359. *The Catalysed Transfer of Hydrogen Chloride from Chlorohydrins to Epoxides. A New Method of Preparing Glycidol and Some of its Derivatives.*

By William Bradley, James Forrest, and Oliver Stephenson.

Experiments are described on the condensation of epichlorohydrin with phenols to form 1-aryloxy-3-chloropropan-2-ols. The reaction is catalysed by bases, pyridine being the most useful catalyst. The reaction furnishes two by-products, αγ-dichlorohydrin and an αα′-diaryl ether of glycerol. It has been found that the transfer of hydrogen chloride from a chlorohydrin to an epoxide takes place readily in the presence of catalysts. The 1-aryloxy-3-chloropropanols first produced lose hydrogen chloride to form aryl glycide ethers. The liberated hydrogen chloride combines with epichlorohydrin to form αγ-dichlorohydrin, and the aryl glycide ethers combine with the phenols to form αα′-diaryl ethers of glycerol. The mode of reaction of the catalysts is discussed. Several applications of the hydrogen chloride transfer reaction are described in the preparation of glycidol and its derivatives.

The condensation of phenols with epichlorohydrin to form 1-aryloxy-3-chloropropan-2-ols (I) has been studied by many authors. Lindemann (*Ber.*, 1891, **24**, 2145) obtained these products in poor yield by heating a mixture of the two reactants. Later, Boyd and Marle (*J.*, 1910, **97**, 1788) and Marle (*J.*, 1912, **101**, 305) improved the yields by carrying out the condensation in the presence of sodium hydroxide at room temperature for a period of six weeks. More recently, Levas and Lefebre (*Compt. rend.*, 1946, **222**, 555, 1439) have employed boron trifluoride, a reagent which necessitates the use of a large excess of the phenols if the 1-aryloxy-3-chloropropan-2-ols are to be prepared in good yield. Several authors (Lindemann, *loc. cit.*; Boyd and Marle, *J.*, 1908, **93**, 838; 1909, **95**, 1807) have reported the formation of αα′-diaryl ethers of glycerol (III) as by-products.

$$\mathrm{ArOH} + \mathrm{CH_2{-}CH{\cdot}CH_2Cl} \longrightarrow \mathrm{ArO{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2Cl} \quad \text{(I.)}$$

$$\text{(II.)} \quad \mathrm{ArO{\cdot}CH_2{\cdot}CH{-}CH_2} \xrightarrow{\mathrm{ArOH}} \mathrm{ArO{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2{\cdot}OAr} \quad \text{(III.)}$$

The readiness of alkali phenoxides to combine with epichlorohydrin harmonizes with a number of observations which have shown that anions react easily with α-epoxides. Sodiomalonic ester (Traube and Lehmann, *Ber.*, 1899, **32**, 720; 1901, **34**, 1971; Haller and Blanc, *Compt. rend.*, 1906, **142**, 1471; Kotz and Hoffmann, *J. pr. Chem.*, 1925, **110**, 105), sodium hydrogen sulphite

(Erlenmeyer, *Z. Chem.*, 1868, 342; Darmstadter, *Annalen*, 1868, **148**, 125; Brunel, *Compt. rend.*, 1903, **137**, 63), and sodium thiosulphate (Ross, *J.*, 1950, 2257) all react additively with α-epoxides and the same is likely to be true of phenoxide ions.

The present study of the condensation of phenols with epichlorohydrin has shown that tertiary amines, *e.g.*, pyridine and triethylamine, are suitable catalysts for the reaction. Primary and secondary amines also may be used but offer no advantages. Good results are obtained by employing the reactants in equimolecular proportions and adding the tertiary amines in amounts equivalent to 0·2—1·0% of the combined weight. At 90—95° the 1-aryloxy-3-chloropropan-2-ols are obtained in 50—70% of the theoretical yield after 4—10 hours' heating. The results compare favourably with the optimum yields of Boyd and Marle (*J.*, 1910, **97**, 1778) and Marle (*loc. cit.*), who obtained yields of 26% and 60—70% after keeping the reactants at room temperatures for 21 and 40—60 days, respectively. As in the older methods of preparation, by-products are formed, the proportion increasing with increase in the proportion of the tertiary base.

The more acidic phenols combine more readily than the weaker with epichlorohydrin. This result is to be expected if the relative concentration of the various phenoxide ions in the reaction mixture is the most important consideration, but the relative reactivities of the phenoxide anions towards epichlorohydrin must also be involved. In this connection Brønsted, Kilpatrick, and Kilpatrick (*J. Amer. Chem. Soc.*, 1929, **51**, 428) observed the following anions to be in order of increasing reactivity towards epichlorohydrin, formate < benzoate < acetate < chloride < bromide < iodide. The anions of the halogen hydracids were more effective than any derived from the weaker organic acids, but within the series of organic anions the anion of the weakest acid was the most effective. The greater reactivity of the more strongly acidic phenols was reflected in the higher yields of 1-aryloxy-3-chloropropan-2-ols obtained by their use.

Whichever condensing agent is employed, the reaction product contains the αα′-diaryl ethers (III). Table I (p. 1594) summarises the yields of (I) and (III), expressed as percentages of the theoretical, when various phenols are condensed with equimolecular amounts of epichlorohydrin; the amounts of catalyst are expressed as percentages of the combined weights of the reactants.

The yields of the 1-aryloxy-3-chloropropan-2-ols are uniformly higher than those of the related αα′-diaryl ethers of glycerol. It appeared that hydrogen chloride was lost from the chlorohydrins, yielding the 1-aryloxy-2 : 3-epoxypropanes (II), which then reacted additively with phenols. The formation of epoxides such as (II) from chlorohydrins (I), however, was believed to require the use of strong alkalis.

Two observations have now been made which suggest the correctness of the second hypothesis; both αγ-dichlorohydrin and the epoxides (II) can be isolated from the reaction products. For example, the condensation of epichlorohydrin with β-naphthol yields 1-chloro-3-naphthoxypropane-2-ol and αγ-dichlorohydrin; phenol and epichlorohydrin yield 1-chloro-3-phenoxypropane-2-ol, glycide phenyl ether, 1 : 3-diphenoxypropan-2-ol, and αγ-dichlorohydrin.

The dichlorohydrin could only have resulted by the addition of hydrogen chloride to epichlorohydrin, and glycide phenyl ether only by loss of hydrogen chloride from 1-chloro-3-phenoxypropan-2-ol. It appeared possible that the two reactions were related, epichlorohydrin acting as a hydrogen chloride acceptor and 1-chloro-3-phenoxypropan-2-ol as a hydrogen chloride donor.

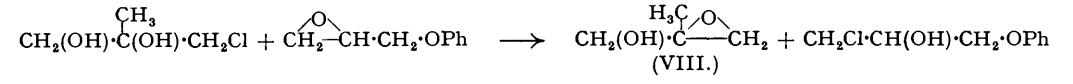
Experiment has shown that the transfer of hydrogen chloride from chlorohydrins to epoxides takes place readily in many instances under appropriate conditions, a new epoxide and chlorohydrin resulting.

$$\underset{\text{(IV.)}}{RO\cdot CH_2\cdot CH(OH)\cdot CH_2Cl} + \underset{\text{(V.)}}{R'O\cdot CH_2\cdot CH\!-\!CH_2} \rightleftharpoons \underset{\text{(VI.)}}{RO\cdot CH_2\cdot CH\!-\!CH_2} + \underset{\text{(VII.)}}{R'O\cdot CH_2\cdot CH(OH)\cdot CH_2Cl}$$

When α-monochlorohydrin (IV; R = H) is heated with glycide phenyl ether (V; R′ = Ph) and the product is fractionally distilled, glycidol (VI; R = H) and 1-chloro-3-phenoxypropan-2-ol (VII; R′ = Ph) are obtained. Similarly, glycidol results together with a 1-chloro-3-aryloxypropan-2-ol when α-monochlorohydrin is heated with glycide *o*-tolyl ether, glycide *p*-tolyl ether, or glycide *p*-chlorophenyl ether. An analogous reaction occurs between monochlorohydrin and quinol bisglycide ether. Under appropriate conditions the yield of glycidol exceeds 95% of the theoretical.

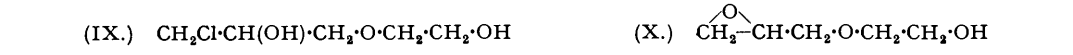
The transfer of hydrogen chloride from a chlorohydrin to an epoxide has enabled many derivatives and analogues of glycidol to be prepared conveniently. β-Methylglycidol (VIII) results by heating 3-chloro*iso*butane-1 : 2-diol with glycide phenyl ether. *O*-Acetylglycidol is

formed by heating 1-acetoxy-3-chloropropan-2-ol with glycide *p*-chlorophenyl ether. Glycide 2-hydroxyethyl ether (X) is produced by heating 1-chloro-3-2′-hydroxyethoxypropan-2-ol



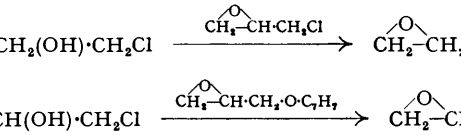
(VIII.)

(IX) with either glycide *p*-chlorophenyl ether or glycide β-naphthyl ether. 1-Chloro-3-2′-hydroxyethoxypropan-2-ol and glycide *p*-chlorophenyl ether yield 1 : 2-epoxy-3-2′-hydroxy-



(IX.) (X.)

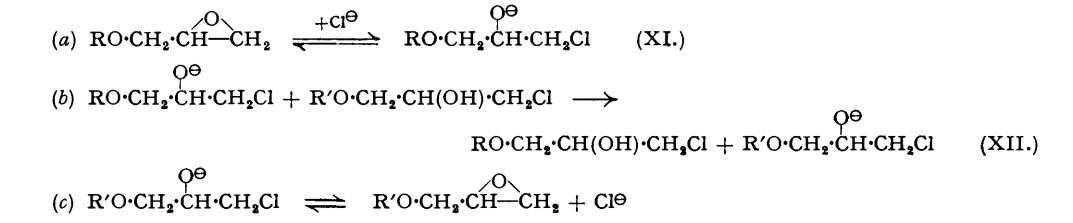
ethoxypropane. This was characterised by combining it with *o*-cresol to give 1-2′-hydroxyethoxy-3-*o*-tolyloxypropan-2-ol. Aryl ethers of glycidol can be prepared by similar processes. 1-Chloro-3-*o*-tolyloxypropan-2-ol, heated with either glycide β-naphthyl ether or *p*-phenylene bisglycide ether, yields glycide *o*-tolyl ether Epichlorohydrin results when glycerol αγ-dichlorohydrin is heated with glycide *o*-tolyl ether; ethylene oxide by heating ethylene chlorohydrin with epichlorohydrin:



The process of hydrogen chloride transfer is not limited to 1 : 2-chlorohydrins. For example heating with glycide phenyl ether transforms 3-bromopropan-1-ol into 1 : 3-epoxypropane (oxetane).

The method enables a number of difficultly accessible epoxides to be prepared from the more readily accessible. The most satisfactory procedure is to mix the chlorohydrin related to the epoxide to be prepared with an epoxide of higher boiling point to function as a hydrogen chloride acceptor. The mixture of chlorohydrin and epoxide is heated and then distilled slowly through an efficient column at an appropriate pressure. The epoxide produced as a result of the reaction distils, leaving behind a chlorohydrin related to the original epoxide reactant. Propylene oxide is conveniently prepared at atmospheric pressure. Glycidol and its simple derivatives are preferably distilled at 10—20 mm. Lower pressures are desirable when the product is a glycide aryl ether. In all the instances investigated the transfer of hydrogen chloride required the presence of a catalyst. Aqueous ammonia, primary and secondary amines such as aniline and piperidine, potassium hydroxide, and potassium carbonate were effective, but tertiary amines such as pyridine, quinoline, and triethylamine were more satisfactory. The most successful catalysts giving the highest rate of transfer were quaternary ammonium salts such as pyridinium ethiodide, *p*-nitrobenzylpyridinium bromide, and 2′ : 3′-dihydroxypropylpyridinium chloride. Table II (p. 1596) summarises the results of several interchange reactions employing various chlorohydrins and epoxides and a range of catalysts. On p. 1595 are summarised results which show the influence of conditions on the progress of one reaction, *viz.*, that between *p*-chlorophenyl glycide ether (2 mols.) and α-monochlorohydrin (1 mol.), which yields glycidol as the volatile product in 0—98% of the theoretical yield, calculated on the α-monochlorohydrin employed.

When the catalyst is a quaternary ammonium salt it is always recoverable unchanged from the product of the reaction. The efficiency of the salts as catalysts recalls the experiments of Brønsted, Kilpatrick, and Kilpatrick (*loc. cit.*) in which the reactivity of epoxides towards halide ions was demonstrated. It would appear that their content of halide ions is important, even



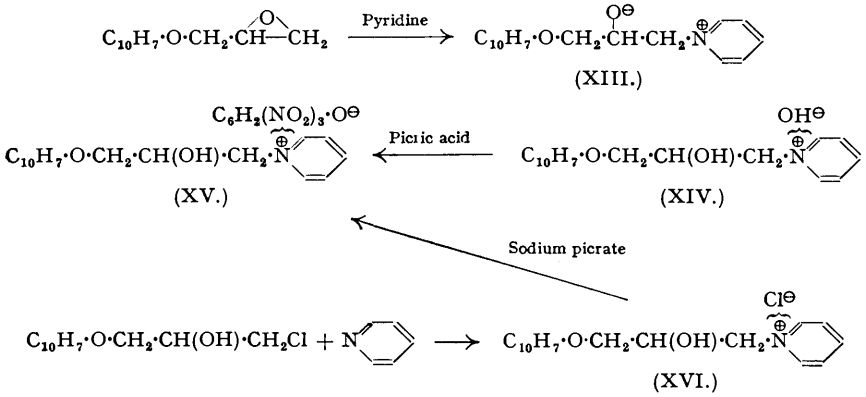
(XI.) (XII.)

if not essential, to the catalytic activity of the quaternary salts. Hammett (" Physical Organic Chemistry," McGraw-Hill Book Co. Inc., p. 301) has postulated the formation of a

complex ion (XI), and it may be expected that such would be in equilibrium with the epoxide and react with one or more of the hydroxylated compounds present, *e.g.*, the chlorohydrin reactant. If the chlorohydrin is involved a new complex ion (XII) will result, and this will decompose, yielding a new epoxide and regenerating a chloride ion.

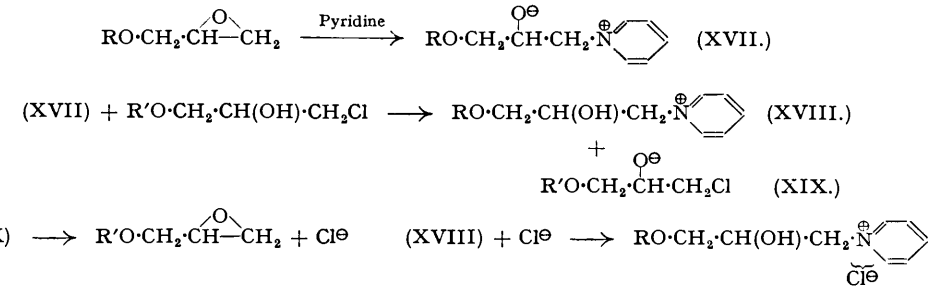
Tertiary amines employed as condensing agents become modified during the reaction, and appear in the product as quaternary ammonium salts; some part of their activity may be due to the salts into which they are transformed. Initially, however, their reaction must involve either the epoxide or the chlorohydrin originally present: the former is the more probable course for the following reasons. In separate experiments it has been shown that the rate of reaction of the chlorohydrins with pyridine is slow, even at high temperatures. By comparison, the rate of reaction of pyridine with epoxides is rapid. Finally, the quaternary salts formed during the reaction are related to the epoxide originally present, not to the chlorohydrin reactant. For example, in the reaction between α-monochlorohydrin and glycide phenyl ether catalysed by pyridine, the base is transformed into 2′-hydroxy-3′-phenoxypropylpyridinium chloride. Only when the molecular concentration of the pyridine approaches that of the epoxide and chlorohydrin reactant are two quaternary salts isolable.

The products obtained by reaction of pyridine with epoxides had the character of internal salts. For example, glycide β-naphthyl ether and pyridine yielded a product, regarded as (XIII), which was soluble in water but insoluble in ether. The aqueous solution, mixed with sodium picrate or picric acid, precipitated 2′-hydroxy-3′-β-naphthoxypropylpyridinium



picrate (XV), identical with the product obtained by reaction of 2′-hydroxy-3′-β-naphthoxypropylpyridinium chloride (XVI) with sodium picrate. Mixed with hydrochloric acid, the aqueous solution yielded 2′-hydroxy-3′-β-naphthoxypropylpyridinium chloride directly. The chloride so formed was identical with the salt obtained by combining pyridine with 1-chloro-3-β-naphthoxypropan-2-ol. It appears that the aqueous solution of the epoxide–pyridine adduct contains the internal salt (XIII) or the related 'onium hydroxide (XIV), or both of these forms.

The catalytic action of pyridine in promoting the transfer of hydrogen chloride from a chlorohydrin to an epoxide may therefore involve the following stages:



Experiments on the character and yield of the quaternary salts isolable from epoxide–chlorohydrin mixtures after they had been heated with pyridine are summarised in Table III.

The results show that when relatively large amounts of pyridine are used the yields of quaternary salts increase markedly with time of heating, and with increase in the proportion of epoxide reactant. Reduction in the proportion of pyridine increases the yields of isolable homogeneous quaternary salts, probably for the reason that with small amounts of pyridine reaction is mainly confined to the formation of one of the two possible salts, which individual is then more easily isolated. The properties of the quaternary chlorides and picrates encountered in these experiments are summarised on pp. 1595, 1597.

Pyridine ethiodide employed as a catalyst in the reaction of epoxides with chlorohydrins was recovered in its original form. The iodide was expected to be more reactive than the chloride in view of the results of Brønsted *et al.* (*loc. cit.*) but the ultimate presence of iodide in the product suggests that the iodide has a lower solubility than the chloride.

The catalytic activity of alkali hydroxides and carbonates probably depends on their ability to liberate chloride ions from the chlorohydrin constituent; these bases are, in fact, changed into alkali chlorides during the reaction. Preformed sodium and potassium chloride have little or no catalytic action, probably because of their insolubility in the reagents. Hydrogen chloride exerts a catalytic effect which is less marked than that of pyridine or pyridinium ethiodide. In this instance chloride ions are present initially, but some become combined with the epoxide reactant, yielding a chlorohydrin, and are not replaced :

$$HCl + >C\overset{O}{\diagup\!\diagdown}CH_2 \longrightarrow >C(OH)\cdot CH_2Cl$$

The rate of transfer of hydrogen chloride increased with the proportion of catalyst employed. When tertiary amines or quaternary ammonium halides were used, 0·02—0·04 mol. of the catalyst per 100 g. of total reactants afforded a convenient rate of transfer. In preparing epoxides that were prone to polymerise, it was important to ensure that the distillate was free from catalyst. In these instances the use of the quaternary ammonium halides was preferred. Alternatively, when tertiary amines were employed the reaction product was heated for some time before distillation to ensure complete conversion of the tertiary base into a non-volatile quaternary ammonium salt.

The preparation of anhydrous glycidol is of considerable practical interest. A convenient method affording almost theoretical yields consists in heating α-monochlorohydrin with a glycide aryl ether in the presence of pyridine or its ethiodide. This procedure may be contrasted with the earlier preparation by Nivière (*Bull. Soc. chim.*, **1914**, **15**, 464) in which a solution of α-monochlorohydrin in ether is treated with sodium.

The present investigation throws light on the mode of formation of the dichlorohydrin observed by Lespieaux (*ibid.*, **1905**, **33**, 462) as a by-product of the reaction between epichlorohydrin and hydrogen cyanide. In this reaction chlorine is eliminated, presumably as chloride ion, and the further reaction of this with epichlorohydrin must lead to dichlorohydrin.

Experimental.

Condensation of p-*Chlorophenol with Epichlorohydrin. Formation of* 1-*Chloro*-3-p-*chlorophenoxypropan*-2-*ol and Glycerol αα′-Di*-p-*chlorophenyl Ether.*—(1) *p*-Chlorophenol (112 g.), epichlorohydrin (81 g.), and 40% aqueous sodium hydroxide (1 c.c.) were mixed and kept at room temperature for 45 days. The product was made just acid with acetic acid, washed with water, dried (Na_2SO_4), and then distilled. The following fractions were collected; (*a*) b. p. up to 144°/1 mm. (12·1 g.); (*b*) b. p. 144—148°/1 mm. (148 g.). There was only a trace of a residue. The second fraction (Found, on hydrolysis : Cl′, 15·9. Calc. for $C_9H_{10}O_2Cl_2$: Cl′, 16·1%) was almost pure 1-chloro-3-*p*-chlorophenoxypropan-2-ol.

(2) When the reactants employed in (1) were heated under reflux for 24 hours instead of being kept at the room temperature, and the product was then distilled, a fraction, b. p. 138—140°/0·5 mm. (94 g.) was obtained. It consisted mainly of 1-chloro-3-*p*-chlorophenoxypropan-2-ol (yield, 52%). Its composition was proved by hydrolysing it to glycerol α-*p*-chlorophenyl ether. This fraction (22·1 g. of redistilled material, b. p. 138°/0·5 mm.) was heated under reflux during 5 hours with a solution of potassium carbonate (13·8 g.) in water (200 c.c.). After cooling, the solid product was collected, washed with water, and dried (yield 19·5 g.; m. p. 72—74°). Recrystallisation from carbon tetrachloride gave glycerol α-*p*-chlorophenyl ether, m. p. 76—78°, not depressed by admixture with an authentic specimen.

A minor fraction, b. p. 200—230°/0·5—1 mm. (21 g.), triturated with ether–light petroleum, gave a white, crystalline solid (19 g.) which after recrystallisation from ether–light petroleum afforded hard white prisms of glycerol *αα′-di*-p-*chlorophenyl ether*, m. p. 89—90° (Found : C, 57·5; H, 4·7; Cl, 22·4. $C_{15}H_{14}O_3Cl_2$ requires C, 57·5; H, 4·5; Cl, 22·7%).

Condensation of β-Naphthol with Epichlorohydrin. Formation of αγ-Dichlorohydrin.—A suspension containing β-naphthol (54 g.) and epichlorohydrin (38·2 g.) in benzene (80 c.c.) was heated until it became homogeneous. Pyridine (1 c.c.) was then added, and the heating continued at 80—90° for 20 hours. The solvent was distilled off, the last portions under somewhat reduced pressure. The residue was distilled, and a fraction, b. p. *ca.* 100°/12 mm., was collected, dried ($MgSO_4$), and redistilled at atmospheric

pressure. The main fraction, b. p. 160—175°, weighed 5·8 g. A few drops mixed with cold, alcoholic sodium hydroxide gave an immediate precipitate of sodium chloride and the characteristic odour of epichlorohydrin. The main portion was shaken with light petroleum (b. p. 40—60°) containing phenyl *iso*cyanate. Clusters of white plates slowly separated, and these, recrystallised from methanol, had m. p. 73°, not depressed when mixed with an authentic specimen of the phenylurethane of αγ-dichlorohydrin.

Condensation of Phenol with Epichlorohydrin. Formation of αγ-Dichlorohydrin and Glycide Phenyl Ether.—Phenol (188 g.), epichlorohydrin (194 g.), and pyridine (2 g.) were mixed and heated to 85—90°. An exothermic reaction occurred, necessitating cooling to prevent rise in temperature. The red-brown liquid was heated at 90° for a further 12 hours and then distilled. The following fractions were collected: (*a*) b. p. 85°/3 mm. (75 g.); (*b*) b. p. 90—115°/3 mm. (4 g.); (*c*) b. p. 120—135°/3 mm. (175 g.); (*d*) b. p. 140—185°/3 mm. (20 g.); (*e*) b. p. 185—195°/3 mm. (60 g.). A residue (15 g.) remained. Fraction (*a*), when redistilled, gave a middle fraction, b. p. 176—182°; when this was mixed with cold sodium hydroxide solution, epichlorohydrin, b. p. 117°, was formed. This result indicated the presence of αγ-dichlorohydrin in fraction (*a*). A further portion of fraction (*a*) was warmed with aqueous alcoholic sodium hydroxide and phenol [2 mols., calculated on assumption that fraction (*a*) was αγ-dichlorohydrin]. The reaction yielded glycerol αα′-diphenyl ether, m. p. 81°, not depressed when mixed with the same product prepared from authentic αγ-dichlorohydrin. Fraction (*b*) was redistilled, and a middle fraction, b. p. 89°/1 mm., collected. It was free from chlorine. Its identity as glycide phenyl ether was proved by mixing it with piperidine and crystallising the condensation product from light petroleum (b. p. 60—80°). The adduct formed large colourless needles, m. p. 55° (Found: C, 71·8; H, 8·4; N, 6·1. $C_{14}H_{21}O_2N$ requires C, 71·4; H, 9·0; N, 6·0%), identical with the 1-*phenoxy*-3-*piperidinopropan*-2-*ol* obtained by combining piperidine with an authentic specimen of glycide phenyl ether. Fraction (*c*) consisted essentially of 1-chloro-3-phenoxypropan-2-ol; the yield was 64% of the theoretical. Fraction

TABLE I.

Ar in ArOH.	Catalyst.	Amount of catalyst.	Reaction: Time.	Reaction: Temp.	Yield, %. Ar·O·CH$_2$·CH(OH)·CH$_2$Cl	Yield, %. Ar·O·CH$_2$·CH(OH)·CH$_2$·OAr
Phenyl	Na_2CO_3	0·25	24 hours	90°	40	—
	K_2CO_3	0·5	100 ,,	90	54	14
	,,	0·5	4 ,,	90—156	34	14
	,,	0·5	9·5 ,,	90—160	44	21
	Pyridine	0·5	20 ,,	90	46	15
	Quinoline	0·3	43 days	20	55	3
	Triethylamine	0·3	34 ,,	20	59	16·5
	Morpholine	0·4	61 ,,	20	66	12·4
m-Tolyl	Triethylamine	0·5	64 days	20	69	16·5
p-Tolyl	Dimethylaniline	1·0	10 hours	90—105	55	11·4
o-Tolyl	KOH	0·2	10 hours	80—90	24	—
	,,	0·2	65 days	20	36·3	9·5
	K_2CO_3	0·5	15 hours	128—153	17	3·5
	Pyridine	0·5	3 ,,	92—102	22·8	14·0
	Quinoline	1·0	64 days	20	44	7·4
	Dimethylaniline	0·75	3·5 hours	92—100	34	16·5
	,,	1·50	4 ,,	92—113	43·5	24·0
	,,	1·0	10 ,,	90—100	51	12·5
	Aniline *	0·5	64 days	20	18	?
	Triethylamine	0·6	3 hours	92—99	25·5	12·5
	,,	0·6	5·5 ,,	92—109	35	16·2
	Triethanolamine	0·5	3 ,,	92	22·3	7·3
p-Chlorophenyl	NaOH	0·2	45 days	20	76	None
	KOH	1·0	66 ,,	20	76·5	11·2
	Quinoline	0·5	69 ,,	20	78	3
	,,	0·5	64 ,,	20	72·8	5
	,, †	0·3	69 ,,	20	49	?
o-Methoxyphenyl	Pyridine	0·5	68 days	20	64	16
β-Naphthyl	Dimethylaniline ‡	1·7	20 hours	90	60	?

* Two molecular proportions of *o*-cresol were used in this experiment.
† Two molecular proportions of epichlorohydrin were used in this experiment.
‡ In this experiment benzene was used as a diluent.

(*e*) solidified on cooling; recrystallisation from aqueous alcohol afforded lustrous plates, m. p. 80—82°, not depressed on admixture with an authentic specimen of glycerol αα′-diphenyl ether.

In the following experiments various phenols were heated with equimolecular amounts of epichlorohydrin in the presence of catalysts, under the conditions summarised in Table I. The products were distilled, and fractions consisting of the 1-aryloxy-3-chloropropan-2-ols and glycerol αα′-diaryl ethers were collected. The yields are given as percentages of the theoretical. The amounts of the catalysts employed are given as percentages of the total weight of reactants.

Reaction of Glycide Phenyl Ether with α-Monochlorohydrin. Formation of Glycidol.—Glycide phenyl ether (844 g., 1·125 mols.), α-monochlorohydrin (552·5 g., 1·0 mol.), and pyridinium ethiodide (47·5 g.) were mixed and heated under reduced pressure, the volatile products being passed through an efficient fractionating column. Glycidol commenced to distil almost at once. It was collected during 2—3 hours, depending on the rate of distillation, as a fraction, b. p. 60—85°/15 mm. (365 g.). Redistillation gave pure glycidol, b. p. 64—65°/14 mm. (355 g.; 96% of theoretical). The residue, a red-brown, somewhat viscous oil, was distilled through a short Vigreux column. A first fraction, b. p. 120—155°/15 mm. (140 g.), consisted mainly of glycide phenyl ether. This was followed by a fraction, b. p. 156—160°/10—11 mm. (835 g.), consisting of 1-chloro-3-phenoxypropan-2-ol (yield, approx. 90%).

In preparing large amounts of glycidol it was found convenient to reconvert the 1-chloro-3-phenoxypropan-2-ol into glycide phenyl ether for further use by stirring it for 2 hours at 25° with a solution of sodium hydroxide (240 g.) in water (1 l.). By this means glycide phenyl ether was recovered in 92% yield calculated on the 1-chloro-3-phenoxypropan-2-ol treated.

Reaction of Glycide o-Tolyl Ether with α-Monochlorohydrin.—A mixture of glycide *o*-tolyl ether (738 g.), α-monochlorohydrin (442 g.), and pyridine (18 g.) was heated at 60—65° until the odour of pyridine had disappeared (10—15 mins.). Distillation of the product afforded glycidol (272 g., 92%) and 1-chloro-3-*o*-tolyloxypropan-2-ol, b. p. 160—165°/10 mm. (680 g., 85%).

Reaction of Glycide Phenyl Ether and Trimethylene Bromohydrin. Formation of 1 : 3-*Epoxypropane.*—A mixture of propylene bromohydrin (100 g.), glycide phenyl ether (120 g.), and pyridinium ethiodide (6 g.) was heated, and the volatile products were passed through an efficient fractionating column. The first fraction, b. p. 45—55°, was collected during 45 mins. On redistillation it gave propylene oxide (1 : 3-epoxypropane), b. p. 47° (38 g., 92%).

The results of several other experiments on the reaction between epoxides and chlorohydrins are summarised in Table II.

Reaction of Glycide p-*Chlorophenyl Ether with* 1-*Chloro-3-2′-hydroxyethoxypropan-2-ol.*—Glycide *p*-chlorophenyl ether (41·8 g.), 1-chloro-3-2′-hydroxyethoxypropan-2-ol (35 g.; Kharasch and Nudenberg, *J. Org. Chem.*, 1943, **8**, 189), and triethylamine (1 c.c.) were mixed and then slowly distilled under reduced pressure. The first portion of the distillate, b. p. 90—96°/1—2 mm. (24 g.), was redistilled. 1 : 2-Epoxy-3-2′-hydroxyethoxypropane, b. p. 72°/0·5 mm., was obtained in a yield of 21 g. The new epoxide was characterised by means of its adduct with *o*-cresol. The epoxide (11·8 g.), *o*-cresol (10·8 g.), and triethylamine (0·2 c.c.) were kept for 3 weeks at room temperature. Distillation under reduced pressure then gave 1-2′-*hydroxyethoxy*-3-*o*-*tolyloxypropan*-2-*ol*, b. p. 175°/0·5 mm. (Found: C, 63·5; H, 8·0. $C_{12}H_{18}O_4$ requires C, 63·7; H, 8·0%), as a colourless, viscous oil (19·5 g., 86%).

A mixture of epichlorohydrin (2 mols.), ethylene chlorohydrin (1 mol.), and pyridinium ethiodide (0·05 mol. per 100 g. of reactants) gave ethylene oxide (0·75 mol.).

Quinol diglycide ether (1 mol.), α-monochlorohydrin (2 mols.), and quinoline (0·015 mol. per 100 g. of reactants) afforded glycidol, b. p. 65°/14 mm. (1·54 mols.). Quinol diglycide ether (1 mol.), 1-chloro-3-*o*-tolyloxypropan-2-ol (2 mols.), and quinoline (0·02 mol. per 100 g. of reactants) yielded glycide *o*-tolyl ether, b. p. 95°/2 mm. (1·0 mol.).

N-(2 : 3-Epoxypropyl)-*N*-methylaniline (1 mol.) and α-monochlorohydrin (1 mol.) reacted without the aid of an added catalyst to yield glycidol, b. p. 65°/14 mm. (0·5 mol.).

Reaction between p-*Chlorophenyl Glycide Ether* (2 *Mols.*) *and α-Monochlorohydrin* (1 *Mol.*). *Influence of Condensing Agent.*—A mixture of the reactants with one or other of the catalysts listed below was heated until glycidol ceased to distil. The yields obtained were: pyridine, 93%; quinoline, 92%; triethylamine, 50%; 2′ : 3′-dihydroxypropylpyridinium chloride, 96—98%; 2′-hydroxy-3′-*o*-tolyloxypropylpyridinium chloride, 96—98%; *p*-nitrobenzylpyridinium chloride, 96—98%; pyridine ethiodide, 96—98%; potassium hydroxide, 58—60%; potassium carbonate, 65%; ammonia (*d* 0·88), 92—95%; ammonium chloride, 85%; aniline, 40%; piperidine, 80%; hydrochloric acid (*d* 1·16), 30%. There was almost no reaction in the absence of added catalyst, or on the addition of metallic copper, zinc, or aluminium, or of sodium chloride or potassium chloride. The reaction induced by hydrogen chloride proceeded very slowly; the four quaternary pyridinium salts gave the most rapid rate of change.

The Condensation of Epoxides with Chlorohydrins in the Presence of Pyridine. Formation of Quaternary Salts.—(i) A mixture of glycide *o*-tolyl ether (20·0 g.), 1-chloro-3-*p*-chlorophenoxypropan-2-ol (25·6 g.), and pyridine (4·8 g.) was heated at 60° for 90 mins. The red-brown solution was added to ethyl acetate (250 c.c.), and the precipitate stirred to induce crystallisation. The crude solid (9·5 g.) was extracted thoroughly by means of cold ethyl acetate and then recrystallised from ethyl acetate–methanol. The pure salt formed white needles (8·1 g.), m. p. 163—164° (Found: C, 64·1; H, 6·5; N, 5·0; Cl, 12·5. $C_{15}H_{18}O_2NCl$ requires C, 64·4; H, 6·4; N, 5·0; Cl, 12·7%) not depressed on mixing with authentic 2′-*hydroxy*-3′-*o*-*tolyloxypropylpyridinium chloride* having the same m. p. Admixture with 3′-*p*-chlorophenoxy-2′-hydroxypropylpyridinium chloride depressed the m. p. to 140—150°. 2′-*Hydroxy*-3′-*o*-*tolyloxypropylpyridinium picrate* crystallised from methanol in orange-yellow needles, m. p. 146—147° (Found: N, 12·0. $C_{21}H_{20}O_9N_4$ requires N, 11·9%).

TABLE II.

Ar in epoxide, $CH_2(O)CH{\cdot}CH_2{\cdot}OAr$	Chlorohydrin.	Molar ratio, epoxide : chlorohydrin.	Catalyst.*	Amount of catalyst, mol. per 100 g. of reactants.	Products. Epoxide.	Yield of epoxide, mols.	B. p. of epoxide.	Yield (mols.) of chlorohydrin.†
Ph	α-Monochlorohydrin	1 : 1	C_5H_5N,EtI	0·015	Glycidol	0·75	65°/14 mm.	—
,,	,,	1·15 : 1	,,	0·015	,,	0·95	,,	0·93
o-C_6H_4Me	,,	2 : 1	C_5H_5N	0·0125	,,	0·95	64°/14 mm.	—
,,	,,	1 : 1	,,	0·013	,,	0·68	63—64°/14 mm.	—
,,	,,	1 : 2	,,	0·013	,,	0·95	,,	—
,,	,,	1 : 1	C_9H_7N	0·01	,,	0·62	65°/14 mm.	0·78
,,	,,	1 : 3	,,	0·005	,,	0·85	,,	—
p-C_6H_4Cl	,,	1 : 2	K_2CO_3	0·1	,,	0·65	,,	0·70
p-C_6H_4Me	,,	1 : 1	C_9H_7N	0·015	,,	0·70	,,	—
,,	,,	1 : 2	,,	0·015	,,	0·80	,,	—
Ph	3-Chloro*iso*butane-1 : 2-diol	1·15 : 1	C_5H_5N,EtI	0·015	2 : 3-Epoxy*iso*-butan-1-ol	0·93	63°/12 mm.	0·60
p-C_6H_4Cl	1-Acetoxy-3-chloro-propan-2-ol	1 : 1	C_9H_7N	0·015	*o*-Acetylglycidol	0·61	64°/15 mm.	0·73
β-$C_{10}H_7$	1-Chloro-3-2′-hydroxyethoxypropan-2-ol	1 : 1	NEt_3	0·02	Glycidol 2-hydroxyethyl ether	0·90	94°/2 mm.	—
o-C_6H_4Me	α-Monochlorohydrin	1 : 1	,,	0·011	Glycidol	0·36	65°/14 mm.	0·49
,,	,,	1 : 2	,,	0·011	,,	0·49	,,	0·55
p-C_6H_4Cl	,,	1 : 2	Piperidine	0·007	,,	0·80	,,	0·74
,,	,,	1 : 2	KOH	0·007	,,	0·58	,,	0·76
,,	,,	1 : 2	A	0·014	,,	*ca.* 1·0	,,	0·76
,,	,,	1 : 2	B	0·014	,,	*ca.* 1·0	,,	0·81
,,	,,	1 : 2	K_2CO_3	0·021	,,	0·72	,,	0·74
,,	,,	1 : 2	NH_4Cl	0·007	,,	0·85	,,	0·72
,,	,,	1 : 2	NH_3 (*d* 0·88)	0·007	,,	0·95	,,	0·73
Ph	,,	1 : 1·15	C_5H_5N,EtI	0·010	,,	0·97	,,	0·93
p-C_6H_4Cl	,,	1 : 1	,,	0·02	,,	0·92	72°/0·5 mm.	—
β-$C_{10}H_7$	1-Chloro-3-*o*-tolyloxypropan-2-ol	1 : 2	C_9H_7N	0·02	Glycide *o*-tolyl ether	0·55—0·58	95°/2 mm.	—
o-C_6H_4Me	αγ-Dichlorohydrin	1 : 1	C_5H_5N	0·01	‡ Epichlorohydrin	0·16	120°/760 mm.	—
p-C_6H_4Cl	,,	1 : 1	C_9H_7N	0·015	‡ ,,	0·2—0·3	,,	—

* A = 4-Nitrobenzylpyridinium chloride; B = 2′-hydroxy-3′-*o*-tolyloxypropylpyridinium chloride.
† In these chlorohydrins, $Ar{\cdot}O{\cdot}CH_2{\cdot}CH(OH){\cdot}CH_2Cl$, Ar is identical with that in col. 1.
‡ These products contained an undetermined amount of acraldehyde.

(ii) A mixture of glycide phenyl ether (16·2 g.), 1-chloro-3-phenoxypropan-2-ol (20·0 g.), and pyridine (4·3 g.), treated as in (i), yielded 9·7 g. of crude 2′-hydroxy-3′-phenoxypropylpyridinium chloride. Crystallisation from ethyl acetate–methanol afforded rosettes of small needles, m. p. 137—138°. The derived *picrate* crystallised from methanol in hexagonal plates, m. p. 151—152° (Found: N, 12·0. $C_{20}H_{18}O_9N_4$ requires N, 12·2%). The ethyl acetate mother-liquor yielded 14·7 g. of glycide phenyl ether and 7·5 g. of 1-chloro-3-phenoxypropan-2-ol.

(iii) A mixture of glycide β-naphthyl ether (40 g.) and pyridine (7·9 g.) was heated at 60° for an hour. 1-Chloro-3-*o*-tolyloxypropan-2-ol (20 g.) was added, and the mixture kept at 60° for one hour longer. The product was added to dry ether (250 c.c.) and vigorously stirred. The insoluble portion was separated and again stirred with ether. The ethereal solutions were combined, and washed in turn by means of water, 0·02N-hydrochloric acid (250 c.c.), and finally water. After being dried (Na_2SO_4), the solution was distilled, giving: (*a*) glycide *o*-tolyl ether, b. p. 78—80°/0·2 mm. (10·2 g.) (Found: C, 72·6; H, 7·4. Calc. for $C_{10}H_{12}O_2$: C, 73·1; H, 7·3%); (*b*) 1-chloro-3-*o*-tolyloxypropan-2-ol, b. p. 95—110°/0·1 mm. (3·4 g.); glycide β-naphthyl ether, b. p. 120—130°/0·1 mm. (20·5 g.); there was a small residue (2 g.).

The ether-insoluble portion was added to water (300 c.c.). The resulting suspension was extracted by means of ether and the clear aqueous solution was diluted to 500 c.c. A portion of the solution (50 c.c.) was mixed with aqueous sodium picrate; an oily precipitate formed which soon solidified. Crystallisation from methanol containing a small proportion of dioxan gave 2·7 g. of *2′-hydroxy-3′-β-naphthoxypropylpyridinium picrate*, m. p. 154—155° (Found: N, 10·9. $C_{24}H_{20}O_9N_4$ requires N, 11·0%).

(iv) Table III summarises the results of a number of experiments in which various epoxide–chlorohydrin pairs were heated together in the presence of pyridine for the periods and at the temperatures stated. The yields of the quaternary chlorides isolated (*d*) are given. In the two experiments involving glycide β-naphthyl ether the quaternary salts were isolated as picrates.

TABLE III.

(*a*.) C_5H_5N (mols.).	(*b*.) $RO\cdot CH_2\cdot CH(O)CH_2$, R =	(*c*.) $R'O\cdot CH_2\cdot CH(OH)\cdot CH_2Cl$, R′ =	Mol. ratio *a* : *b* : *c*.	Temp.	Time (hrs.).	Yield of (*d*),* %.
0·1	*o*-C_6H_4Me	*o*-C_6H_4Me	1 : 1 : 1	60°	0·5	20
0·1	,,	,,	,,	,,	1·0	30
0·1	,,	,,	1 : 2 : 2	,,	1·5	65
0·1	,,	*p*-C_6H_4Cl	1 : 2 : 2	55	1·25	*ca.* 50
0·1	*m*-C_6H_4Me	*m*-C_6H_4Me	1 : 2 : 2	60	1·5	65
0·1	*p*-C_6H_4Me	*p*-C_6H_4Me	1 : 2 : 2	60	1·5	65
0·1	*p*-C_6H_4Cl	*p*-C_6H_4Cl	1 : 2 : 2	60	1·5	65
0·1	Ph	Ph	1 : 2 : 2	60	1·5	60
0·1	β-$C_{10}H_7$	β-$C_{10}H_7$	1 : 2 : 2	60	1·5	*ca.* 55
0·1	,,	*m*-C_6H_4Me	1 : 2 : 2	55	1·25	*ca.* 50
0·1	*p*-C_6H_4Cl	,,	1 : 2 : 2	60	1·25	55
0·05	H	H	1 : 1 : 4	30	1·0	*ca.* 25

* The quaternary chloride (*d*) = $RO\cdot CH_2\cdot CH(OH)\cdot CH_2\cdot NC_5H_5\}Cl$, where R is the same as in col. (*b*).

(v) Following are the properties of the other quaternary salts referred to in Table III: *2′-Hydroxy-3′-m-tolyloxypropylpyridinium chloride*, needles, m. p. 127—128° (Found: C, 64·1; H, 6·5; N, 4·9. $C_{15}H_{18}O_2NCl$ requires C, 64·4; H, 6·4; N, 5·0%); the *picrate* crystallised from methanol in yellow needles, m. p. 136—137° (Found: N, 11·7. $C_{21}H_{20}O_9N_4$ requires N, 11·9%). *2′-Hydroxy-3′-p-tolyloxypropylpyridinium chloride*, needles, m. p. 158—159° (Found: C, 64·5; H, 6·4; N, 4·9%); the *picrate* crystallised from methanol in yellow rhombs, m. p. 135° (Found: N, 11·8%). *3′-p-Chlorophenoxy-2′-hydroxypropylpyridinium chloride*, lustrous needles, m. p. 176—177° (Found: C, 55·8; H, 5·2; N, 4·5. $C_{14}H_{15}O_2NCl_2$ requires C, 56·0; H, 5·0; N, 4·7%); the *picrate* separated from methanol–dioxan in lustrous yellow needles, m. p. 164° (Found: N, 11·3. $C_{20}H_{17}O_9N_4Cl$ requires N, 11·4%).

In the following instance the crude chloride was not crystallised. It was dissolved in water, and sodium picrate added to precipitate the quaternary picrate. *2′-Hydroxy-3′-m-methoxyphenoxypropylpyridinium picrate* crystallised from methanol in fine yellow needles, m. p. 137—138° (Found: N, 11·6%).

Reaction of Pyridine with Glycide β-Naphthyl Ether.—A mixture of pyridine (7·9 g.) and glycide β-naphthyl ether (40 g.) was heated at 60° for an hour. The dark red-brown viscous product was added to dry ether (250 c.c.) with good stirring. The supernatant solution was decanted from the undissolved gum and this was stirred thoroughly with two additional 150-c.c. portions of dry ether. The residue weighed 13 g. It was used in the following experiments:

(*a*) 4 G. of the gum were shaken with distilled water (150 c.c.); an emulsion formed and this was extracted twice by means of ether. The clear aqueous solution which resulted was mixed with an excess of aqueous picric acid or, better, sodium picrate. An immediate precipitate formed; it was a gum initially, but it gradually solidified. Crystallisation from methanol containing a small proportion of dioxan afforded glistening, feathery, yellow plates (2·2 g.), m. p. 153—154°, not depressed on admixture with 2′-hydroxy-3′-β-naphthoxypropylpyridinium picrate (Found: N, 10·8%) (above). (*b*) A similar 4-g. portion of the gum was treated as in (*a*) except that 2N-hydrochloric acid (150 c.c.) was used instead

of picric acid. To the resulting solution was added an excess of aqueous picric acid. A picrate, m. p. 153—154° (2 g.), identical with that prepared in (*a*) separated. (*c*) 2 G. of the gum were mixed with 2N-sodium hydroxide solution (75 c.c.). The emulsion which formed gradually settled; after 12 hours the red-brown supernatant solution was decanted, neutralised with dilute acetic acid, and mixed with aqueous sodium picrate. A gum separated, followed by a solid. Crystallisation of the solid from methanol gave 0·1 g. of a product m. p. 153—154°, identical with the picrate prepared in (*a*).

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