved in anhydrous pyridine (30 cc.). The reaction mixture was allowed to stand three days at room temperature (24°). About 5 cc. water were added to dissolve the separated pyridinium chloride and the mixture was then added to cold water. The sirup that separated was dissolved in chloroform and the chloroform solution washed several times with water. The

chloroform solution was dried over anhydrous sodium sulphate, filtered and concentrated *in vacuo* to remove the solvent and traces of pyridine. The light-yellow sirup was dissolved in 99% ethanol (100 cc.) and the solution was treated with decolorizing charcoal and finally filtered. The colorless residue formed a glass that would not crystallize from any of the solvents used. Yield was 4.8 gm. (68%) and decomposition of 1.13 gm. of the substance with concentrated sulphuric acid yielded 0.68 gm. tritanol, showing the presence of one terminal hydroxyl group as the theoretical yield is 0.70 gm.

*1,5-Anhydro-2,4-O-methylene-6-O-p-tolylsulphonyl-*D*-glucitol (XII)*

1,5-Anhydro-2,4-*O*-methylene-D-glucitol (20 gm.) was dissolved in anhydrous pyridine (200 gm.) and the solution was cooled to 0°. *p*-Toluenesulphonyl chloride (21.0 gm.) was added and the mixture was allowed to stand four hours at 24°. The mixture was concentrated to $\frac{1}{4}$ vol. and the sirupy residue mixed with cold water (500 cc.). The sirup did not solidify; it was dissolved in chloroform and the chloroform solution washed twice with ice-cold 2% sulphuric acid to remove pyridine and once with water. The chloroform solution was dried over anhydrous sodium sulphate, filtered, and concentrated to dryness. A white crystalline substance separated in a yield of 31 gm. (81%). This was dissolved in hot 95% ethanol (200 cc.) and a trace of color removed by means of decolorizing charcoal. The clear solution was allowed to cool and crystallization occurred. The product melted at 118–119°. Further recrystallization from ethanol did not change the melting point. It rotated $(\alpha)_D^{23°}$ –16.6° ($CHCl_3$; *c*, 6.0092). Anal.: Calc. for $C_{14}H_{18}SO_7$: C, 50.91; H, 5.45; S, 9.69. Found: C, 50.83; H, 5.66; S, 9.7.

*1,5:3,6-Dianhydro-2,4-O-methylene-*D*-glucitol (IV)*

1,5-Anhydro-2,4-*O*-methylene-6-*O*-*p*-tolylsulphonyl-D-glucitol (15 gm.) was dissolved in chloroform (250 cc.) and sodium (2 gm.) in methanol (100 cc.) was added. The mixture became milky and after about 10 min. glistening crystals of sodium *p*-toluenesulphonate separated. The slight excess of sodium methoxide was converted to carbonate with carbon dioxide and the mixture was then concentrated to dryness *in vacuo*. The dry solid mass was broken up and extracted twice with boiling chloroform and the mixture filtered. The clear, colorless filtrate was concentrated to dryness and the solid residue was soluble in hot ether and hot ethyl acetate. Recrystallized once from ethyl acetate and twice from ether it melted at 79.5–80° and rotated $(\alpha)_D^{22°}$ –44.9° ($CHCl_3$; *c*, 1.112). The yield after recrystallization was 5.7 gm. (79%). Anal.: Calc. for $C_7H_{10}O_4$: C, 53.16; H, 6.33. Found: C, 53.07; H, 6.47.

*2,3,4-Tri-O-acetyl-1,5-anhydro-6-O-p-tolylsulphonyl-*D*-glucitol (XVIII)*

2,3,4-6-Tetra-*O*-acetyl-1,5-anhydro-D-glucitol (24.5 gm.) was dissolved in chloroform (300 cc.). Methanolic sodium methoxide (25 cc. of 0.2 *N*) was added and the mixture allowed to stand 36 hr. at 5°. The sodium methoxide was converted to carbonate and the solvents removed *in vacuo*. The thick sirupy product containing sodium carbonate and bicarbonate was dissolved in hot anhydrous pyridine (45 cc.) and after the solution was cooled to 0°,

tosyl chloride (13.0 gm.) was added. The reaction mixture was then allowed to stand for two hours at 22° and again cooled to 0°. Acetic anhydride (30 cc.) was added and the reaction mixture allowed to stand overnight at room temperature. The mixture was added to cold water and a sirup separated. The sirup did not crystallize after two days and it was therefore extracted with chloroform. The chloroform solution was washed with cold 5% hydrochloric acid to remove pyridine, washed twice with water, and finally dried over anhydrous sodium sulphate. The mixture was filtered and the chloroform filtrate concentrated *in vacuo*. The resulting sirup was dissolved in ether and the ether solution on cooling and scratching deposited crystals. Petroleum ether (30–60°) was added to force complete crystallization. The crude product was then recrystallized from 95% ethanol and it melted at 143.5–144.5°. It rotated $(\alpha)_D^{24°}$ 62.2° ($CHCl_3$; 1,2; *c*, 1.3816). The yield was 19.9 gm. (61%). Anal.: Calc. for $C_{19}H_{24}SO_{10}$: C, 51.35; H, 5.45; S, 7.27; Acetyl, 26.8. Found: C, 51.1; H, 5.7; S, 7.3; Acetyl, 26.5.

*Conversion of 2,3,4-Tri-O-acetyl-1,5-anhydro-6-O-p-tolylsulphonyl-*D*-glucitol to 1,5:3,6-Dianhydro-*D*-glucitol* (D-*Neoglucide*) (*XIII*)

2,3,4-Tri-*O*-acetyl-1,5-anhydro-6-*O*-*p*-tolylsulphonyl-D-glucitol (11.4 gm.) was dissolved in anhydrous methanol (150 cc.) containing sodium (0.5 gm.) in solution. The reaction mixture was allowed to stand two hours at 24° and then heated to boiling under reflux for an additional two hours. The solution was cooled to 10°, the slight excess of sodium methoxide neutralized with dilute sulphuric acid, and the neutral solution concentrated to dryness *in vacuo*. The resulting gummy mass was heated with chloroform (250 cc.) and filtered. The residue consisting mainly of sodium *p*-toluenesulphonate was extracted once with hot chloroform (75 cc.) and the combined filtrates were concentrated *in vacuo*. The resulting sirup, which was soluble in ethyl acetate, chloroform, methanol, ethanol, acetone, water, and dioxane, was heated with isopropyl ether (120 cc.) and the solution was slowly concentrated until it became turbid. Scratching the flask caused immediate precipitation. The solid mass was removed by filtration and it was recrystallized once more from a large volume of isopropyl ether. The melting point was 150–152° and the rotation was $(\alpha)_D^{24°}$ 4.1° (water: 1; 2; *c*, 1.6116). The yield was 4.9 gm. (67.5%). Anal.: Calc. for $C_6H_{10}O_4$: C, 49.25; H, 6.87. Found: C, 49.08; H, 6.97.

Lead Tetraacetate Oxidation of D-*Neoglucide* (*XIII*)

A sample (0.4062 gm.) of D-neoglucide was dissolved in 0.543 *M* lead tetraacetate in glacial acetic acid solution and then made up to 100.0 ml. in a volumetric flask with the same solution. The lead tetraacetate solution was not reduced after 2, 24, and 48 hr. This indicated the absence of a 1,2-glycol group.

Methyleneation of D-*Neoglucide*

A sample (0.3 gm.) of D-neoglucide was dissolved in 37% aqueous formaldehyde (1 cc.) and concentrated hydrochloric acid (1 cc.). The reaction mixture was allowed to stand for 20 hr. at 40–45° and the hydrochloric acid removed

with silver carbonate. Water (50 cc.) was added and the mixture filtered. The filtrate was treated with hydrogen sulphide to remove dissolved silver ions and the silver sulphide removed by filtration through a thin layer of charcoal. The filtrate was concentrated to dryness *in vacuo* and the resulting colorless sirup was dissolved in ether (3 cc.) and seeded with a crystal of 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol. The mixture was cooled to −20° for 48 hr. The crystalline product was filtered and recrystallized once more from a small volume of ether. The yield was 0.11 gm. (35%) and the product, in admixture with a sample of 1,5:3,6-dianhydro-2,4-*O*-methylene-D-glucitol, prepared as described earlier, melted at 77–80°.

Effect of Sodium Periodate and Lead Tetraacetate on 1,5:3,6-Dianhydro-2,4-O-methylene-D-glucitol (IV)

Samples of the above (IV) did not reduce either standard periodate or lead tetraacetate. This showed the absence of 1,2-glycol groups.

Effect of Acetic Anhydride on 1,5:3,6-Dianhydro-2,4-O-methylene-D-glucitol (IV)

A sample (2 gm.) of (IV) was dissolved in acetic anhydride (5 cc.) and anhydrous pyridine (5 cc.) was added. The reaction mixture was allowed to stand for 72 hr. at 23° and then converted to a thick sirup *in vacuo*. The sirupy residue was dissolved in chloroform and the chloroform solution washed once with ice-cold 2% sulphuric acid, once with saturated ice-cold sodium bicarbonate, and then with water. The chloroform solution was dried over anhydrous sodium sulphate, filtered, and concentrated to dryness *in vacuo*. The white solid residue was recrystallized once from hot ether. The yield was 1.6 gm. (80%) and the mixed melting point with the starting material (IV) was 79–80°. This indicated the absence of hydroxyl groups.

Effect of Hot Water on 1,5:3,6-Dianhydro-2,4-O-methylene-D-glucitol (IV)

A sample of the above (0.4 gm.) was dissolved in water (50 cc.) and boiled under reflux for one hour. The water was removed *in vacuo* and the distillate did not give a dimethone test for formaldehyde. The residue on recrystallization from ether was found to be unchanged starting material in a yield of 0.38 gm. (96%).

Effect of 0.01 N Hydrochloric Acid on 1,5:3,6-Dianhydro-2,4-O-methylene-D-glucitol (IV)

A sample of the above (0.35 gm.) was heated under reflux in 0.01 *N* hydrochloric acid (50 cc.) for one hour. The solution was neutralized with silver carbonate and then filtered. The filtrate was treated with hydrogen sulphide to remove traces of silver ions and after filtration the filtrate was concentrated to dryness and the white residue recrystallized from ether. The yield was 0.28 gm. (82%) and the mixed melting point with starting material was 78–80°.

Effect of 1 N Hydrochloric Acid on IV

The above experiment was repeated with 0.3 gm. of IV and 1 *N* hydrochloric acid. After one hour a trace of formaldehyde was formed. The solution was

then slowly distilled in a stream of nitrogen and the volume was kept constant by addition of distilled water. After six hours all the formaldehyde was evolved and 0.47 gm. (86%) of the dimethone of formaldehyde was isolated, washed, and dried. It melted at 187–189° and the melting point was not depressed with authentic formaldehyde dimethone. The residue in the distilling flask was neutralized with silver carbonate and after filtration the traces of silver ions were removed as sulphide. The filtrate was concentrated to dryness and the cloudy sirup dissolved in chloroform; the latter solution was treated with charcoal and then filtered. The clear, colorless filtrate was concentrated *in vacuo* to a thick sirup. The sirup was extracted with a large volume of boiling isopropyl ether. The solvent was allowed to evaporate slowly and crystallization occurred. The oily crystals were filtered and recrystallized once more from isopropyl ether. The yield was 0.13 gm. (48%) and the melting point was 150–152°. A mixed melting point determination with authentic 1,5:3,6-dianhydro-D-glucitol showed identity.

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