641. *The Preparation of α-Aryl Ethers of* iso*Butane*-1 : 2 : 3-*triol.*

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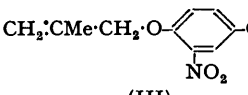
The recognition of muscle-relaxing properties amongst α-aryl ethers of glycerol has led to a study of the means of preparing analogous ethers of its β-methyl derivative (*iso*butane-1 : 2 : 3-triol).

The ethers can be prepared by forming the 2-methylallyl ethers of phenols and oxidising these by means of peracetic or performic acid. The course of the oxidation is discussed. The same ethers of *iso*butane-1 : 2 : 3-triol are obtained in better yield and more conveniently by condensing phenols with 1 : 2-epoxy-3-hydroxy*iso*butane (β-methylglycidol) in the presence of pyridine. A third method of preparation consists in oxidising 2-methylallyl chloride with peracetic acid to form 3-chloro*iso*butane-1 : 2-diol and condensing this with phenols. The three methods of preparation yield identical ethers of *iso*butane-1 : 2 : 3-triol.

The investigation of the α-aryl ethers of glycerol already reported (*J.*, 1951, 1589) has been extended to include the preparation of analogous ethers of *iso*butane-1 : 2 : 3-triol. The ready availability of 2-methylallyl chloride (I; R = Cl) enabled a series of aryl 2-methylallyl ethers (I; R = OAr) to be obtained, and from these the ethers (II; R = OAr, R′ = OH) by oxidation.

(I) $CH_2{:}CMe{\cdot}CH_2R$ $\qquad\qquad$ $R{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH_2R'$ (II)

Several authors (Bortz, Miller, and Adams, *J. Amer. Chem. Soc.*, 1935, **57**, 371; Mauthner, *J. pr. Chem.*, 1937, **148**, 95) have described the formation of 2-methylallyl ethers of phenols by heating phenols with 2-methylallyl chloride and aqueous-alcoholic sodium hydroxide or a suspension of anhydrous potassium carbonate in dry acetone. We have employed the same conditions in preparing the 2-methylallyl ethers of *m*- and *p*-nitrophenol, 4-chloro-3-methylphenol, butyl *m*- and *p*-hydroxybenzoate, butyl 4-hydroxy-3-nitrobenzoate, and *p*-hydroxybenzoic acid. The more acidic phenols reacted slowly and in these cases it was found advantageous to employ 2-methylallyl iodide, prepared *in situ* from 2-methylallyl chloride and sodium iodide. Care was required in purifying the 2-methylallyl ethers because of their tendency to rearrange during distillation (Bortz, Miller, and Adams, *loc. cit.*), except that butyl 4-2′-methylallyloxy-3-nitrobenzoate (III), unlike the corresponding allyl ether, distilled almost unchanged at 180° under reduced pressure.



(III)

The oxidation of the 2-methylallyl ethers was effected by means of peracetic acid prepared by warming 100-vol. hydrogen peroxide with glacial acetic acid at 80° for an hour. Oxidation occurred readily at 60° and cooling was required to prevent undue rise in temperature. The oxidation products consisted of the methylglycerol ethers (II; R = OAr, R′ = OH) together with *O*-acetates of undetermined constitution. After separation of the product from the medium, and its hydrolysis with either aqueous-alcoholic sulphuric acid or a suspension of anhydrous potassium carbonate in alcohol (Fischer, *Ber.*, 1920, **53**, 1634), the whole of the oxidation product was obtained in the form of the methylglycerol ether (II; R = OAr, R′ = OH). The yields of these ethers varied greatly (from 6 to 68%) with the nature of the nuclear substituents in the aryl 2-methylallyl ether oxidised. The use of performic acid (Swern, Billen, Findley, and Scanlar, *J. Amer. Chem. Soc.*, 1945, **67**, 1786) afforded greatly improved yields in the case of the *m*-methyl (25%) and 3 : 4-dimethyl (50%) derivatives of 2-methylallyl phenyl ether.

When the oxidation was carried out by means of peracetic acid the methylglycerol ethers (II; R = OAr, R′ = OH) could usually be readily obtained crystalline. The mother-liquors contained the *O*-acetate of the methylglycerol ether, the amounts of which could be estimated by hydrolysis with aqueous-alcoholic sulphuric acid to the methylglycerol ether. It was thus found, in one experiment, that when 2-methylallyl phenyl ether was oxidised the ratio of methylglycerol ether to its *O*-acetate was 3·1 : 1. In a similar experiment with 2-methylallyl *p*-tolyl ether the ratio was 1·2—1·3 : 1, and in several experiments with *p*-chlorophenyl 2-methylallyl ether the ratio varied from 0·8 : 1 to 2·0 : 1 according to the conditions.

(IV) $CH_2\overset{O}{\frown}CMe{\cdot}CH_2{\cdot}OR$ $\qquad$ $ArO{\cdot}CH_2{\cdot}CMe(OH){\cdot}CH_2{\cdot}NR_2$ (V)

When the oxidation with peracetic acid was carried out for a shorter time and at a higher temperature (80°) it was often possible to isolate the epoxide (IV; R = Ar) in good yield. Epoxides were readily prepared from the 2-methylallyl ethers of phenol, *o*-cresol, *p*-cresol, and *p*-chlorophenol, and their occurrence in the oxidation product supports the conclusion of Swern *et al.* (*loc. cit.*) that the appearance of epoxides in oxidation processes is not limited to reactions in non-hydroxylic solvents. The persistence of an epoxide depends upon the ease of its reaction with the medium in which it is formed. In this connection it may be mentioned that the epoxides derived from the 2-methylallyl ethers of phenols are notably more stable towards acid hydrolysis than the corresponding epoxides of allyl ethers.

The epoxides isolated after oxidations with peracetic acid reacted with glacial acetic acid or with a solution of peracetic acid in acetic acid to form the methylglycerol ethers (II; R = OAr, R′ = OH) and the related *O*-acetates in approximately the same proportions as those in which these compounds occurred in the product of oxidising the 2-methylallyl ethers. This supports the view that the first product of the oxidation of an aryl 2-methylallyl ether is the related epoxide, which then reacts with the medium to form the methylglycerol ether (II; R = OAr, R′ = OH) and its *O*-acetate.

Another factor affecting the proportion of the *O*-acetate found in the oxidation products is the esterification of acetic acid by the methylglycerol ether formed at an earlier stage. This was shown by experiments with 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol. The importance of the esterification factor is considerable when the oxidation time is prolonged and the proportion of water in the medium is small. The product is probably a 1-acetoxy-3-aryloxy*iso*butan-2-ol (II; R = OAr, R′ = OAc), in view of the greater ease of acylation of primary than of tertiary alcohols.

Although the oxidation of aryl 2-methylallyl ethers sometimes affords low yields of the corresponding methylglycerol ethers, the method of preparation is of value because the constitution of the products follows from their mode of preparation.

The use of potassium permanganate in acetone as an oxidant was studied in the case of *p*-chlorophenyl 2-methylallyl ether. The corresponding ether of methylglycerol was obtained but the yield was much inferior to that of the preparation by use of peracetic acid.

It was later found that 2-methylallyl chloride was readily oxidised to 3-chloro*iso*butane-1 : 2-diol (II; R = Cl, R′ = OH) by peracetic acid. This intermediate enabled a number of aryl ethers of methylglycerol to be prepared directly in good yield. Reaction with *p*-iodophenol gave 3-*p*-iodophenoxy*iso*butane-1 : 2-diol (II; R = OH, R′ = $O{\cdot}C_6H_4I$-*p*) in 68% yield, and the yields obtained with other derivatives of phenol were 33—78%. In the case of the *m*-methyl and 3 : 5-dimethyl derivatives of 3-phenoxy*iso*butane-1 : 2-diol (II; R = OH, R′ = OPh), direct comparison showed that the methylglycerol ethers obtained by the use of 3-chloro*iso*butane-1 : 2-diol were identical with the ethers derived by oxidising the 2-methylallyl ethers of the corresponding phenols.

The oxidation of 2-methylallyl chloride by means of peracetic acid yields in the first instance a mixture of (II; R = Cl, R′ = OH) and an *O*-acetate. 3-Chloro*iso*butane-1 : 2-diol (II; R = Cl, R′ = OH) can be prepared in good yield by heating the mixture with aqueous-alcoholic sulphuric acid. A suspension of potassium carbonate in alcohol may also be used, but *iso*butane-1 : 2 : 3-triol 1-ethyl ether (II; R = OEt, R′ = OH) then appears as a by-product. For most purposes the mixture of (II; R = Cl, R′ = OH) and its *O*-acetate could be employed, the condensation products with phenols being obtained free from esters by ester-exchange with the solvent during the reaction.

A convenient procedure has been devised to prepare β-methylglycidol (IV; R = H) from 3-chloro*iso*butane-1 : 2-diol or from the mixture of this with its *O*-acetate following Rider and Hill's method (*J. Amer. Chem. Soc.*, 1930, **52**, 1521). In the presence of catalysts (IV;

R = H) condensed readily with phenols to form aryl ethers of methylglycerol in good yield (*m*-nitrophenol, 10%; 7 others, 55—70%). The products obtained by condensing β-methylglycidol with phenol, *m*-cresol, *p*-cresol, 4-chloro-3-methylphenol, and *m*-nitrophenol were shown to be identical with the corresponding 3-aryloxy*iso*butane-1 : 2-diols (II; R = OAr, R′ = OH) obtained by the oxidation of the 2-methylallyl ethers of phenols. The structure of the products obtained by condensing β-methylglycidol with phenols indicates that in this reaction it is the terminal carbon atom of the oxide ring which is reactive towards phenols or phenoxide ions.

$$CH_2\!<\!\overset{O}{}\!>\!CMe\cdot CH_2\cdot OH + Ar\cdot OH \longrightarrow HO\cdot CH_2\cdot CMe(OH)\cdot CH_2\cdot OAr$$

By analogy, the *O*-acetates derived by the action of acetic acid on the epoxides (IV; R = Ar) are most probably 1-acetoxy-3-aryloxy*iso*butan-2-ols (II; R = OAr, R′ = OAc), and the same constitution must be assigned to the *O*-acetates which occur in the products of the oxidation of aryl 2-methylallyl ethers by means of peracetic acid, because these also are derived from the epoxides (IV; R = Ar). Further, for the same reason the *O*-acetate which accompanies the 3-chloro*iso*butane-1 : 2-diol prepared by the action of peracetic acid on 2-methylallyl chloride is doubtless 1-acetoxy-3-chloro*iso*butan-2-ol (II; R = Cl, R′ = OAc).

In experiments designed to estimate the yields of epoxides, β-methylglycerol ethers, and *O*-acetates resulting from the oxidation of aryl 2-methylallyl ethers, it was found convenient in several instances to add a secondary amine such as piperidine or diethylamine to the isolated crude oxidation product with the object of converting the epoxide constituent into an adduct with the amine. The reaction occurred readily in all the cases encountered. The products were probably 1-aryloxy-3-piperidino*iso*butan-2-ols (V; NR_2 = piperidino) or the corresponding 3-diethylamino-compounds (V; R = Et).

The product obtained by oxidising 2-methylallyl phenyl ether with peracetic acid and combining the derived epoxide with piperidine was therefore 1-phenoxy-3-piperidino*iso*butane-2-ol (V; Ar = Ph, NR_2 = piperidino). Analogously, the products obtained by oxidising the 2-methylallyl ethers of *o*-cresol, *p*-cresol, and *p*-chlorophenol by means of peracetic acid and combining the derived epoxides with diethylamine were (V; R = Et, Ar = *o*-C_6H_4Me, *p*-C_6H_4Me, or *p*-C_6H_4Cl).

Experimental.

3-m-*Tolyloxy*iso*butane*-1 : 2-*diol*.—(1*a*) 2-Methylallyl *m*-tolyl ether (50 g.) was added at 40° to a solution of hydrogen peroxide (100-vol.; 75 g.) in acetic acid (240 c.c.), which had been previously warmed to 80° for an hour and then cooled. When the mixture was warmed to 60° the ether dissolved, forming a solution which became orange-red. This was heated at 70° for an hour and then poured into water (2 vols.) and extracted by means of chloroform. The extract was washed with dilute sodium hydroxide solution then with water, and the solvent was removed by distillation. The residual reddish oil was dissolved in a mixture of water (50 c.c.) and alcohol (100 c.c.) containing concentrated sulphuric acid (2 c.c.), and the solution was heated under reflux for 1·5 hours. Water was added, and the product extracted by means of chloroform. Evaporation of the extract gave the *diol* as a solid which, after crystallisation from ether–light petroleum, was obtained in colourless crystals, m. p. 71—72° (3·7 g.) (Found: C, 67·0; H, 7·8. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

(1*b*) The same product was obtained in better yield by suspending 2-methylallyl *m*-tolyl ether (40 g.) in formic acid (125 c.c.), cooling the suspension in ice-water, and stirring it vigorously while hydrogen peroxide (100-vol.; 30 c.c.) was added dropwise. The deep red-brown product (18 g.) so obtained, crystallised from ether–light petroleum, had m. p. 71—72°; the final yield was 10·2 g.

(2) A mixture of *m*-cresol (10·8 g.), β-methylglycidol (8·8 g.), and pyridine (0·1 g.) was heated at 90° for 2 hours. The resulting brown product was added to water and the mixture then extracted by means of chloroform (150 c.c.). The extract was washed twice with water, then concentrated by distilling a portion of the solvent. and finally mixed with light petroleum. On cooling, needles, m. p. 70—72°, separated. The m. p. was raised to 71—72° after three recrystallisation from ether–light petroleum. The product (11·5 g.) was identical with that obtained by the oxidation of 2-methylallyl *m*-tolyl ether. The same compound was formed when *m*-cresol was condensed with 1-chloro*iso*butane-1 : 2-diol.

3-o-*Tolyloxy*iso*butane*-1 : 2-*diol*.—This was prepared similarly both (i) by oxidising 2-methylallyl *o*-tolyl ether and (ii) by condensing *o*-cresol with β-methylglycidol. (i) 2-Methylallyl *o*-tolyl ether (121·5 g.) was added in one portion to peracetic acid prepared from hydrogen peroxide (100-vol; 171 g.) and acetic acid (420 c.c.). When heated and shaken, the mixture became homogeneous at 55°, and then the temperature rose sharply to 80°. After 5 minutes at this temperature the deep red solution was cooled rapidly and then poured into water. The oil which separated was taken up in chloroform and fractionated to give: (*a*) mainly unchanged 2-methylallyl *o*-tolyl ether, b. p. 54°/0·5 mm. (48 g.); (*b*) a fraction, b. p. 54—100° (mainly 76—80°)/0·5 mm., 46·5 g.; (*c*) a fraction, b. p. 140—150°/0·5 mm. Redistillation of fraction (*b*) gave 1 : 2-epoxy-3-*o*-tolyloxy*iso*butane, b. p. 78—80°/0·5 mm. (26·1 g.)

In a similar preparation, in which 2-methylallyl *o*-tolyl ether was oxidised by means of peracetic acid (prepared from 2·1 mols. of hydrogen peroxide) at 65—70° for 2·5 hours, the product was isolated

by addition of water and extraction with chloroform, and then recovered and hydrolysed by heating it with aqueous-alcoholic sulphuric acid. Isolation by means of chloroform and distillation gave 3-*o*-*tolyloxy*iso*butane*-1 : 2-*diol*, b. p. 124—126°/0·05 mm. (30%) (Found: C, 67·1; H, 7·9. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

(ii) The same product was obtained in 55% yield by condensing *o*-cresol (1·05 mols.) with β-methylglycidol (1·0 mol.) for 3·5 hours at 90—95° in the presence of pyridine. It was also prepared (yield, 63%) by condensing *o*-cresol (1 mol.) with 3-chloro*iso*butane-1 : 2-diol (1·5 mols.) in alcohol containing potassium carbonate.

1-*Diethylamino*-3-*o*-*tolyloxy*iso*butan*-2-*ol*.—This *alcohol* resulted when 1 : 2-epoxy-3-*o*-tolyloxy*iso*butane was mixed with diethylamine in slight excess. Distillation gave a fraction, b. p. 144—145°/0·5 mm. (Found: C, 71·4; H, 10·0; N, 5·5. $C_{15}H_{25}O_2N$ requires C, 71·7; H, 10·0; N, 5·6%).

3-(3 : 5-*Dimethylphenoxy*)iso*butane*-1 : 2-*diol*.—3 : 5-Dimethylphenyl 2-methylallyl ether (44 g.) was added at 40°, with shaking, to a solution of peracetic acid prepared from acetic acid (180 c.c.) and hydrogen peroxide (100-vol.; 57 g.). Treatment as described for 3-*m*-tolyloxy*iso*butane-1 : 2-diol (1*a*) gave almost pure *diol* (3 g.), m. p. 74° (Found: C, 68·6; H, 8·5. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·6%). The same percentage yield was obtained when 3 : 5-dimethylphenyl 2-methylallyl ether (22 g.) was oxidised at 5° by means of a solution of 100-vol. hydrogen peroxide (11·3 g.) in formic acid (125 c.c.).

3-(3 : 4-*Dimethylphenoxy*)iso*butane*-1 : 2-*diol*.—3 : 4-Dimethylphenyl 2-methylallyl ether (80 g.) was heated for an hour at 60—70° with peracetic acid prepared from acetic acid (360 c.c.) and hydrogen peroxide (100-vol.; 114 g.). The product was heated for 30 minutes at 90—95° with a solution containing concentrated sulphuric acid (2 c.c.) in a mixture of water (40 c.c.) and methanol (100 c.c.). The hydrolysed product, recrystallised from ether, afforded white needles of the *diol* (20 g.), m. p. 96° (Found: C, 68·4; H, 8·2. $C_{12}H_{18}O_3$ requires C, 68·6; H, 8·6%).

The yield was considerably improved when performic acid was used instead of peracetic acid. 3 : 4-Dimethylphenyl 2-methylallyl ether (37 g.) was vigorously stirred for an hour with a solution of hydrogen peroxide (100-vol.; 30 c.c.) in formic acid (125 c.c.), the temperature being kept below 30°. All the ether had then dissolved. After 30 minutes' more stirring at room temperature, the product was isolated and hydrolysed with aqueous-methanolic sulphuric acid as in the preceding preparation. The yield of the pure methylglycerol ether, m. p. 96°, was 20·2 g.

3-*Phenoxy*iso*butane*-1 : 2-*diol*.—(1*a*) To a solution of peracetic acid, prepared from acetic acid and 2·1 mols. of hydrogen peroxide, was added 2-methylallyl phenyl ether (1 mol.). The mixture was kept at 65—70° for 2—3 hours and then the product was isolated and heated with aqueous-alcoholic sulphuric acid. 3-*Phenoxy*iso*butane*-1 : 2-*diol* had m. p. 91° (Found: C, 66·1; H, 7·6. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%); yield 42%.

(1*b*) 2-Methylallyl phenyl ether (74 g.) was added at 40° to a cooled solution of peracetic acid, prepared by heating hydrogen peroxide (114 g.) with acetic acid (280 c.c.) at 80° for 2 hours. The mixture was heated at 60°, and then became homogeneous. An exothermic reaction ensued, the temperature rising to 80° during 5 minutes. At this point the solution was cooled rapidly and poured into a large volume of water. The oil which separated was taken into chloroform and washed successively with water, dilute sodium carbonate solution, and again with water. Distillation then gave the following fractions; (*a*) b. p. 54—58°/1 mm. (23 g.); (*b*) b. p. 80—85°/1 mm. (25 g.). There was a residue (7 g.). Fraction (*a*) consisted of unchanged 2-methylallyl phenyl ether. Fraction (*b*) was mainly 1 : 2-epoxy-3-phenoxy*iso*butane. The yield of this was determined by adding the whole of the fraction (25 g.) to an excess of piperidine. The mixture was warmed to initiate the reaction, which soon occurred with evolution of heat, necessitating cooling. On distillation the product yielded piperidine, 2-methylallyl phenyl ether, and then 1-phenoxy-3-piperidino*iso*butan-2-ol, b. p. 134°/0·5 mm., identified by conversion into the *hydrochloride*, m. p. 150° (see below). The yield was 28 g., equivalent to a yield of 18·5 g. of 1 : 2-epoxy-3-phenoxy*iso*butane in fraction (*b*).

In a second similar experiment the mixture of 2-methylallyl phenyl ether and peracetic acid was allowed to react until the temperature reached 86°. This temperature was maintained for 2 minutes and then the product was isolated and distilled. The following fractions were obtained; (*a*) b. p. 52—60°/1 mm. (16 g.), (*b*) b. p. 60—85°/1 mm. (20 g.), (*c*) b. p. 85—130°/1 mm. (5 g.), (*d*) b. p. 140°/1 mm. (22 g.). Fraction (*a*) was mainly unchanged 2-methylallyl phenyl ether. Fraction (*b*) boiled mainly at 82°/1 mm. It contained 10·8 g. of 1 : 2-epoxy-3-phenoxy*iso*butane, because when it reacted with an excess of piperdine it gave 16·2 g. of 1-phenoxy-3-piperidino*iso*butan-2-ol, b. p. 135°/0·5 mm. Fraction (*c*) was warmed with a small volume of carbon tetrachloride. On cooling, crystals of 3-phenoxy*iso*butane-1 : 2-diol (11 g.) separated, m. p. 89—90° not depressed when mixed with an authentic sample. The mother-liquor was evaporated and the residue heated under reflux with aqueous-alcoholic sodium carbonate solution during 2 hours; ethyl acetate was formed. Water was added to the solution, and the product extracted by means of chloroform. The extract after being washed with water, concentrated, and mixed with light petroleum gave 3-phenoxy*iso*butane-1 : 2-diol (3·5 g.), m. p. 90° not depressed when mixed with an authentic sample.

(2) A mixture of phenol (20 g.) and β-methylglycidol (18·6 g.), heated at 90° for 2—3 hours with the addition of 2 or 3 drops of pyridine, gave white needles, m. p. 89—91° (24 g.), identical with the product obtained by oxidising 2-methylallyl phenyl ether. When pyridine ethiodide was substituted for pyridine and the condensation was conducted at 115° for 3 hours the yield was slightly improved (70%). Heating with pyridine ethiodide at 90—95° for 6·5 hours gave only a 12·5% yield of the product.

1-*Phenoxy*-3-*piperidino*iso*butane*-2-*ol Hydrochloride*.—The product, b. p. 134°/0·5 mm., obtained by reaction of 1 : 2-epoxy-3-phenoxy*iso*butane with piperidine, was dissolved in aqueous hydrochloric acid, and the *hydrochloride* recovered by evaporation of the solution. It crystallised from ether–methanol in small, white plates, m. p. 150° (Found: N, 4·6; Cl, 12·2. $C_{15}H_{24}O_2NCl$ requires N, 4·9; Cl, 12·4%).

3-p-*Methoxyphenoxy*iso*butane*-1 : 2-*diol*.—*p*-Methoxyphenol (12·4 g.) and β-methylglycidol (8·8 g.) heated at 90—95° for 2 hours with the addition of pyridine (0·1 c.c.), afforded the *diol* (14·3 g.), m. p. 103—104°. A similar yield was obtained when the same reactants were heated at 115° for 3 hours or at 90—95° for 3 hours. The product was identical with that prepared from *p*-methoxyphenol and 3-chloro*iso*butane-1 : 2-diol; that had m. p. 104° (Found: C, 62·2; H, 7·5. $C_{11}H_{16}O_4$ requires C, 62·3; H, 7·6%).

3-(4-*Chloro*-3-*methylphenoxy*)iso*butane*-1 : 2-*diol*.—(1) 4-Chloro-3-methylphenyl 2-methylallyl ether (50 g.; see below) was added at 45° to a solution of peracetic acid prepared from acetic acid (240 c.c.) and hydrogen peroxide (100 vol; 75 g.). On being heated to 70° all the ether dissolved, and the reactants were kept at this temperature for an hour. The product was dissolved in ether–light petroleum, and the solution cooled in ice. A solid (A), m. p. 77—78° (7·85 g.), separated. The mother-liquor was evaporated and the residual oil hydrolysed, to give 19·2 g. of material (B), m. p. 78° (Found: C, 57·4; H, 6·7. $C_{11}H_{15}O_3Cl$ requires C, 57·3; H, 6·6%). Both the products (A) and (B) consisted of the almost pure 4-*chloro*-3-*methylphenyl ether* of methylglycerol.

The 4-*chloro*-3-*methylphenyl* 2-*methylallyl ether* used in this preparation as obtained in 75% yield by heating an equimolecular mixture of 4-chloro-3-methylphenol and 2-methylallyl chloride in aqueous alcohol in the presence of potassium hydroxide. It was an oil, b. p. 108°/1 mm. (Found: C, 67·0; H, 6·7. $C_{11}H_{13}OCl$ requires C, 67·15; H, 6·7%).

(2) The same diol was obtained in 65% yield when a mixture of β-methylglycidol (1 mol.) and 3-chloro-4-methylphenol (1·05 mol.) was heated for 3·5 hours at 90—95° in the presence of pyridine (0·01 mol. per 100 g. of reactants).

3-m-*Nitrophenoxy*iso*butane*-1 : 2-*diol*.—(1) 2-Methylallyl *m*-nitrophenyl ether (1 mol.) was oxidised during 4 hours at 70° with a solution of peracetic acid prepared from hydrogen peroxide (2·1 mols.). The product was isolated and then hydrolysed with aqueous-alcoholic sulphuric acid to 3-m-*nitrophenoxy*iso*butane*-1 : 2-*diol*, m. p. 68° (Found: C, 53·6; H, 6·3; N, 5·9. $C_{10}H_{13}O_5N$ requires C, 52·9; H, 5·7; N, 6·2%), in 33% yield. The 2-*methylallyl* m-*nitrophenyl ether* employed in this preparation was prepared in 45% yield by condensing equimolecular amounts of 2-methylallyl iodide and *m*-nitrophenol in aqueous alcohol in the presence of potassium hydroxide. The product was an oil, b. p. 95—98°/0·1 mm. (Found: C, 61·8; H, 5·9; N, 7·1. $C_{10}H_{11}O_3N$ requires C, 62·2; H, 5·7; N, 7·3%.

(2) The same diol was obtained in 10% yield by condensing *m*-nitrophenol (1·05 mols.) with β-methylglycidol (1·0 mol.) for 3·5 hours at 95° in the presence of pyridine (0·01 mol. per 100 g. of reactants).

3-m-*Carbobutoxyphenoxy*iso*butane*-1 : 2-*diol*.—2-Methylallyl chloride (20 g.) was added to a solution containing butyl *m*-hydroxybenzoate (38·8 g.) and potassium hydroxide (11·2 g.) in a mixture of alcohol (200 c.c.) and water (25 c.c.), and the whole heated under reflux for 75 minutes; the resulting m-*carbobutoxyphenyl* 2-*methylallyl ether* (31·1 g.; 62%) was isolated as a colourless, viscous oil, b. p. 153—154°/1 mm. (Found: C, 72·2; H, 7·9. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%).

The product (30 g.) was added at 35° to a solution of peracetic acid prepared from acetic acid (80 c.c.) and hydrogen peroxide (100-vol.; 25 g.). When warmed to 70° the mixture became homogeneous. It was kept for an hour at 70—75° and then the product was treated as described for the 3-*m*-tolyloxy-analogue (1*a*, p. 2879). The *diol* was obtained as a pale yellow, viscous oil, and this was heated at 90° for 2 hours at 1 mm., but not distilled (Found: C, 63·1; H, 7·7. $C_{15}H_{22}O_5$ requires C, 63·8; H, 7·9%).

3-p-*Carbobutoxyphenoxy*iso*butane*-1 : 2-*diol* was prepared similarly by oxidising butyl *p*-2-methylallyloxybenzoate (1 mol.) during 3—4 hours at 70° with peracetic acid prepared from acetic acid and hydrogen peroxide (100-vol.; 2·1 mols.), the product being finally hydrolysed with aqueous-alcoholic sulphuric acid. The diol (yield, 50%) has m. p. 56° (Found: C, 63·5; H, 7·7%). The *butyl* p-2-*methylallyloxybenzoate* used in this preparation was obtained in 40% yield by condensing equimolecular amounts of butyl *p*-hydroxybenzoate and 2-methylallyl chloride in acetone in the presence of anhydrous potassium carbonate. It was an oil, b. p. 218—220°/33 mm. (Found: C, 72·1; H, 7·8. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·1%).

None of the β-methylglycerol derivative could be isolated from a similar oxidation of p-2-*methylallyloxybenzoic acid*, which was prepared (yield 90%) by condensing equimolecular amounts of *p*-hydroxybenzoic acid and 2-methylallyl chloride in alcoholic potassium hydroxide. It had m. p. 132° (Found: C, 67·9; H, 6·4. $C_{11}H_{12}O_3$ requires C, 68·5; H, 6·3%).

3-p-*Tolyloxy*iso*butane*-1 : 2-*diol*.—(1) 2-Methylallyl *p*-tolyl ether (1 mol.) was heated at 65—70° during 2·5 hours with peracetic acid prepared from hydrogen peroxide (2·1 mols.). The reaction product was isolated and heated with aqueous-alcoholic sulphuric acid, then recovered and crystallised from carbon tetrachloride. The *diol* was obtained as needles, m. p. 106° (Found: C, 67·7; H, 8·2. $C_{11}H_{16}O_3$ requires C, 67·3; H, 8·2%).

(2) A solution of peracetic acid was prepared from hydrogen peroxide (100-vol.; 171 g.) and acetic acid (420 c.c.), and then 2-methylallyl *p*-tolyl ether (121·5 g.) was added at 50°. The temperature rose to 80° during 12 minutes and at this point the solution was cooled, kept at 35° for an hour, and then added to water (2 vols.). The precipitated oil was extracted by chloroform (4 × 250 c.c.), isolated, and distilled. The following fractions were obtained: (*a*) b. p. 58°/0·7 mm. (36 g.); (*b*) b. p. 58—72°/0·5 mm. (12 g.); (*c*) b. p. 80°/0·5 mm. (17 g.); (*d*) b. p. 140—155°/1—2 mm. (37 g.). Fraction (*a*) was mainly 2-methylallyl *p*-tolyl ether, fraction (*c*) mainly 1 : 2-epoxy-3-*p*-tolyloxy*iso*butane, and fraction (*b*) contained both these constituents. Fraction (*d*) was a viscous oil. Fraction (*c*) was characterised by reaction with diethylamine in slight excess. 1-*Diethylamino*-3-p-*tolyloxy*iso*butan*-2-*ol*

was formed readily. It was obtained by distillation as a pale yellow oil, b. p. 146°/0·5 mm. (Found: C, 72·1; H, 9·9; N, 5·6. $C_{15}H_{25}O_3N$ requires C, 71·7; H, 10·0; N, 5·6%). Fraction (*d*) crystallised from carbon tetrachloride, yielding 3-*p*-tolyloxy*iso*butane-1 : 2-diol (14 g.), m. p. 104—105°, unchanged when mixed with an authentic sample. The mother-liquor was evaporated, and the residue heated with dilute alcoholic sulphuric acid. The hydrolysed residue was recovered and recrystallised from carbon tetrachloride. In this way an additional 10·5 g. of the ether, m. p. 104—105°, were obtained.

Hydrolysis of 1 : 2-*epoxy*-3-p-*tolyloxy*iso*butane*. Fraction (*c*) was redistilled to give the pure glycide ether, which (4·45 g.) was heated with a mixture of glacial acetic acid (14 c.c.) and water (5·7 c.c.) for 2 hours at 95°. The product was isolated by pouring the mixture into water, extraction into chloroform, and recovery. It was then crystallised from carbon tetrachloride, yielding 1·8 g. of the ether, m. p. 104—105°. The mother-liquor was evaporated, and the residue heated with alcoholic sulphuric acid. After addition of water, extraction into chloroform, recovery, and crystallisation from carbon tetrachloride, an additional 1·5 g. of the ether, m. p. 104—105°, were obtained.

In a similar experiment the same amount of the glycide ether was caused to react under the same conditions with peracetic acid prepared from acetic acid (14 c.c.) and hydrogen peroxide (100-vol; 5·7 c.c.). Crystallisation of the product from carbon tetrachloride afforded the ether (1·6 g.), m. p. 105—106°, and more (1·3 g.) of the same ether resulted when the mother-liquor was evaporated and the residue hydrolysed by means of alcoholic sulphuric acid.

(3) A mixture of *p*-cresol (21·6 g.) and β-methylglycidol (17·6 g.) containing two drops of pyridine was heated at 90—95° for 3·5 hours. 3-*p*-Tolyloxy*iso*butane-1 : 2-diol (28 g.), m. p. 105°, was obtained after crystallisation of the product from carbon tetrachloride. An almost identical yield was obtained when the pyridine was replaced by its ethiodide, and the reaction carried out at 115° for 3 hours.

3-p-*Chlorophenoxy*iso*butane*-1 : 2-*diol*.—(1) *p*-Chlorophenyl 2-methylallyl ether (1 mol.) was heated at 70° for 3—4 hours with a solution of peracetic acid, prepared from 2·1 mols. of hydrogen peroxide. The product was isolated, and then heated with a 1% solution of concentrated sulphuric acid in 50% aqueous alcohol. The *diol* thus obtained crystallised from carbon tetrachloride, m. p. 103° (Found: C, 55·7; H, 6·1. $C_{10}H_{13}O_3Cl$ requires C, 55·4; H, 6·1%).

(2) *p*-Chlorophenyl 2-methylallyl ether (91·3 g.) was added to a solution of peracetic acid prepared from glacial acetic acid (280 c.c.) and hydrogen peroxide (100-vol.; 114 g.). The mixture was heated at 67° until it became homogeneous (2 minutes), and then the temperature was allowed to rise during 4 minutes to 85°. The product was quickly cooled to 30°, kept at this temperature for 3 hours, and then poured into water. The precipitated oil was taken up in chloroform, washed, dried, and distilled. The following fractions were obtained: (*a*) b. p. 80—100°/1 mm. (20 g.); (*b*) b. p. 100—120°/1 mm. (30·5 g.); (*c*) b. p. 120—170°/1 mm. Fraction (*a*) was mainly *p*-chlorophenyl 2-methylallyl ether. Fraction (*b*) distilled mainly at 112°/1 mm. and again at this temperature on redistillation. It was 3-*p*-chlorophenoxy-1 : 2-epoxy*iso*butane, as shown by its conversion into 1-diethylamino-3-*p*-chlorophenoxy*iso*butan-2-ol by reaction with diethylamine. Fraction (*c*) crystallised from carbon tetrachloride yielding 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol (18 g.), m. p. 101—102° not depressed on admixture with the product of preparation (1). The mother-liquor gave a tacky residue on evaporation, and this was heated under reflux with a 1% solution of concentrated sulphuric acid in 50% aqueous alcohol. After isolation of the hydrolysed product and recrystallisation from carbon tetrachloride an additional 9·1 g. of 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol, m. p. 100—101°, were obtained.

(3) A solution of potassium permanganate (15·8 g.) in water (1 l.) was added during 1 hour to a stirred solution of *p*-chlorophenyl 2-methylallyl ether (27·4 g.) in acetone (300 c.c.), the temperature being kept at 0°. The oxidation complete, the precipitated manganese dioxide was filtered off and washed with chloroform. The filtrate was extracted by means of chloroform, and the combined chloroform solutions were evaporated. The residue (2 g.) crystallised from carbon tetrachloride in small feathery plates, m. p. 102—103° not depressed on mixing with 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol obtained as in (2), above.

(4) *p*-Chlorophenol (1·05 mols.) and β-methylglycidol (1·0 mol.) were heated at 90—95° for 3·5 hours in the presence of pyridine (0·01 mol. per 100 g. of total reactants). The product, crystallised from carbon tetrachloride, was obtained, m. p. 98—100°, in 60% yield. When an equimolecular amount of pyridinium ethiodide was used at 115° in this preparation instead of pyridine an almost identical yield was obtained.

Action of Acetic Acid on 3-p-*Chlorophenoxy*iso*butane*-1 : 2-*diol*.—A solution containing this diol (10·8 g.) in a mixture of acetic acid (28 c.c.) and water (11·4 c.c.) was heated at 95° for 5 hours, then cooled and added to water, and the product extracted by means of chloroform. The chloroform was evaporated, and the residue crystallised from carbon tetrachloride. 3-*p*-Chlorophenoxy*iso*butane-1 : 2-diol (8·2 g.), m. p. 103°, was recovered by this means. The mother-liquor was concentrated and then mixed with light petroleum. Crystals, m. p. 60—62°, slowly separated (1·5 g.). The product recrystallised from light petroleum (b. p. 40—80°) in small, hard, white prisms, m. p. 65—66° (Found: C, 55·6; H, 5·8; Cl, 13·4. $C_{12}H_{15}O_4Cl$ requires C, 55·7; H, 5·9; Cl, 13·7%). This compound was 3-p-*chlorophenoxy*iso*butane*-1 : 2-*diol monoacetate*.

In several similar experiments the concentration of the acetic acid employed was varied. In each experiment heating was carried out under reflux for 8 hours. The proportions of methylglycerol ether recovered and *O*-acetate formed were:

Concn. of acetic acid (% by vol.)	100	72·1	51·2
Methylglycerol ether recovered, %	None	50	77·8
Methylglycerol ether *O*-acetate isolated, %	85	36·4	11·6

Action of Acetic and Peracetic Acids on 3-p-*Chlorophenoxy*-1 : 2-*epoxy*iso*butane*.—(1) The epoxide (9·98 g.) was added to 2 mols. of peracetic acid prepared from acetic acid (28 c.c.) and hydrogen peroxide (100-vol.; 11·4 g.). The mixture was heated for an hour at 75°, then diluted, and the product extracted by means of chloroform. The chloroform solution was washed and then concentrated, and light petroleum was added to turbidity. Crystals of 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol, m. p. 100—101°, separated (4·3 g.). The mother-liquor was evaporated and the residue heated for an hour with a 1% solution of concentrated sulphuric acid in 50% aqueous alcohol. The hydrolysed product was extracted by means of chloroform; it crystallised when light petroleum was added. A second crop (2·3 g.) of the diol, m. p. 100—101°, was thus obtained. The second crop being assumed to have been derived by hydrolysis of an acetate, the yields of the methylglycerol ether obtained at the two stages indicate that the methylglycerol ether and its *O*-acetate were formed in the ratio 1·87 : 1 by the action of a solution of peracetic acid in acetic acid on 3-(*p*-chlorophenoxy)-1 : 2-epoxy*iso*butane.

(2) In a similar experiment in which the solution of peracetic acid was replaced by a mixture of acetic acid (28 c.c.) and water (11·4 c.c.) the yield of 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol first obtained was 5·0 g. Hydrolysis of the non-crystallising constituent then afforded an additional 2·4 g. of the same methylglycerol ether. The relative amounts of 3-*p*-chlorophenoxy*iso*butane-1 : 2-diol obtained at the two stages indicate the formation of the methylglycerol ether and its *O*-acetate in the ratio 2·04 : 1 by the action of acetic acid on 3-*p*-chlorophenoxy-1 : 2-epoxy*iso*butane.

3-p-*Chlorophenoxy*-1-*diethylamino*iso*butan*-2-*ol*.—Fraction (*b*), b. p. 112°/1 mm., obtained in the oxidation of *p*-chlorophenyl 2-methylallyl ether by means of peracetic acid (p. 2882) reacted with diethylamine with evolution of heat. The *adduct* was obtained as a yellow oil, b. p. 155°/0·5 mm. (Found: C, 62·15; H, 8·1; N, 4·7; Cl, 13·2. $C_{14}H_{22}O_2NCl$ requires C, 61·8; H, 8·2; N, 5·2; Cl, 13·1%).

3-*Chloro*iso*butane*-1 : 2-*diol*.—(1) To a solution of peracetic acid prepared from acetic acid (1500 c.c.) and hydrogen peroxide (100-vol.; 450 g.) was added 2-methylallyl chloride (181 g.). The mixture was kept at 25° for 5 days and then concentrated under reduced pressure. Distillation gave: (*a*) unchanged 2-methylallyl chloride (10 g.); (*b*) a fraction, b. p. 70—80°/1 mm. (10—12 g.); (*c*) 3-chloro*iso*butane-1 : 2-diol and its *O*-acetate, b. p. 79—80°/0·5 mm. (170—175 g.); (*d*) a fraction of higher b. p. (25—30 g.).

(2) The same reactants, mixed at the room temperature and then heated at 70° for an hour, gave the following products: (*a*) unchanged 2-methylallyl chloride (30 g.); (*b*) 3-chloro*iso*butane-1 : 2-diol and its *O*-acetate, b. p. 78—83°/0·5 mm. (140—145 g.); (*c*) a higher-boiling fraction (20 g.).

The mixture of 3-chloro*iso*butane-1 : 2-diol and its *O*-acetate (60 g.), obtained under either of the conditions described, was heated under reflux for an hour with a 1% solution of concentrated sulphuric acid in 50% aqueous alcohol. The yield of recovered 3-chloro*iso*butane-1 : 2-diol was 48 g.

β-Methylglycidol.—A solution of potassium hydroxide (56 g.) in dry ethanol (200 c.c.) was added dropwise to a solution of 3-chloro*iso*butane-1 : 2-diol (125 g.) in alcohol (100 c.c.), which was cooled in water to keep the temperature at 13—15°. The mixture was kept for 20 minutes after the addition was complete. It was then filtered, and the filtrate concentrated to half volume under reduced pressure. Salts were then precipitated by adding ether (2 vols.) to the residue. The suspension was filtered, and the filtrate distilled. The fraction, b. p. 70—85°/18—20 mm., was collected and redistilled to give pure β-methylglycidol, b. p. 80°/21 mm. (70 g., 80%).

Several condensations of phenols with 3-chloro*iso*butan-1 : 2-diol, not describe above, are summarised in the attached table.

Reactants						Products						
							Found, % :			Reqd., % :		
Phenol deriv.	Wt. (g.)	Diol (g.)	EtOH (c.c.)	K_2CO_3 (g.)	Reflux time (hr.)	M. p.	C	H	Formula	C	H	Yield (g.)
m-Me	5·4	7·8	50	6·9	3	—	—	—	—	—	—	6·1
3 : 5-Me_2	24·4	24·9	250	27·6	4	77	—	—	—	—	—	21·7
o-Cl	21·5	31·2	150	34·5	3	56 [a]	55·0	6·1	$C_{10}H_{13}O_3Cl$	55·4	6·1	—
o-I	22	15·6	150	35	3	71 [a]	39·1	4·0	$C_{10}H_{13}O_3I$	39·0	4·3	22
p-I	22	15·6	150	35	3	106 [b]	39·2	4·2	,,	,,	,,	24·8
o-OMe	30	40	150	40	4	77 [a]	62·4	7·7	$C_{11}H_{16}O_4$	62·3	7·6	—
m-OMe	30	33	150	35	3	90 [b]	62·3	7·4	,,	,,	,,	—
p-OMe	22	30	150	30	3	104 [b]	62·2	7·5	,,	,,	,,	15
p-NHAc	21·5	19·8	150	27·6	5	147 [a]	60·2	7·0 *	$C_{12}H_{17}O_4N$	60·2	7·2	26

[a] Needles. [b] Prisms. * Found: N, 5·5. Reqd.: N, 5·9%.

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