11. *Anhydrides of Polyhydric Alcohols. Part XVI.* The Action of Phenols on Some Ethylene Oxide Derivatives.*

By G. P. McSweeney, L. F. Wiggins, and D. J. C. Wood.

A study has been made of.the action of certain phenols on 1 : 2-5 : 6-diepoxyhexane, 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol, and 1 : 3-2 : 4-diethylidene 5 : 6-anhydrosorbitol. The products obtained are designated as 1 : 6-diaryloxyhexane-2 : 5-diol, 1 : 6-diaryl 3 : 4-*iso*propylidene mannitol, and 6-aryl 1 : 3-2 : 4-diethylidene sorbitol respectively. The phenyl groups are attached to the primary carbon atoms since, when propylene oxide is treated in an exactly similar manner, the product is proved, by an alternative synthesis, to be 1-phenoxypropan-2-ol. The product of the action of phenol on 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol is synthesized by an alternative route which indicates that it is 1 : 6-diphenyl 3 : 4-*iso*propylidene mannitol.

Earlier communications of this series have recorded some reactions of 1 : 2-5 : 6-diepoxyhexane (I), 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol (II) (*J.*, 1950, 1566; 1946, 384), and 1 : 3-2 : 4-diethylidene 5 : 6-anhydrosorbitol (III) (*J.*, 1946, 388). This work has now been extended to a study of the behaviour of these ethylene oxide derivatives towards various phenols.

It is known that ring fission of ethylene oxide ring compounds by phenols may be brought about under a variety of conditions. For example, a slow combination occurs when phenols and ethylene oxide itself are heated under pressure (Roithner, *Monatsh.*, 1894, **15**, 665); reaction is more rapid in the presence of an alkali-metal derivative of the phenol in a solvent such as water or alcohol (Boyd and Marle, *J.*, 1910, 1788; 1914, 2117). In the present work the reactions were effected by heating the appropriate phenol with the epoxy-compound in dry benzene solution in the presence of a suspension of the sodium derivative of the phenol, usually for about 7 hours. The products were isolated by addition of water and in most cases were crystalline.

The treatment of 1 : 2-5 : 6-diepoxyhexane (I) with phenol led to a crystalline product which was separated by fractional recrystallisation into approximately equal amounts of two diphenoxyhexanediols. Each isomeride gave rise to crystalline diacetyl and ditoluene-*p*-sulphonyl derivatives. *p*-Cresol and (I) also gave a mixture of two solid di-*p*-tolyloxyhexanediols, each of which gave a crystalline diacetate. With *m*-cresol, the reaction similarly led to two solid isomerides. In each of these three cases, the melting points of the pairs of isomerides were found to differ by about 30°. When the reaction with diepoxyhexane was carried out with *o*-cresol, only one solid di-*o*-tolyloxyhexanediol could be obtained.

In the earlier communication on the reactions of 1 : 2-5 : 6-diepoxyhexane (Part XIV, *J.*, 1950, 1566), theoretical considerations were shown to suggest that two isomeric forms of the epoxide should exist and the experimental results described supported this idea. The existence of isomerism in the products of the reaction of diepoxyhexane with phenols is in conformity with this view and it would accordingly be expected that, of the two isomerides obtained, one would be a *meso*- or *cis*-form while the other would be a racemic mixture of the corresponding D- and L- or *trans*-forms. If the aryloxy-groups are assumed to be attached to the primary carbon atoms of the hexane chain, the two forms of the condensation product from phenol, for example, would be represented by the 1 : 6-diphenoxyhexane-2 : 5-diols (IV) and (V). This assumption appears to be justified by the fact that, in all our previous work on diepoxyhexane involving its ring fission under conditions similar to those used here, no evidence was found to suggest that ring opening occurred in any manner other than that leading to combination of the anionic part of the

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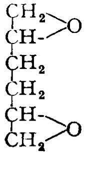
* Part XV, *J.*, 1951, 1180.

reagent molecule with the primary carbon atoms. Nevertheless, the possibility of ring fission occurring in the reverse direction, giving isomeric 2 : 5-diphenoxyhexane-1 : 6-diol, cannot be completely dismissed and in an attempt to decide the question the ditoluene-*p*-sulphonates of the two diphenoxyhexanediols were each treated with sodium iodide and acetone at 100° according to Oldham and Rutherford's method (*J. Amer. Chem. Soc.*, 1932, **54**, 366) for distinguishing between primary and secondary hydroxyl groups. It was expected that no reaction would occur in either case, but, in fact, both toluene-*p*-sulphonates reacted readily to give a high yield of sodium toluene-*p*-sulphonate.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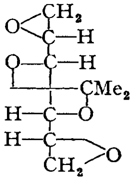
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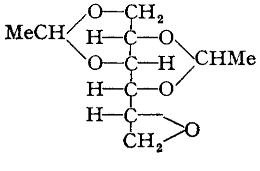
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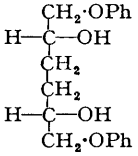
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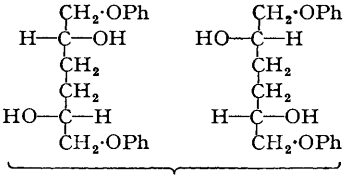
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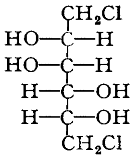
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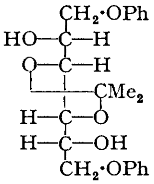
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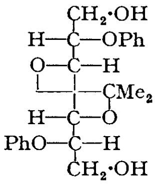
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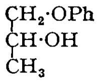
(IX)

In view of the exceptions observed to Oldham and Rutherford's rule, it was thought desirable to seek further evidence. This was obtained by a study of the action of phenol on 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol (II) under the same conditions as those employed with diepoxyhexane. A crystalline compound was obtained which ultimate analysis showed to be a diphenyl *iso*propylidene hexitol. The same compound was obtained by an alternative route, namely, the condensation of a di*iso*propylidene derivative of 1 : 6-dichloro-1 : 6-dideoxymannitol (VI) with sodium phenoxide in acetone. Further proof of the identity of the two specimens of this compound was supplied by the acid hydrolysis of each to give the same 1 : 6-diphenyl mannitol, benzoylation of which yielded 2 : 3 : 4 : 5-tetrabenzoyl 1 : 6-diphenyl mannitol. During this reaction an unexpected complication arose inasmuch as one of the *iso*propylidene groups attached to the mannitol molecule became detached and it is not possible to state, at present, a reason for this. The chlorine atoms in the starting material were known to be attached to $C_{(1)}$ and $C_{(6)}$ by reason of the preparation of the compound from 1 : 6-dichloro-1 : 6-dideoxymannitol (Wiggins, *J.*, 1946, 384), and it therefore follows that the phenoxy-groups in the condensation product should also be at positions 1 and 6. However, because it is not known how the one *iso*propylidene residue from the original di*iso*propylidene 1 : 6-dichloro-1 : 6-dideoxymannitol became dislodged, this cannot be regarded as a rigid proof for the allocation of the phenol residues to $C_{(1)}$ and $C_{(6)}$. Nevertheless, the result obtained above very strongly suggests that the diphenyl *iso*propylidene hexitol, whether obtained from the dichloro-compound or from *iso*propylidene dianhydromannitol is 1 : 6-diphenyl 3 : 4-*iso*propylidene mannitol (VII). Ring fission of the dianhydride in the reverse direction would imply the probable occurrence of Walden inversion on $C_{(2)}$ and $C_{(5)}$ (these atoms becoming transitional carbonium cations), which would lead to the formation of a L-iditol derivative (VIII).

Therefore it is most probable that the action of phenol on 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol results in ring fission at the bonds between the oxiran-oxygen atoms and the primary carbon atoms with the resultant attachment of phenoxy-groups to the latter. By analogy, these observations provide strong support for the idea that ring fission of 1 : 2-5 : 6-diepoxyhexane by phenol occurs in a similar manner, giving 1 : 6-diphenoxyhexane-2 : 5-diol.

Still further evidence in support of this contention has been obtained by studying the reaction of propylene oxide with phenol in benzene in the presence of sodium phenoxide under the conditions used for the reaction with 1 : 2-5 : 6-diepoxyhexane. The product was a liquid which showed the properties recorded by Hurd and Perlitz (*J. Amer. Chem. Soc.*, 1946, **68**, 38) for 1-phenoxypropan-2-ol (IX). It yielded a crystalline toluene-*p*-sulphonate. Its structure was proved by its synthesis from methylmagnesium iodide and phenoxyacetaldehyde, which can lead only to 1-phenoxypropan-2-ol. The crystalline toluene-*p*-sulphonate was identical with that obtained from the product of reaction of propylene oxide with phenol. This shows conclusively that the reaction between phenol and propylene oxide leads to the addition of the phenoxy-group at the primary carbon atom. It is reasonable to assume that this takes place also in the condensation of phenols with 1 : 2-5 : 6-diepoxyhexane and 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol and that the products of these reactions are therefore 1 : 6-diaryloxyhexane-2 : 5-diols and 1 : 6-diaryl 3 : 4-*iso*propylidene mannitol respectively.

In an attempt to explain the reactivity of the ditoluene-*p*-sulphonyl derivatives of the two isomeric diphenoxyhexanediols towards sodium iodide, the behaviour, under the same conditions, of the ditoluene-*p*-sulphonate of 1 : 6-diphenyl 3 : 4-*iso*propylidene mannitol (VII) and of the toluene-*p*-sulphonate of 1-phenoxypropan-2-ol was examined. Reaction of (VII) with toluene-*p*-sulphonyl chloride in pyridine solution did not proceed at room temperature but was effected by prolonged heating of the mixture at 130°; doubtless there is steric hindrance by the phenyl and the *iso*propylidene groups. The ditoluene-*p*-sulphonate did not react with sodium iodide in acetone, as might be expected, but the same was true after the *iso*propylidene group, and hence the possible steric hindrance, had been removed by acid hydrolysis. 1-Phenoxyprop-2-yl toluene-*p*-sulphonate, which indisputably contains a toluene-*p*-sulphonyl residue attached to a secondary carbon atom, reacted readily with sodium iodide in acetone solution and furnished 0·92 mol. of sodium toluene-*p*-sulphonate. It appears that the difference in the behaviour of the toluene-*p*-sulphonates of, on the one hand, diphenoxyhexanediol and 1-phenoxypropan-2-ol and, on the other, diphenyl *iso*propylidene mannitol must be ascribed to the presence of the deoxy-groupings at $C_{(3)}$ and $C_{(4)}$ in the hexane derivative and at $C_{(3)}$ in the propane derivative.

3 : 4-*iso*Propylidene 1 : 2-5 : 6-dianhydromannitol was also treated with *p*-chlorophenol and with *m*-cresol. The two crystalline products obtained were 1 : 6-di-*p*-chlorophenyl 3 : 4-*iso*propylidene mannitol and 3 : 4-*iso*propylidene 1 : 6-di-*m*-tolyl mannitol respectively. Acid hydrolysis of these afforded 1 : 6-di-*p*-chlorophenyl and 1 : 6-di-*m*-tolyl mannitol.

When 1 : 3-2 : 4-diethylidene 5 : 6-anhydrosorbitol (III) was treated under similar conditions with phenol and *o*- and *m*-cresol, three crystalline products were isolated which, by analogy, are the 6-phenyl and 6-*o*- and 6-*m*-tolyl derivatives of 1 : 3-2 : 4-diethylidene sorbitol. Hydrolysis of the *o*- or *m*-tolyl compound yielded syrupy 6-tolyl sorbitols, characterised as their crystalline penta-acetates. 1 : 3-2 : 4-Diethylidene 6-*o*-tolyl sorbitol yielded a crystalline toluene-*p*-sulphonate which did not react with sodium iodide in acetone at 105°.

Although the study of the reaction of ethylene oxide compounds, particularly those containing two epoxy-rings, with phenols was of interest from the theoretical viewpoint, this was not the main reason for undertaking this work. It has been shown (Berger and Bradley, *Brit. J. Pharmacol.*, 1946, **1**, 265) that certain aryl ethers of glycerol, particularly the *o*-tolyl ethers (3-*o*-tolyloxypropane-1 : 2-diol, " Myanesin "), show muscle-relaxing activity, and the aryl ethers of mannitol and sorbitol described above were prepared in order that their pharmacological activity might be examined. This phase of the work is now being studied by others and the results will be published elsewhere.

EXPERIMENTAL

Action of Phenol on 1 : 2-5 : 6-*Diepoxyhexane.*—To a solution of phenol (5 g.) in benzene (20 c.c.), in which sodium (0·2 g.) had been dissolved, diepoxyhexane (1·2 g.) was added, and the mixture heated on the boiling-water bath for 7 hours. Water was then added to the cooled mixture, and the white crystalline solid which separated, collected, and washed with dilute sodium hydroxide solution and with water. The crude product (2·3 g.), after being once recrystallized from alcohol, gave fine, feathery needles (1·3 g.), m. p. 135—143°. Fractional recrystallization from a large volume of alcohol effected separation of this material into two components: colourless plates (0·24 g.) of 1 : 6-*diphenoxyhexane*-2 : 5-*diol*, m. p. 163—164·5° (Found: C, 71·3; H, 7·35. $C_{18}H_{22}O_4$ requires C, 71·5; H, 7·3%); and stout needles (0·16 g.), m. p. 135—136·5°, of an *isomer* (Found: C, 71·7; H, 7·3%).

The diol of m. p. 163—164·5° (0·09 g.) and acetic anhydride (0·5 c.c.) in dry pyridine (2 c.c.) were kept at about 30° for 24 hours, then poured into water; the solid *diacetate* produced was collected, washed with water, and recrystallized from alcohol in needles (0·09 g.), m. p. 102—103° (Found: C, 68·1; H, 6·7. $C_{22}H_{26}O_6$ requires C, 68·4; H, 6·7%).

The diol of m. p. 135—136·5° similarly gave a *diacetate* (0·10 g.) [from light petroleum (b. p. 60—80°)] as prisms, m. p. 70—71·5° (Found: C, 68·4; H, 6·8%).

The diol of m. p. 163—164·5° (0·09 g.) and toluene-*p*-sulphonyl chloride (0·24 g.) in dry pyridine (5 c.c.), first at 0° and then at about 30° (overnight), gave the *ditoluene*-p-*sulphonate*, m. p. 177—178° (decomp.), as needles from chloroform (Found: C, 62·6; H, 5·7. $C_{32}H_{34}O_8S_2$ requires C, 63·0; H, 5·6%). The derivative (0·057 g.) was heated with dry sodium iodide (0·25 g.) and dry acetone (10 c.c.) in a sealed tube at 100° for 7 hours. The precipitate of sodium toluene-*p*-sulphonate which rapidly formed was collected, washed with a little dry acetone and dried at 110°; the yield was 0·032 g. (1·78 equivs.)

The isomeric diol (0·12 g.) similarly gave a *ditoluene*-p-*sulphonate* as needles (0·1 g.), m. p. 124—125° (from alcohol) (Found: C, 63·0; H, 5·6%). With dry sodium iodide (0·4 g.) and dry acetone (10 c.c.) in a sealed tube at 100° for 8 hours, it rapidly gave sodium toluene-*p*-sulphonate (0·057 g., 2·0 equivs.).

Action of o-*Cresol on* 1 : 2-5 : 6-*Diepoxyhexane*.—A solution of *o*-cresol (2·5 g.) and sodium (0·1 g.) in dry benzene (10 c.c.) was treated with diepoxyhexane (0·5 g.) and the whole heated for 7 hours. Water was added, the benzene layer separated, and the aqueous layer extracted with benzene. The combined extracts were dried ($MgSO_4$) and evaporated to a syrup (1·1 g.) which partly crystallized. After addition of ether and light petroleum, the crystalline material (0·33 g.) was collected and recrystallized from alcohol, forming prisms of 1 : 6-*di*-o-*tolyloxyhexane*-2 : 5-*diol*, m. p. 95—97° (Found: C, 72·7; H, 7·7. $C_{20}H_{26}O_4$ requires C, 72·8; H, 7·9%)

Action of m-*Cresol on* 1 : 2-5 : 6-*Diepoxyhexane*.—Diepoxyhexane was treated with *m*-cresol as described for *o*-cresol. When heating of the reaction mixture was complete, dilute sodium hydroxide solution was added and the separated solid collected, washed free from cresol, and recrystallized from aqueous alcohol, to give clusters of fine needles (0·4 g.), m. p. 95—106°. The benzene layer from the reaction mixture was evaporated to a solid, which, recrystallized from alcohol, formed shining plates (0·11 g.), m. p. 93·5—94·5°. It was 1 : 6-*di*-m-*tolyloxyhexane*-2 : 5-*diol* (Found: C, 72·5; H, 8·15%). Fractional recrystallization of the product of m. p. 95—106° yielded a first fraction (0·02 g.) which formed needles, m. p. 119—120°, and was the isomeric *diol* (Found: C, 72·8; H, 8·3%), and a final fraction (0·03 g.) which crystallized in plates, m. p. 92—94°, and was identical with the compound, m. p. 93·5—94·5°, isolated from the benzene layer.

Action of p-*Cresol on* 1 : 2-5 : 6-*Diepoxyhexane*.—The previous experiment was repeated using *p*-cresol. The crude condensation product crystallized from alcohol in feathery needles (0·4 g.), m. p. 143—155°. Fractional recrystallization from alcohol separated the compound into two isomeric 1 : 6-*di*-p-*tolyloxyhexane*-2 : 5-*diols*; the first fraction (0·025 g.) formed plates, m. p. 173—174·5° (Found: C, 73·2; H, 7·6%), and the final fraction small prisms (0·043 g.), m. p. 143·5—145° (Found: C, 72·5; H, 8·0%).

The mixture (0·20 g.) of m. p. 143—145° was heated with acetic anhydride (0·5 c.c.) and dry pyridine (2·5 c.c.) on a boiling-water bath for 2½ hours. The product, isolated by addition of water, formed small nodules (0·19 g.), m. p. 92—120°, from alcohol. Recrystallization from alcohol yielded two isomeric *diacetates*, the first fraction forming needles (0·04 g.), m. p. 49·5—51° (Found: C, 69·3; H, 7·0%), and the final fraction prismatic needles (0·03 g.), m. p. 123—125° (Found: C, 69·4; H, 7·1%).

Action of Phenol on 3 : 4-iso*Propylidene* 1 : 2-5 : 6-*Dianhydromannitol*.—A solution of sodium (0·25 g.) and phenol (5 g.) in dry benzene (20 c.c.) was treated with *iso*propylidene dianhydromannitol (1 g.) and the whole heated for 5 hours. After the mixture had cooled, water (20 c.c.) was added and the benzene layer diluted with twice its volume of light petroleum. The separated solid was collected and washed successively with sodium hydroxide solution and water. Recrystallization from light petroleum (b.p. 100—120°) gave 1 : 6-*diphenyl* 3 : 4-iso-

propylidene mannitol (1·9 g.) in long colourless needles, m. p. 115° (Found : C, 67·5; H, 6·6. $C_{21}H_{26}O_6$ requires C, 67·5; H, 6·9%).

This product (0·1 g.) was heated with 0·1N-sulphuric acid (25 c.c.) and alcohol (5 c.c.) on the boiling-water bath for 3 hours. The solid (0·08 g.) which separated was collected, washed with water, and recrystallized from acetone, forming 1 : 6-*diphenyl mannitol* in small plates, m. p. 200—204° (Found : C, 64·9; H, 6·7. $C_{18}H_{22}O_6$ requires C, 64·7; H, 6·6%). This (0·04 g.) was dissolved in dry pyridine (2 c.c.) and benzoyl chloride (0·5 c.c.) added. After being kept at about 30° for 48 hours, the solution was poured into water and extracted with chloroform; the extract was washed successively with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, dried ($MgSO_4$), and evaporated to a viscous syrup (0·075 g.), which crystallized on trituration with alcohol. 2 : 3 : 4 : 5-*Tetrabenzoyl* 1 : 6-*diphenyl mannitol* recrystallized from alcohol formed clusters of needles, m. p. 122—123° (Found : C, 74·0; H, 5·3. $C_{46}H_{38}O_{10}$ requires C, 73·6; H, 5·1%).

Condensation of 2 : 3-4 : 5-*Di*iso*propylidene* 1 : 6-*Dichloro*-1 : 6-*dideoxymannitol with Sodium Phenoxide.*—Di*iso*propylidene 1 : 6-dichloro-1 : 6-dideoxymannitol (0·5 g.) {the liquid isomer, n_D^{20} 1·4750, $[\alpha]_D$ −5·4° (in chloroform); see Wiggins, *J.*, 1946, 384} and sodium phenoxide (0·6 g.) in dry acetone (15 c.c.) were heated at 120° for 22 hours. The mixture was filtered hot and diluted with alcohol and water; the precipitated solid (0·4 g.) was collected and recrystallized from light petroleum (b. p. 100—120°), forming needles, m. p. 113—115·5° (Found : C, 67·5; H, 7·1. Calc. for $C_{21}H_{26}O_6$: C, 67·5; H, 6·9%). The product was 3 : 4-*iso*propylidene 1 : 6-diphenyl mannitol; the m. p. was not depressed on admixture with a specimen obtained from 3 : 4-*iso*propylidene 1 : 2-5 : 6-dianhydromannitol as described above. Hydrolysis with sulphuric acid and subsequent benzoylation of the product gave 1 : 6-diphenyl mannitol and its tetrabenzoate, respectively, the m. p. of which were unchanged on admixture with specimens prepared by the alternative method.

Treatment of 1 : 6-*Diphenyl* 3 : 4-iso*Propylidene Mannitol with Toluene*-p-*sulphonyl Chloride.*—(i) 1 : 6-Diphenyl 3 : 4-*iso*propylidene mannitol (0·5 g.) and toluene-*p*-sulphonyl chloride (1·0 g.) in dry pyridine (10 c.c.) were kept at 30° overnight and then poured into water. The precipitated solid recrystallized from alcohol as needles, m. p. 112—114°, alone or on admixture with the starting material. The recovery was almost quantitative. Repetition of the reaction at 60° for 5 hours also yielded only the starting material.

(ii) 1 : 6-Diphenyl 3 : 4-*iso*propylidene mannitol (0·5 g.) and toluene-*p*-sulphonyl chloride (1·0 g.) in dry pyridine (10 c.c.) were heated (oil-bath) at 120—130° for 8 hours, then poured into water and extracted with chloroform; the extract was washed successively with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, and dried ($MgSO_4$). Evaporation of the solvent gave a syrup (0·7 g.), which crystallized on trituration with alcohol. The solid was recrystallized from light petroleum (b. p. 100—120°), yielding 1 : 6-*diphenyl* 3 : 4-iso-*propylidene* 2 : 5-*ditoluene*-p-*sulphonyl mannitol* as needles, m. p. 107—108° (Found : C, 61·8; H, 5·6. $C_{35}H_{38}O_{10}S_2$ requires C, 61·6; H, 5·6%).

This ditoluene-*p*-sulphonate (0·10 g.) did not react with dry sodium iodide (0·25 g.) in dry acetone (10 c.c.) at 100° during 7½ hours. The starting material was recovered in 90% yield.

Hydrolysis. (i) The *iso*propylidene compound (0·26 g.) was heated under reflux with 0·1N-sulphuric acid (20 c.c.) and alcohol (25 c.c.) for 1½ hours. The solution yielded only unchanged starting material.

(ii) The *iso*propylidene compound (0·19 g.) was heated under reflux with 0·5N-sulphuric acid (20 c.c.) and alcohol (20 c.c.) for 8½ hours. The solution was then neutralized with sodium hydrogen carbonate and extracted with chloroform. Evaporation of the dried ($MgSO_4$) extract gave a crystalline residue (0·2 g.) which, recrystallized from alcohol–chloroform, afforded 1 : 6-*diphenyl* 2 : 5-*ditoluene*-p-*sulphonyl mannitol* in fine needles (0·1 g.), m. p. 185—186° (Found : C, 60·1; H, 5·6. $C_{32}H_{34}O_{10}S_2$ requires C, 59·8; H, 5·3%). This did not react with dry sodium iodide and dry acetone at 100° (8 hours); a small amount of sodium toluene-*p*-sulphonate was obtained on further heating at 150° for 8 hours.

Action of Phenol on Propylene Oxide.—To a solution of sodium (0·2 g.) and phenol (10 g.) in dry benzene (40 c.c.), propylene oxide (3 g.) was added and the mixture heated under reflux on the water-bath for 5 hours. After the mixture had cooled, water was added and the benzene layer separated; the aqueous layer was extracted with benzene, and the combined solutions were washed with dilute sodium hydroxide solution and with water and finally dried ($MgSO_4$). Evaporation of the benzene gave a residual oil (2·8 g.) which was distilled under reduced pressure; 1-phenoxypropan-2-ol was collected as a colourless oil (1·9 g.), b. p. (bath-temp.) 134—136°/15 mm., n_D^{17} 1·5239. Hurd and Perlitz (*loc. cit.*) record b. p. 130°/21 mm., n_D 1·5232.

1-*Phenoxyprop*-2-*yl Toluene*-p-*sulphonate*.—1-Phenoxypropan-2-ol (0·57 g.) and toluene-*p*-sulphonyl chloride (1·1 g.) in dry pyridine (5 c.c.), were kept, first at 0° and then at about 30° (overnight), the solution was poured into water, and the solid derivative (1·2 g.) collected, washed with water, and recrystallized from aqueous alcohol, giving 1-*phenoxyprop*-2-*yl toluene*-p-*sulphonate* in clusters of fine needles (0·9 g.), m. p. 93—94° (Found : C, 62·5; H, 5·9. $C_{16}H_{18}O_4S$ requires C, 62·8; H, 5·9%).

The toluene-*p*-sulphonyl derivative (0·151 g.) was heated with dry sodium iodide (0·36 g.) and dry acetone (10 c.c.) at 95—100° for 6 hours. The precipitate of sodium toluene-*p*-sulphonate was then collected, washed with a little dry acetone, and dried at 110°; the yield was 0·088 g. (92%).

Phenoxyacetaldehyde.—Phenoxyacetaldehyde diethylacetal (Dey, *J*., 1937, 1057) (5 g.) was hydrolysed on the boiling water-bath for 1 hour with 1% sulphuric acid (50 c.c.) and acetic acid (20 c.c.). The reaction mixture was neutralised with sodium hydrogen carbonate and extracted with ether. The extract was dried ($MgSO_4$) and evaporated to give an oil (3·9 g.) which, on distillation, yielded phenoxyacetaldehyde (1·9 g.), b. p. (bath-temp.) 130—135°/15 mm., n_D^{20} 1·5321. Rotbart (*Ann. Chim*., 1934, **1**, 479), records b. p. 101—103°/15 mm., n_D^{21} 1·5381. The product gave a semicarbazone, m. p. 145°, in agreement with the value recorded by Rotbart.

Action of Methylmagnesium Iodide on Phenoxyacetaldehyde.—Phenoxyacetaldehyde (0·93 g.) in dry ether (7 c.c.) was added dropwise at room temperature to methylmagnesium iodide (from Mg, 0·2 g.) in ether (10 c.c.). The mixture was heated under reflux on the water-bath for 1½ hours and thereafter poured into ice-water acidified with sulphuric acid. The ethereal layer was separated, the aqueous layer was extracted with more ether, and the combined ether extracts were washed successively with sodium hydrogen carbonate solution and water. Evaporation of the dried ($MgSO_4$) solution gave a residual oil (1·0 g.) from which 1-phenoxypropan-2-ol (0·49 g.) distilled at 138—140° (bath-temp.)/15 mm. It showed n_D^{20} 1·5269. Treatment of the product (0·15 g.) with toluene-*p*-sulphonyl chloride in pyridine as described above gave 1-phenoxyprop-2-yl toluene-*p*-sulphonate (0·20 g.), m. p. 91—92·5° alone or in admixture with a specimen of the compound obtained from propylene oxide.

Action of p-*Chlorophenol on* 3 : 4-iso*Propylidene* 1 : 2-5 : 6-*Dianhydromannitol*.—Sodium (0·25 g.) was dissolved, with warming, in a solution of *p*-chlorophenol (1·4 g.) in dry benzene (70 c.c.) and *iso*propylidene dianhydromannitol (0·5 g.) added. After the mixture had been heated under reflux for 8 hours, it was cooled, decanted from a little unchanged sodium, and shaken with 20% sodium hydroxide solution. The benzene layer was separated, washed with water, and dried ($MgSO_4$). Evaporation of the solvent gave a residual syrup which crystallised on trituration with chloroform–light petroleum (b. p. 40—60°); recrystallization from the same mixture of solvents yielded 1 : 6-*di*-p-*chlorophenyl* 3 : 4-iso*propylidene mannitol* as needles (0·3 g.), m. p. 111—114° (Found : C, 57·0; H, 5·6. $C_{21}H_{24}O_6Cl_2$ requires C, 57·1; H, 5·4%).

The *iso*propylidene compound (0·1 g.) was heated under reflux with N-sulphuric acid (25 c.c.) and alcohol (30 c.c.), for 10 hours. The solid which separated on cooling was collected, washed with water, and recrystallized from aqueous alcohol, forming 1 : 6-*di*-p-*chlorophenyl mannitol* as colourless needles (0·06 g.), m. p. 177—178° (Found : C, 53·6; H, 4·8. $C_{18}H_{20}O_6Cl_2$ requires C, 53·6; H, 5·0%).

Action of m-*Cresol on* 3 : 4-iso*Propylidene* 1 : 2-5 : 6-*Dianhydromannitol*.—*m*-Cresol (4·06 g.) was dissolved in dry benzene (50 c.c.) and sodium (0·25 g.) added in small pieces. After the reaction had ceased, *iso*propylidene dianhydromannitol (1·0 g.) was added and the reaction carried out as in the case of the *p*-chlorophenol. The syrup obtained on evaporation of the benzene solution distilled as a yellow viscid syrup at 160—170° (bath-temp.)/0·05 mm. (Found : C, 68·1; H, 7·7. Calc. for $C_{23}H_{30}O_6$: C, 68·7; H, 7·5%). The syrup crystallized on trituration with methyl alcohol and recrystallized from methyl alcohol–water as colourless needles of 3 : 4-iso*propylidene* 1 : 6-*di*-m-*tolyl mannitol monohydrate* (0·9 g.), m. p. 68—70°, $[\alpha]_D^{17}$ +22·4° (*c*, 3·22 in pyridine) (Found : C, 68·6; H, 7·7. $C_{23}H_{30}O_6,H_2O$ requires C, 68·7; H, 7·6%). The substance becomes liquid when dried over phosphoric anhydride.

This compound (0·73 g.) was heated under reflux for 7 hours with 0·1N-sulphuric acid (30 c.c.). After the solution had been allowed to cool, the solid formed was collected by filtration and recrystallized from absolute alcohol, to yield 1 : 6-*di*-m-*tolyl mannitol* (0·31 g.) as small plates, m. p. 139·5—140·5°, $[\alpha]_D^{15}$ +24·6° (*c*, 1·38 in pyridine) (Found : C, 66·5; H, 7·2. $C_{20}H_{26}O_6$ requires C, 66·3; H, 7·2%). The di-*m*-tolyl mannitol (0·08 g.) was dissolved in dry pyridine, treated with benzoyl chloride (0·3 g.) at 0°, and kept at 30° overnight. The usual treatment afforded a syrup which crystallized on trituration with methyl alcohol. Recrystallization from the same solvent yielded 2 : 3 : 4 : 5-*tetrabenzoyl* 1 : 6-*di*-m-*tolyl mannitol* as colourless needles, m. p. 101—102°, $[\alpha]_D$ +30·2° (*c*, 2·98 in pyridine) (Found : C, 73·9; H, 5·5. $C_{48}H_{42}O_{10}$ requires C, 74·0; H, 5·4%).

Action of o-*Cresol on* 1 : 3-2 : 4-*Diethylidene* 5 : 6-*Anhydrosorbitol.*—*o*-Cresol (14·4 g.) was dissolved in dry benzene (10 c.c.), and sodium (0·9 g.) added in small pieces. When the reaction had ceased, diethylidene anhydrosorbitol (7·2 g.) was added and the mixture heated under reflux for 9 hours. It was then diluted with benzene, water added, and the benzene layer separated and washed with sodium hydroxide solution. After being washed with water, the extract was dried ($MgSO_4$) and evaporated to a syrup which was dissolved in hot aqueous alcohol. On cooling, the solution yielded 1 : 3-2 : 4-*diethylidene* 6-o-*tolyl sorbitol* (7·0 g.) as prisms, m. p. 134·5—135·5°, $[\alpha]_D^{18}$ +4·07° (*c*, 4·94 in chloroform) (Found : C, 62·9; H, 7·5. $C_{17}H_{24}O_6$ requires C, 63·0; H, 7·4%).

This diethylidene compound (0·5 g.) and toluene-*p*-sulphonyl chloride (0·5 g.) in dry pyridine (8 c.c.) at 25° (3 days) gave 1 : 3-2 : 4-*diethylidene* 5-*toluene*-p-*sulphonyl* 6-o-*tolyl sorbitol* (0·41 g.) as colourless needles, m. p. 143—144°, $[\alpha]_D^{20\cdot5}$ −14·8° (*c*, 2·55 in dry pyridine), from aqueous alcohol (Found : C, 60·0; H, 6·1; S, 7·0. $C_{24}H_{30}O_8S$ requires C, 60·3; H, 6·3; S, 6·7%); this did not react with dry sodium iodide in dry acetone at 105—110° (7 hours), the starting material being recovered in 83% yield.

Hydrolysis. Diethylidene *o*-tolyl sorbitol (6·0 g.) was heated under reflux with 2N-sulphuric acid (20 c.c.) and alcohol (20 c.c.) for 6 hours. The solution was neutralised with barium carbonate and filtered. Evaporation of the filtrate yielded liquid 6-o-*tolyl sorbitol*. After being dried at 50°/0·01 mm. it showed $[\alpha]_D$ +12·4° (*c*, 7·7 in ethyl alcohol) (Found : C, 57·4; H, 7·4. $C_{13}H_{20}O_6$ requires C, 57·4; H, 7·4%). It formed a crystalline *penta-acetate*, m. p. 89·5—90·5° (Found : C, 57·2; H, 6·2. $C_{23}H_{30}O_{11}$ requires C, 57·3; H, 6·2%).

Action of m-*Cresol on* 1 : 3-2 : 4-*Diethylidene* 5 : 6-*Anhydrosorbitol.*—*m*-Cresol (3 g.) was dissolved in dry benzene (35 c.c.) and treated with sodium (0·9 g.) and diethylidene anhydrosorbitol (1·3 g.) as in the case of the *o*-isomer. The syrupy 1 : 3-2 : 4-*diethylidene* 6-m-*tolyl sorbitol* obtained on evaporation of the benzene solution crystallized in the form of colourless plates (1·4 g.), m. p. 88°, $[\alpha]_D^{19}$ −8·1° (*c*, 3·46 in pyridine) (Found : C, 62·9; H, 7·8%).

The *m*-tolyl ether was hydrolysed as described for the *o*-isomer. The 6-m-*tolyl sorbitol* obtained was dried at 50°/0·005 mm. and showed $[\alpha]_D^{18\cdot5}$ +13·9° (*c*, 6·06 in ethyl alcohol) (Found : C, 57·2; H, 7·7%). Acetylation with acetic anhydride and anhydrous sodium acetate afforded stout prisms of the *penta-acetate*, m. p. 110—111°, $[\alpha]_D^{18}$ −28·5° (*c*, 3·72 in pyridine) (Found : C, 57·0; H, 6·4%).

Action of Phenol on 1 : 3-2 : 4-*Diethylidene* 5 : 6-*Anhydrosorbitol.*—Phenol (1·3 g.) was dissolved in dry benzene (30 c.c.), sodium (0·32 g.) added, followed by diethylidene anhydrosorbitol (1 g.), and the mixture was treated as above. The syrup obtained on evaporation of the benzene solution crystallized from light petroleum (b. p. 40—60°) as colourless needles of 1 : 3-2 : 4-diethylidene 6-phenyl sorbitol (0·7 g.), m. p. 98—99°, $[\alpha]_D^{17\cdot5}$ +11·3° (*c*, 2·82 in ethyl alcohol).

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