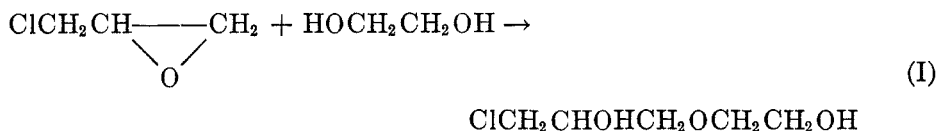


CONDENSATION OF EPICHLOROHYDRIN WITH ETHYLENE GLYCOL: SOME NEW POLYFUNCTIONAL DERIVATIVES

M. S. KHARASCH AND W. NUDENBERG

Received January 18, 1948

Fourneau and Ribas (1) have reported the condensation of epoxyalkanes with alcohols in the presence of sulfuric acid. By suitable modifications (described in the Experimental Part), their method is here extended to the condensation of epichlorohydrin (3-chloro-1,2-epoxypropane) and ethylene glycol (1,2-ethanediol).



The 1-chloro-3-(β -hydroxyethoxy)-2-propanol (I) thus obtained was used to synthesize a number of new compounds.

EXPERIMENTAL PART

The preparation of 1-chloro-3-(β -hydroxyethoxy)-2-propanol (I). To 278 g. (3 moles) of epichlorohydrin (obtained from the Shell Development Company) was added 379 g. (6 moles) of ethylene glycol. Since the two liquids are immiscible, the mixture was vigorously agitated, and concentrated sulfuric acid was added a few drops at a time. The mixture became homogeneous after the addition of 1 cc. of sulfuric acid. Since further addition of acid caused a considerable rise in temperature, the flask was cooled with running water during the subsequent addition. A total of 13 cc. of sulfuric acid was added. The product was then refluxed on a steam-bath for 12 hours and neutralized with excess barium carbonate (38 g.). The material was distilled directly at 3 mm. pressure. Two main fractions were obtained: (a) unidentified material (b.p. below 135°); (b) 1-chloro-3-(β -hydroxyethoxy)-2-propanol (b.p. 135–139°) (I). The 260 g. of material in fraction (b) represents a 56% yield.

Anal. Calc'd for $\text{C}_5\text{H}_{11}\text{ClO}_3$: Cl, 22.94. Found: Cl, 22.40.

Some unidentified high-boiling material remained in the flask.

Preparation of 1,3-bis-(β -hydroxyethoxy)-2-propanol (III). This compound may be prepared by treating compound (I) with the monosodium salt of ethylene glycol. It has, however, proved more satisfactory to prepare the substance directly from epichlorohydrin by the following method. The monosodium salt of ethylene glycol was prepared by adding 23 g. of sodium (in small pieces) to 92 g. of ethylene glycol dissolved in liquid ammonia. The solvent was then removed by evaporation. To 101 g. of the monosodium salt of glycol suspended in 200 g. of glycol, was added 112 g. of epichlorohydrin (20 g. at a time). During this addition, the mixture was vigorously agitated, and heated. After the addition (which required 3 hours) was complete, the reaction mixture was refluxed for 13 hours. The fraction (48 g.) which distilled at 188–192° at 2–3 mm. was identified by its analysis and reactions as 1,3-bis-(β -hydroxyethoxy)-2-propanol (III). After the liquid had stood for 24 hours at room temperature, the liquid solidified (m.p. 30°). To obtain a sample for analysis, this solid was redistilled. It boiled at 188–192° at 2–3 mm.

Anal. Calc'd for $\text{C}_7\text{H}_{16}\text{O}_5$: C, 46.65; H, 8.95.

Found: C, 46.20; H, 8.75.

Preparation of 3-(β -hydroxyethoxy)-1,2-epoxypropane (II). The method of preparation was that used by Rider and Hill (2) for the preparation of glycidol. Nineteen grams

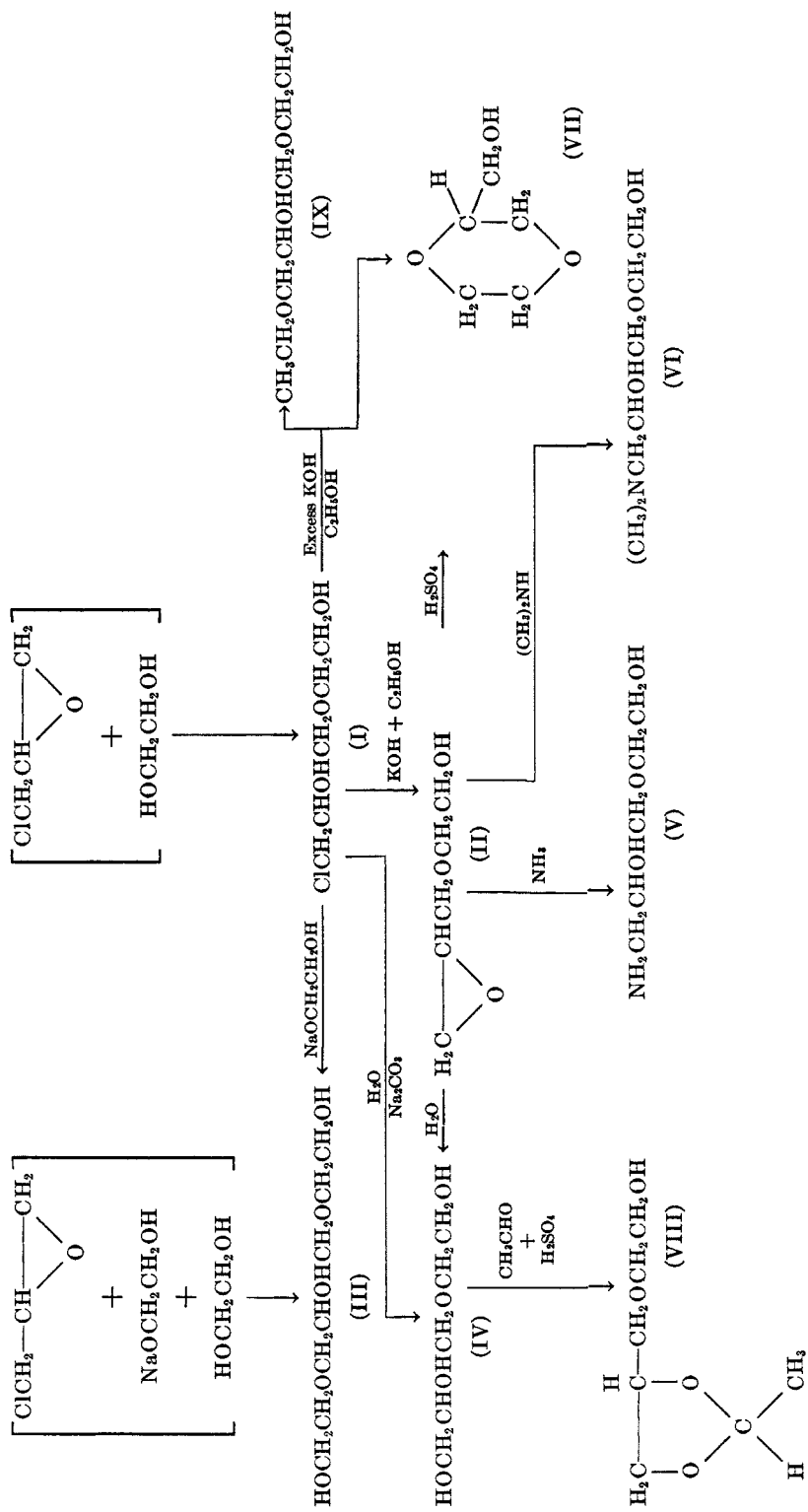


DIAGRAM I

(0.33 mole) of potassium hydroxide pellets was added to 135 cc. of absolute alcohol in a 500-cc. round-bottom, three-necked flask fitted with a stirrer and dropping-funnel. The alcoholic potassium hydroxide solution was cooled to 2°. Then 54 g. (0.33 mole) of 1-chloro-3-(β -hydroxyethoxy)-2-propanol (I) dissolved in 67 cc. of absolute alcohol was slowly added. Stirring was continued for one hour after the addition of the chloro compound. The precipitated potassium chloride was collected on a filter and washed several times with absolute alcohol; the washings were added to the main filtrate. The alcohol was removed from this filtrate by distillation at 76 mm. through a one-foot column. The residue was distilled at 1–2 mm., and the portion of the material boiling at 90–94° was collected. This portion (32 g.) was redistilled, and the fraction boiling at 92–94° was collected. This portion (32 g.) was redistilled, and the fraction boiling at 92–94° at 2 mm. was used for analysis; n_D^{20} 1.4480.

Anal. Calc'd for $C_5H_{10}O_3$: C, 50.80; H, 8.55.

Found: C, 50.44; H, 8.39.

Preparation of 3-(β -hydroxyethoxy)-1,2-propanediol (IV). To 9 g. of twice distilled 3-(β -hydroxyethoxy)-1,2-epoxypropane (II) was added 19 g. of distilled water. The mixture was refluxed for 5 hours, and the water then removed by evaporation on a steam-bath. The residue was distilled at 3 mm. The material boiling at 162–164° at 3 mm. (n_D^{20} 1.4723) was collected as the desired product.

Anal. Calc'd for $C_5H_{12}O_4$: C, 44.09; H, 8.88.

Found: C, 43.07; H, 8.36.

This ether was also prepared directly from 1-chloro-3-(β -hydroxyethoxy)-2-propanol (I). To 161 g. (1.04 mole) of (I) was added a solution of 60 g. (0.5 mole) of sodium carbonate in 1200 cc. of water. The mixture was heated on a steam-bath for 16 hours. Water was removed by evaporation on a steam-bath. Methyl alcohol was added to the residue, and the sodium chloride removed by filtration. The filtrate was concentrated on a steam-bath, and the residue distilled. A considerable amount of sodium chloride separated during distillation. The portion boiling at 161–191° at 2–5 mm. was collected. This portion was submitted to a slow distillation and the fraction (90 g. = 66% yield) boiling at 145–150° at 1 mm. was collected (n_D^{20} 1.4722).

Preparation of 2-methyl-4-(β -hydroxyethoxymethyl)-1,3-dioxolene (VIII). To 52 g. (0.382 mole) of (IV) in a 500-cc. round-bottom, three-necked flask was added 2 cc. of 50% sulfuric acid. Then 18 g. of paraldehyde was slowly added while the reaction flask was heated on a steam-bath and its contents stirred. After the addition of the paraldehyde was complete, heating was continued for three hours. Then the reaction mixture was extracted with ether. The ether extract was dried with anhydrous potassium carbonate, and the ether removed by distillation on a water-bath. The residue was distilled, and the fraction boiling at 112–114° (8 mm.) was collected. The yield was 27 g. (43% of the calculated amount). This material was subjected to another distillation, and the fraction boiling at 113–115° (8 mm.) (n_D^{20} 1.4453) was used for analysis.

Anal. Calc'd for $C_7H_{14}O_4$: C, 51.82; H, 8.63.

Found: C, 51.92; H, 8.26.

Preparation of 1-amino-3-(β -hydroxyethoxy)-2-propanol (V). Twenty-five grams of (II) was added to 2.5 liters of concentrated ammonium hydroxide. The reaction mixture was allowed to stand at room temperature for 5 hours; then the water and ammonia were removed by evaporation on a steam-bath. The residue was distilled. A very small amount (1 g.) distilled below 141° at 2–4 mm. The main portion (23 g., 81% yield) distilled from 141–144° at 2–4 mm. The amine is extremely hygroscopic and readily absorbs carbon dioxide from the air. These properties may account for the somewhat low nitrogen content of the substance.

Anal. Calc'd for $C_5H_{13}NO_3$: N, 10.35. Found: N, 9.44.

Preparation of 1-dimethylamino-3-(β -hydroxyethoxy)-2-propanol (VI). The method used for this preparation was similar to that which Rider and Hill (2) used for the preparation of 1-dimethylamino-2,3-propanediol. Thirty grams (0.25 mole) of epoxide (II) was slowly added to 60 g. of dimethylamine solution (30% solution obtained from Commercial Solvents

Corporation) in a 200-cc. three-necked flask fitted with a stirrer and a reflux condenser. Since the reaction was slightly exothermic, the reaction vessel was cooled with ice-water. The reaction mixture was stirred for two hours at room temperature after the addition of the epoxide was complete; then the water was removed on a steam-bath. The residue was distilled at 1–2 mm. A few cubic centimeters boiled below 102°. The main fraction, 34.5 g., distilled at 102–105°; (n_D^{20} 1.4638). The yield was 85%. This material was analyzed without further purification.

Anal. Calc'd for $C_7H_{17}NO_3$: N, 8.57. Found: N, 7.87.

Preparation of 2-hydroxymethyl-1,4-dioxane (VII). Thirty-nine grams of epoxide (II) was placed in a flask fitted with a reflux condenser, and 1.3 cc. of concentrated sulfuric acid was added, a few drops at a time. Much heat was evolved at each addition of sulfuric acid. The reaction mixture was then heated on a steam-bath for 6 hours. The thick, syrupy reaction product was transferred to a Claisen flask and 4 g. of barium carbonate added. After the evolution of carbon dioxide had ceased, the material was distilled. Two fractions were collected: (a) 10 cc. (b.p. 94–96° at 9 mm.); (b) higher-boiling material which appeared to decompose when heated to 200° at 3–4 mm. Fraction (b) was probably a linear condensation product of the epoxide compound. Fraction (a) was the 2-hydroxymethyl-1,4-dioxane (VII). This fraction was redistilled, and the material which boiled at 92–93° at 8 mm. was used for analysis; n_D^{20} 1.4617.

Anal. Calc'd for $C_6H_{10}O_3$: C, 50.80; H, 8.55.

Found: C, 50.57; H, 8.34.

Preparation of dinitrobenzoate of 2-hydroxymethyl-1,4-dioxane. Two cubic centimeters of the material boiling at 92–93° under 8 mm. pressure was treated with 0.7 g. of 3,5-dinitrobenzoyl chloride in the manner of Shriner and Fuson (3). The 3,5-dinitrobenzoate was crystallized three times from alcohol-water. The compound melted at 106–108° (dec.).

Anal. Calc'd for $C_{12}H_{12}N_2O_8$: N, 8.97. Found: N, 9.27.

Preparation of 1-ethoxy-3-(β -hydroxyethoxy)-2-propanol (IX) and 2-hydroxymethyl-1,4-dioxane (VII). Potassium hydroxide pellets (85 g.) were added to 370 cc. of 95% ethyl alcohol. To the stirred solution (cooled to 0°), 200 g. of 1-chloro-3-(β -hydroxyethoxy)-2-propanol (I) in 100 cc. of alcohol was slowly added. The reaction mixture was stirred for 14 hours, after which the potassium chloride which had formed was removed by filtration. This potassium chloride was washed several times with ethyl alcohol, and the washings added to the original filtrate. The excess potassium hydroxide in the filtrate was neutralized (phenolphthalein) with alcoholic hydrogen chloride. The alcoholic solution was then treated with an excess of solid anhydrous potassium carbonate. The solid was collected on a filter, and the alcohol removed from the filtrate by distillation through a one-foot column at 30° and 76–78 mm. pressure. After most of the alcohol had been removed, the solution was transferred to a modified 500-cc. Claisen flask and distilled at 2 mm. pressure. The following major fractions were collected: (a) 40.1 g. = 27% (b.p. 88–93°) identified as 2-hydroxymethyl-1,4-dioxane; (b) 31 g. = 15% (b.p. 115–122°) identified as 1-ethoxy-3-(β -hydroxyethoxy)-2-propanol (IX); (c) (b.p. 137–165°) identified as material consisting largely of unreacted chloro compound. There was a higher-boiling residue which was not distilled. Fraction (a) was redistilled at 87–88° at 1–2 mm. It had the correct index of refraction (n_D^{20} 1.4611) and composition for IX.

Anal. Calc'd for $C_7H_{16}O_4$: C, 51.19; H, 9.81.

Found: C, 50.61; H, 9.41.

In order to prove the structure of VII, 25 g. of fraction (a) (b.p. 88–93° at 2 mm.) was treated with 2.5 liters of concentrated ammonium hydroxide. After the mixture had stood for 7 hours, the ammonia and water were removed by evaporation. The residue was distilled. Practically all of it distilled at 88–93° under 2 mm. pressure (n_D^{20} 1.4618). Since this material was not the amino compound (b.p. 141° at 1 mm.), the original material must have been the dioxane derivative rather than the epoxide.

An attempt was made to effect the isomerization of the epoxide (II) to 2-hydroxymethyl-1,4-dioxane by refluxing the material at atmospheric pressure (220–230°) for 1.5 hours. A

fraction boiling at 78–82° under 3–4 mm. pressure (n_D^{20} 1.4618) was thus obtained; this material was presumably the dioxane derivative or the isomeric 3-(β -hydroxyethoxy)-2-propional derivative. The yield was 30%. The major portion of the epoxy compound was converted to higher-boiling materials.

Other attempts to convert the epoxide to the dioxane derivative were made by using acids or bases in ether solution. In these experiments, the major portion of the starting material was recovered practically unchanged.

SUMMARY

Eight new compounds derived from 1-chloro-3-(β -hydroxyethoxy)-2-propanol are described.

CHICAGO, ILL.

REFERENCES

- (1) FOURNEAU AND RIBAS, *Bull. soc. chim.*, **41**, 1046 (1927).
- (2) RIDER AND HILL, *J. Am. Chem. Soc.*, **52**, 1522 (1930).
- (3) SHRINER AND FUSON, "Systematic Identification of Organic Compounds," Wiley and Sons, New York, 1935.