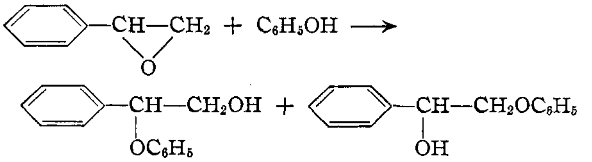
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA]

The Reaction of Styrene Oxide with Phenol

BY CYRUS O. GUSS

From the results of previous studies of the alkali-catalyzed reaction of olefin oxides with phenol it was concluded that the products were ether-alcohols. In the case of propylene oxide, an unsymmetrical olefin oxide, the early work[1] indicated that an isomeric mixture of the two possible ether-alcohols was obtained. Recent work[2,3] has shown, however, that the alkali-catalyzed reaction of propylene oxide with phenols produced predominantly or entirely the isomer having a secondary alcohol group. Alcohols were reported[3,4,5] to react with propylene oxide in a similar manner.

In the present investigation it was found that the alkali-catalyzed reaction of styrene oxide with phenol proceeded as shown



I II

Both isomers were isolated and their structures proved by independent synthesis. In most cases the primary alcohol (I) was formed in greater amount, a result in contrast to the analogous reaction of propylene oxide with phenol under similar conditions.

In Table I are summarized some data obtained in this study. The alkali-catalyzed reactions were run in water, or dioxane, and excess phenol. In the presence of water the isomeric mixture was found to consist of approximately three parts of the primary alcohol (I) to one part of the secondary alcohol (II). In dioxane the relatively slower reaction produced the two isomers in more nearly equal amounts. Thus, there was an apparent effect of the reaction medium on the course of the ring-opening reaction. It was also noted, as shown in Table I, that as the concentration of sodium phenoxide was increased, the relative amount of the secondary alcohol (II) formed also increased. This effect of sodium phenoxide concentration was most pronounced in dioxane.

The separation of the two isomers from each other was most easily accomplished by taking advantage of the differences in their rate of reaction with phthalic anhydride.[6] However, since the separation by this method was not attained quantitatively, it was necessary to resort to other means to ascertain the composition of the isomeric mixture more precisely. The use of a phase diagram made it possible to obtain the composition data in Table I.

TABLE I

REACTION OF 0.1 MOLE OF STYRENE OXIDE WITH 0.3 MOLE OF PHENOL[a]

Solvent used	Catalyst	Time, hr.	Yield of mixture, I + II, %	I in mixture, %
15 cc. of water	0.005 mole NaOH	2.5	65.9	78
15 cc. of water	.1 mole NaOH	1.0	85.0	76
15 cc. of water	.3 mole NaOH	1.0	74.8	70
20 cc. of water	.2 mole NaOH	1.0	76.6	75[b]
25 cc. of dioxane	.004 mole Na	3.5	74.8	68
25 cc. of dioxane	.1 mole Na	3.5	89.7	49
25 cc. of dioxane	.25 mole Na	3.0	66.8	39
25 cc. of dioxane	.15 mole Na	3.0	74.7	53[b]
None	None	4.0	32.2[c]	88
15 cc. of water	0.0016 mole HOTs[d]	1.0	14.0[e]	67
None	0.0026 mole HOTs	0.5	..[f]	

[a] All runs in dioxane were at reflux temperature, the uncatalyzed run and those in water at 100°-bath. The last run in the table was at 200°-bath. [b] Styrene bromohydrin (0.1 mole, b. p. 114–115° (3 mm.), $n^{20}\text{D}$ 1.5780) was used instead of styrene oxide. [c] A large amount of higher boiling material was also formed. [d] *p*-Toluenesulfonic acid monohydrate. [e] Other products were phenyl glycol (11.6%) and higher boiling material, part of which was alkali soluble. [f] A solid product formed which softened at 80–100° and was alkali soluble. Only 0.1 mole of phenol was used in this run.

Styrene bromohydrin gave the same relative amounts of primary alcohol (I) and secondary alcohol (II) in the isomeric mixture as styrene oxide when it was used instead of styrene oxide in the alkali-catalyzed reaction, showing that the oxide was undoubtedly the species reacting with the phenol. This result excluded the use of the bromohydrin in the reaction as a means for structure proof, and it also seriously jeopardized the validity of the structure proof employed by Emerson[7] in his study of the reaction of styrene oxide with alcohols.

The uncatalyzed reaction of styrene oxide with phenol gave a relatively low yield of the isomeric mixture in which the primary alcohol (I) was present in a ratio of nearly nine to one.

The use of *p*-toluenesulfonic acid to catalyze the reaction of styrene oxide with phenol gave a product that was alkali soluble. When water was present also, as indicated in Table I, a low yield of the isomeric mixture of I and II was formed together with phenyl glycol and higher-boiling materials, part of which was alkali soluble. The alkali-soluble material must have resulted from a reaction of the oxide with the nucleus of the phenol. A study of this latter type of reaction is nearly completed and will be reported upon soon.

The structures of I and II were assigned on the

---

(1) Boyd and Marle, *J. Chem. Soc.*, **105**, 2117 (1914).

(2) Hurd and Perletz, THIS JOURNAL, **68**, 38 (1946).

(3) Sexton and Britton, *ibid.*, **70**, 3606 (1948).

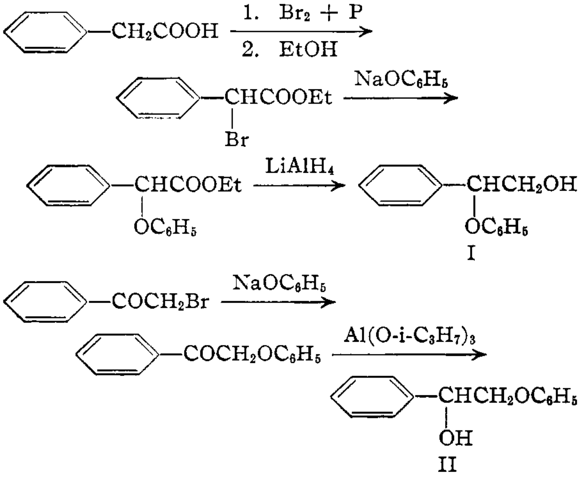
(4) Chitwood and Freure, *ibid.*, **68**, 680 (1946).

(5) Swern, Billen and Knight, *ibid.*, **71**, 1152 (1949).

(6) Cox, Nelson and Cretcher, *ibid.*, **49**, 1080 (1927).

(7) Emerson, *ibid.*, **67**, 516 (1945).

basis of identity with the products from the reaction sequences



The results from the present study supplement the knowledge of the effect of groups and media on the direction of the ring opening of substituted ethylene oxides. Since propylene oxide is found to give the secondary alcohol in the alkali-catalyzed reaction with alcohols[4,5] or with phenols,[2,3] the course of the reaction is said to be guided by the electron-releasing action of the methyl group.[4,5] In 3,4-epoxy-1-butene, in which the vinyl group is present instead of the methyl group as in propylene oxide, one interpretation that is suggested[5] to account for an observed formation of a primary alcohol exclusively in the reaction of the oxide with sodium alloxide in allyl alcohol is also based on an electron release by the vinyl group. Alternatively, Bartlett and Ross,[8] who find that 3,4-epoxy-1-butene reacts with sodium methoxide in methanol to give the secondary alcohol predominantly but also some primary alcohol, suggest that allylic resonance in a transition state might account for the formation of the primary alcohol. If this concept of resonance in a transition state is applied to the alkali-catalyzed reaction of styrene oxide with alcohols and with phenols, the expected result would be to find the formation of the primary alcohol predominant or exclusive, since the lowering of the energy of the transition state leading to the primary alcohol ought to be greater in the case of styrene oxide than in the case of 3,4-epoxy-1-butene. The present results can be cited in support of this interpretation, as can also the finding by Swern, Billen and Knight[5] that styrene oxide reacts with allyl alcohol and sodium alloxide to give the primary alcohol predominantly. The latter authors explain their results on the basis of an electron-attracting action by the phenyl group. On the other hand, Russell and VanderWerf[9] present the point of view that the phenyl group in styrene oxide is electron releasing in the reaction with sodium diethyl malonate. Perhaps a study of the effect of temperature and other factors of the reaction environment might help to resolve some of the present difficulties in the interpretation of the ring-opening reactions of olefin oxides.

Experimental[10]

Reaction of Styrene Oxide with Phenol.—The runs reported in Table I were all made in a similar manner. The phenol, water or dioxane, and the sodium hydroxide, or sodium, or *p*-toluenesulfonic acid were brought together in a three-necked flask equipped with stirrer, condenser and a dropping funnel. As soon as but one phase existed at the temperature used, the styrene oxide[11] (n^{20}_{D} 1.5352) was added dropwise over a period of five to ten minutes. Heating and stirring were continued for the indicated time. These reactions, except for the first run in Table I, were one-phase. The amber or red reaction mixture was then poured into 200 g. of an ice-water mixture containing sufficient sodium hydroxide to react with the excess free phenol. The insoluble material was then taken up in two 75-cc. portions of ether, and the ether solution was dried over anhydrous potassium carbonate or anhydrous sodium sulfate. After distillation of the ether, the residue was distilled in a 50-cc. modified Claisen flask packed with 3″ of $^1/_8$″ glass helices. A small amount of material boiling in the range 50–60° (0.5 mm.) was usually obtained, after which the temperature rose immediately to 150–160° (0.5 mm.) over which interval the mixture of I and II distilled. A higher-boiling residue that remained was usually not distilled, but it was noted on one occasion to have a boiling point above 200° (0.5 mm.). The fraction boiling at 150–160° (0.5 mm.) rapidly solidified. It was this material whose melting point was now measured to determine the relative amounts of I and II present by the use of the phase diagram.

Determination of Composition of Mixture of Isomers I and II.—The apparatus used was similar to the Beckmann freezing-point depression arrangement, employing a thermometer calibrated in 0.5°. A system of crossed polaroid glasses was used to observe the disappearance of the last crystal. Table II gives the melting points thus obtained for the mixtures of known composition.

TABLE II

MELTING POINTS OF KNOWN MIXTURES OF I AND II

I, %	M. p., °C.	I, %	M. p., °C.
4.88	60.25	40.20	46.00
9.33	58.50	47.68	53.50
16.99	55.50	68.88	65.75
28.97	50.50	86.97	74.50
35.00	47.00		

The graph made from these data was used in the usual manner to determine the composition of the mixture of isomers resulting from the interaction of styrene oxide and phenol.

Separation of I and II.—It was found that isomer I was much more easily esterified than II, and it was this observation that led to the use of the following procedure to separate the two isomers.

A solution of the mixture of isomers (5 g., 0.0234 mole, 76% I), phthalic anhydride (7.4 g., 0.05 mole), and pyridine (4.9 g., 0.062 mole) in dioxane (25 cc.) was allowed to stand at room temperature for five hours. This solution was then dissolved in 100 cc. of ether. The ether solution was shaken with 100 cc. of water containing 10 cc. of concd. hydrochloric acid to remove the pyridine. The half-ester of I and any phthalic acid were removed by shaking the ether solution with 150 cc. of 7.5% sodium carbonate.

---

[8] Bartlett and Ross, THIS JOURNAL, **70**, 926 (1948).

[9] Russell and VanderWerf, *ibid.*, **69**, 11 (1947).

[10] Microanalyses reported in this paper were performed by the analyst at the California Institute of Technology, Pasadena, California. All melting points are uncorrected.

[11] Alquist and Guss, U. S. Patent 2,237,284 (April 8, 1941).

The remaining ether solution was then washed with 100 cc. of water, dried over anhydrous potassium carbonate, and the removal of the ether then left a white solid. Two or three recrystallizations from heptane left 0.5 g., m. p. 62–64°, identified as **1-phenyl-2-phenoxyethanol** (II) by mixed melting with an authentic sample.

To the aqueous solution of the half-ester of I was added 4 g. of sodium hydroxide and the solution refluxed for one hour. The insoluble material that separated was taken up in 75 cc. of ether and the ether solution dried over anhydrous potassium carbonate. After removal of the ether and two recrystallizations of the resulting solid from heptane, 3.0 g., m. p. 80–81° was obtained and identified as **2-phenyl-2-phenoxyethanol** (I) by mixed melting point.

The above procedure thus gave a 70% yield of the two pure isomers. The separation was not found to be clean-cut, and the remaining 30% consisted of mechanical loss and a mixture of approximately equal parts of the two isomers. An initial mixture containing 49% I gave a 60% yield of pure I and pure II when carried through the above procedure. The reprocessing of the unseparated portion would undoubtedly lead to a higher over-all yield of the two separated isomers.

Preparation of 2-Phenyl-2-phenoxyethanol (I).—Ethyl α-bromophenylacetate (b. p. 102–104° (0.4 mm.), $n^{20}\mathrm{D}$ 1.5380) was prepared in 70.7% yield by the procedure of Anschütz[12] from phenylacetic acid, bromine, phosphorus and absolute ethanol. This ester (36.5 g., 0.15 mole) was added dropwise in fifteen minutes to sodium phenoxide (0.15 mole) and phenol (0.15 mole) in dry dioxane (23 cc.) at 100°. After forty-five minutes the reaction mixture was cooled and added to 300 cc. of water. The organic layer was extracted with 200 cc. of ether, dried over anhydrous sodium sulfate, and distilled to give 26.1 g. (68%), b. p. 155–156° (0.8 mm.), $n^{20}\mathrm{D}$ 1.5452. That this material was ethyl α-phenoxyphenylacetate was shown by its hydrolysis in refluxing 4% sodium hydroxide to α-phenoxyphenylacetic acid, m. p. 108–109.5°. Meyer and Boner[13] have reported m. p. 108°.

Ethyl α-phenoxyphenylacetate was reduced to 2-phenyl-2-phenoxyethanol (I), needles, m. p. 80–81°, in 84% yield by the use of lithium aluminum hydride according to the usual procedure.[14] Heptane was used for recrystallization. This product mixed with I from the styrene oxide and phenol reaction melted without depression.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.50; H, 6.60.

The *p*-nitrobenzoate of this alcohol was prepared in the usual manner[15] with the exception that the reaction mixture was not heated externally but allowed to stand for one hour before working up. The ester was recrystallized from ethanol as platelets, m. p. 86–87°.

Anal. Calcd. for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72. Found: C, 69.63; H, 4.88.

Preparation of 1-Phenyl-2-phenoxyethanol (II).—Phenacyl bromide was converted into ω-phenoxyacetophenone, m. p. 71–72°, by the procedure of Mohlau[16] in 61% yield; oxime, m. p. 113–114°, as reported by Fritz.[17] The 2,4-dinitrophenylhydrazone was made by the ordinary method,[18] m. p. 183–184°. It was recrystallized from an ethanol–ethyl acetate mixture.

Anal. Calcd. for $C_{20}H_{16}N_4O_5$: C, 61.22; H, 4.11. Found: C, 61.11; H, 4.14.

The ω-phenoxyacetophenone was reduced with aluminum isopropoxide to the corresponding alcohol, 1-phenyl-2-phenoxyethanol (II), needles, m. p. 63–64° in 86.5% yield. The recrystallization solvent was heptane. This product was shown to be identical with II resulting from the reaction of styrene oxide with phenol by the absence of a mixed melting point depression.

Anal. Calcd. for $C_{14}H_{14}O_2$: C, 78.48; H, 6.59. Found: C, 78.75; H, 6.58.

The *p*-nitrobenzoate, prepared in the manner employed for the isomer above, crystallized from ethanol as fine needles, m. p. 83–84°.

Anal. Calcd. for $C_{21}H_{17}NO_5$: C, 69.41; H, 4.72. Found: C, 69.72; H, 4.96.

Summary

1. Styrene oxide was found to undergo an alkali-catalyzed reaction with phenol to give 66–90% yields of an isomeric mixture of 2-phenyl-2-phenoxyethanol (I) and 1-phenyl-2-phenoxyethanol (II) in which the content of I varied from 39 to 78% depending on the conditions used. Resonance stabilization of a transition state is mentioned to explain this difference in the direction of ring opening relative to propylene oxide.

2. The uncatalyzed reaction produced low yields of the isomeric mixture in which I constituted 88% of the total.

3. Acid catalysis of the reaction gave large amounts of an alkali-soluble material presumed to result from the reaction of the oxide with the nucleus of the phenol.

4. Styrene bromohydrin gave the same relative amounts of I and II as styrene oxide in the alkali-catalyzed reaction, indicating intermediate formation of the oxide.

LOS ANGELES 7, CALIFORNIA RECEIVED MAY 20, 1949

---

[12] Anschütz, *Ann.*, **354**, 127 (1907).

[13] Meyer and Boner, *ibid.*, **220**, 51 (1883).

[14] Nystrom and Brown, THIS JOURNAL, **69**, 1197 (1947).

[15] Shriner and Fuson, "The Systematic Identification of Organic Compounds," John Wiley and Sons, New York, N. Y., 1948, p. 164.

[16] Mohlau, *Ber.*, **15**, 2497 (1882).

[17] Fritz, *ibid.*, **28**, 3028 (1895).

[18] Reference 15, p. 171.