[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

THE REACTION OF ETHYLMAGNESIUM BROMIDE WITH EPICHLOROHYDRIN

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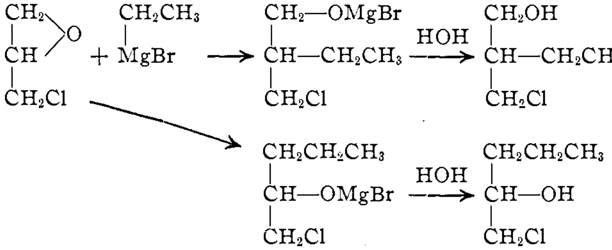
In connection with some work being carried on in this Laboratory it was desired to prepare 2-chloromethylbutanol-1 (I). It was thought that the reaction between ethylmagnesium bromide and epichlorohydrin might yield this particular compound, its isomer (II), or both, according to the reactions



(I)

(II)

The reaction was carried out in the usual manner, but when the reaction product was isolated and weighed it was apparent that the reaction had taken a different course from that shown above, for if the product formed was considered to be a chloro-amyl alcohol, the yield was approximately 115% of the theoretical.

The literature was then consulted, and it was found that the above reaction had been studied by a number of investigators, and that there was considerable disagreement as to the products that were formed. Iozitsch[1] reported that he obtained a chloro-amyl alcohol from the reaction between ethylmagnesium bromide and epichlorohydrin but made no mention of any other products. A little later Kling,[2] using methylmagnesium iodide to react with epichlorohydrin, obtained nothing but a glycerol chloro-iodohydrin. Iozitsch repeated his work and stated that he did obtain a glycerol chlorobromohydrin, but that he was able to separate it from the chloro-amyl alcohol by fractional distillation. The yield of neither product was given. Later, Fourneau and Tiffeneau[3] studied the action of ethyl-, propyl-, butyl- and amylmagnesium bromides on

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[1] The papers of Iozitsch on this subject are *J. Russ. Phys.-Chem. Soc.*, **34**, 96 (1902); *ibid.*, **36**, 6 (1904); but this journal was not available for reference. Neither could reference to this author's work be found in the *Centralblatt* or in the *British Chemical Abstracts*. All of the information concerning Iozitsch's work was found in the articles of Kling and of Fourneau and Tiffeneau.

[2] Kling, *Bull. soc. chim.*, [3] **31**, 14 (1904).

[3] Fourneau and Tiffeneau, *ibid.*, [4] **1**, 1227 (1907).

epichlorohydrin under numerous conditions of reaction, and were unable to duplicate Iozitsch's results. Glycerol chlorobromohydrin was the only product that they could isolate from the reaction mixture regardless of which alkylmagnesium bromide was used. These investigators were able, however, to obtain good yields of the expected chloro-alcohols when phenyl-, *p*-methoxyphenyl- and benzylmagnesium bromides were used instead of the alkylmagnesium bromides, although there was always some glycerol chlorobromohydrin formed. Delaby[4] reported that ethylmagnesium bromide and ethyl glycerol epibromohydrin reacted to form 1,3-dibromopentanol-2, which corresponds to the results obtained by Fourneau and Tiffeneau, and by Kling.

An investigation of the reaction product from ethylmagnesium bromide and epichlorohydrin in this Laboratory showed the presence of at least two different compounds. On repeated fractional distillation under reduced pressure, the product was separated into two fractions, one boiling at 70–75° (20 mm.) and the other boiling at 100–105° (20 mm.). Analyses of these two fractions indicated that the lower-boiling fraction was a chloro-amyl alcohol, and that the higher-boiling fraction was a glycerol chlorobromohydrin. This latter compound was proved to be 1-chloro-3-bromopropanol-2 by preparing the known 1,3-diphenoxypropanol-2 from it.

Since Iozitsch did not determine the structure of the chloro-amyl alcohol which he prepared, the product obtained in this work was further investigated in order to determine which of the two possible isomers it was. Reduction to the corresponding amyl alcohol seemed to be the simplest way of determining the structure, but such reducing agents as zinc dust with acetic or hydrochloric acid, the zinc–copper couple in aqueous alcohol and catalytic platinum with hydrogen were without action. Sodium amalgam removed the halogen, but none of the amyl alcohol could be isolated. Oxidation of the chloro-alcohol with alkaline potassium permanganate converted it into butyric acid, but it is conceivable that both isomers (I and II) might yield butyric acid with this reagent.

The chloro-alcohol was then converted by thionyl chloride into a dichloropentane. This latter compound reacted slowly with sodium iodide in acetone solution to liberate free iodine. This behavior, as van Duin[5] has shown, indicates that the halogens in the dichloropentane were on adjacent carbon atoms and that the chloro-amyl alcohol in question has the structure II. Finally, 1,2-dichloropentane was prepared by the addition of chlorine to pentene-1. The dichloropentane prepared from the chloro-amyl alcohol was identical with the 1,2-dichloropentane prepared from pentene-1.

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[4] Delaby, *Compt. rend.*, **176**, 1153 (1923); *Ann. chim.*, **20**, 56 (1923).

[5] Van Duin, *Rec. trav. chim.*, **43**, 341 (1924).

These results leave no doubt that Iozitsch's observations, rather than those of Fourneau and Tiffeneau, on the products of the reaction between epichlorohydrin and ethyl magnesium bromide were correct and that the particular chloro-amyl alcohol which is formed is 1-chloropentanol-2.

Various reaction conditions were tried in an effort to find the optimum conditions for the formation of the chloro-alcohol, but the maximum yield which it was possible to obtain amounted to only 19% of the theoretical. The remainder of the reaction product was the glycerol chlorobromohydrin mentioned above. With ethylmagnesium chloride approximately the same amounts of the chloro-alcohol along with a corresponding quantity of the glycerol dichlorohydrin were obtained.

Experimental

1-Chloropentanol-2.—The following procedure was found to give the best yield of this product. A solution of ethylmagnesium bromide prepared from 109 g. (1 mole) of ethyl bromide and 26.5 g. (1.1 atom) of magnesium in 300 cc. of ether was added slowly with stirring to 92.5 g. (1 mole) of epichlorohydrin dissolved in 100 cc. of ether contained in a three-necked flask fitted with a stirrer, reflux condenser and dropping funnel. During the addition the flask was cooled with running water. The mixture was refluxed for one hour and allowed to stand for two days at room temperature, the flask being closed with a soda-lime tube. At the end of this time, no appreciable precipitate had formed in the reaction mixture. A solution of 75 g. of acetic acid in 200 cc. of water was then added slowly with stirring and external cooling. The ether layer was separated, washed with dilute sodium carbonate solution until neutral, and the ether distilled off on a water-bath at 60°. The remaining oil was fractionated five times under reduced pressure, fractions being taken every 5° from 70 to 105° (20 mm.). The total weight of these fractions was 135–140 g. The fractions boiling to 85° were refractionated three times at atmospheric pressure, the part boiling at 157–160° (735 mm.) being practically pure chloropentanol; yield, 20–23 g. (16–19% of the theoretical); d_{25}^{25} 1.0143; n_{D}^{25} 1.4404.

Anal. Calcd. for $C_5H_{11}OCl$: Cl, 28.9. Found: Cl, 28.7.

The following variations in the preparation were tried. (a) After the reactants had been mixed, the ether was distilled off and simultaneously replaced by higher-boiling inert solvents such as benzene and toluene. There was no appreciable precipitate formed in the benzene (or toluene) solution even after four to five hours of refluxing. When the reaction mixture was fractionated, the boiling point range of the product indicated that only a small amount of chloro-alcohol had been formed. (b) After the reactants had been mixed, the ether was distilled off and the dry addition product was heated on a water-bath.[6] This treatment caused the rearrangement to take place with explosive violence, and a carbonaceous, ash-like mass was left from which none of the chloro-alcohol could be isolated. (c) The reactants were mixed and allowed to stand for two weeks in ether. After about three days, a white precipitate settled out of the solution. On longer standing, an inflammable gas, which analysis showed to be a mixture of ethylene, ethane and hydrogen, was given off from the reaction mixture. Only 6.5 g. of chloro-amyl alcohol was obtained when the reaction mixture was worked up in the usual way. (d) *n*-Butyl ether was used as a solvent instead of ordinary ethyl ether, and the reactants were heated at various temperatures up to the boiling point

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[6] *Cf.* Grignard, *Bull. soc. chim.*, [3] **29**, 944 (1903).

of the solvent (140°). By these procedures it was not possible to isolate any of the chloro-alcohol. It was apparent, however, that some fundamental change had occurred in the reaction mixture, for when the reactants were mixed in butyl ether, a white crystalline precipitate formed which on further heating changed into a brown, porous, brittle mass from which not even the glycerol chlorobromohydrin could be isolated. If the initial precipitate from the butyl ether was hydrolyzed immediately, glycerol chlorobromohydrin was the only product obtained.

Acetate of 1-Chloropentanol-2.—Ten grams of the chloro-alcohol was warmed with an equal weight of acetyl chloride on the water-bath until no more hydrogen chloride was given off. Water was then added, the oil washed with dilute sodium carbonate solution and dried over calcium chloride. The acetate distilled at 186–188° (740 mm.); d_{25}^{25} 1.0825; n_D^{25} 1.4328.

Anal. Calcd. for $C_7H_{13}O_2Cl$: Cl, 21.2. Found: Cl, 21.1.

3,5-Dinitrobenzoate of 1-Chloropentanol-2.—A mixture of 2.5 g. of the chloro-alcohol and 4.61 g. of 3,5-dinitrobenzoyl chloride was heated on an oil-bath to 135° until no more hydrogen chloride was given off. The sirupy brown liquid was dissolved in hot alcohol and on cooling the ester crystallized out in colorless plates which melted after another recrystallization from alcohol at 83–84°.

Anal. Calcd. for $C_{12}H_{13}O_6N_2Cl$: Cl, 11.3. Found: Cl, 11.5.

To a solution of 11 g. of potassium permanganate in 100 cc. of water was added 2.5 g. of 1-chloropentanol-2 and the solution refluxed until the permanganate color was destroyed. The manganese dioxide was then filtered off and the filtrate acidified with sulfuric acid and distilled. The distillate, after neutralization with sodium hydroxide, was evaporated to dryness. The resulting sodium butyrate was converted into the *p*-toluidide of the acid, which after recrystallization melted at 70–72°.

1,2-Dichloropentane from 1-Chloropentanol-2.—Twelve grams of the alcohol was mixed with 15 g. of freshly distilled diethylaniline in a flask fitted with a reflux condenser. The mixture was cooled while 24 g. of thionyl chloride was added through a dropping funnel.[7] The mixture solidified and became brown during the addition, but it liquefied when all of the thionyl chloride had been added. The reaction was completed by heating on the water-bath until the evolution of sulfur dioxide had ceased. Water was added and the oil steam distilled out. After washing with concd. sulfuric acid and then sodium carbonate solution, and drying with calcium chloride, the oil was fractionated. The yield was 9.6 g. of a product boiling at 145.8–146.2° (739 mm.); d_{25}^{25} 1.0767; n_D^{25} 1.4448.

Anal. Calcd. for $C_5H_{10}Cl_2$: Cl, 50.3. Found: Cl, 50.1.

To a solution of 15 g. of dry sodium iodide in 100 cc. of dry acetone was added 5 g. of the dichloropentane as obtained above. The solution was refluxed for about six hours, after which time the solution was distinctly colored with free iodine and a precipitate of about 1 g. of sodium chloride had formed. The acetone was distilled off and water added to the residue. The insoluble oil was taken up in ether, washed with sodium thiosulfate, dried, and after removal of the ether, distilled. The dichloropentane that was recovered amounted to 3.2 g.

1,2-Dichloropentane from Pentene-1.—Pentene-1 was prepared according to the method of Kirrmann.[8] Seven grams of pentene-1 was dissolved in 50 cc. of carbon tetrachloride. The solution was cooled with ice and chlorine was passed in under diffused artificial light until the yellow color remained in the solution for about thirty seconds after the current of chlorine had been stopped. After the removal of the carbon tetra-

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[7] *Cf.* Darzens, *Compt. rend.*, **152**, 1314 (1911).

[8] Kirrmann, *Bull. soc. chim.*, **39**, 988 (1926).

chloride from the product by fractional distillation, the dichloropentane distilled at 146.0–146.2°; yield, 7 g.; d_{25}^{25} 1.0773; n_D^{25} 1.4453.

Anal. Calcd. for $C_5H_{10}Cl_2$: Cl, 50.3. Found: Cl, 49.8.

1-Chloro-3-Bromopropanol-2.—The fraction boiling at 100–105° (20 mm.) from the preparation of 1-chloropentanol-2 was refractionated under reduced pressure into a part boiling at 95–98° (15 mm.) which was the glycerol chlorobromohydrin described by Fourneau and Tiffeneau.[3] The compound was colorless when freshly distilled but darkened rapidly on exposure to light. It boiled with much decomposition at 190–200° (740 mm.), and for this reason was best purified by distillation under diminished pressure; d_{25}^{25} 1.7456; n_D^{25} 1.5140.

Anal. Calcd. for C_3H_6OClBr: Cl, 20.4; Br, 46.1. Found: Cl, 20.1; Br, 45.3.

No effort was made to secure the maximum yield of this compound. Presumably, however, about 100 g. of it was available from a run of one mole of epichlorohydrin, since the total weight of reaction product was about 140 g. and about 23 g. of chloropentanol was obtained from this. The intermediate fractions weighed 10–15 g.

The chlorobromohydrin was further identified by preparing the known 1,3-diphenoxypropanol-2 from it by the procedure described by Rössing[9] for the preparation of this substance from α-dichlorohydrin. The melting point of the diphenoxy compound after recrystallization from alcohol was 80–81°.

Summary

1. It has been shown that ethylmagnesium bromide reacts with epichlorohydrin to give a chloro-amyl alcohol as well as glycerol chlorobromohydrin.

2. The chloro-amyl alcohol which is formed has been found to be 1-chloropentanol-2.

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[Contribution from the Laboratory of Physical Chemistry of the Polytechnic Institute]

STUDIES ON HYDRAZINE. THE HYDROLYSIS OF DIMETHYLKETAZINE AND THE EQUILIBRIUM BETWEEN HYDRAZINE AND ACETONE

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One of the most important properties of hydrazine and its organic substitution products is their capacity to react with the carbonyl group of ketones and aldehydes, forming hydrazones or azines by elimination of water. This reaction takes place most generally in neutral or alkaline solution, while in acid the product is to a greater or less extent, depending on the particular components, hydrolyzed. A study of this type of hydrolysis, using the product formed in the reaction of hydrazine with the simplest ketone, acetone, has been made in the work here presented.

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[9] Rössing, *Ber.*, **19**, 64 (1886).

[1] Fellow of the John Simon Guggenheim Memorial Foundation.