[Contribution from the Kedzie Chemical Laboratory, Michigan State College]

THE REACTIONS OF 1,2-EPOXYPROPANE WITH ALKYLMAGNESIUM CHLORIDES

RALPH C. HUSTON and HARLAN E. TIEFENTHAL

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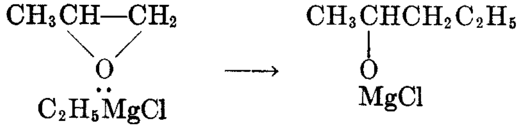
When cooled solutions of ethylmagnesium bromide are treated with equimolecular quantities of 1,2-epoxyethane (1), 1,2-epoxypropane (2), or 2,3-epoxybutane (3) the predominant reactions are with the magnesium-bromide bond of the Grignard reagent.

When ethylmagnesium chloride is treated with 2,3-epoxybutane under the same conditions the relative amount of reaction with the ethyl-magnesium bond is greatly increased (3) and when this Grignard reagent is treated with 1,2-epoxyethane the predominant reaction is with the ethyl-magnesium bond (4).

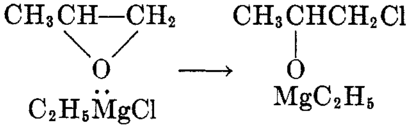
The treatment of ethylmagnesium chloride with equimolecular portions of 1,2-epoxypropane also gives a slight predominance of reaction with the ethyl-magnesium bond:

1.

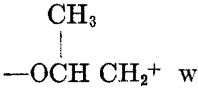


as compared with reaction with the magnesium-chlorine bond:

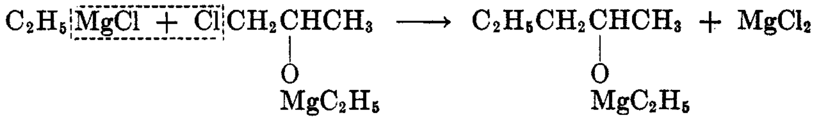
2.



and the yield of 2-pentanol exceeds slightly that of 1-chloro-2-propanol. Treatment of the higher alkylmagnesium chlorides with 1,2-epoxypropane gives predominance to reaction with the magnesium-chlorine bond; however, reaction with the alkyl-magnesium bond is in general more extensive than is the case when the same alkylmagnesium bromide is used (2). Primary chlorides gave better yields of secondary alcohol than did the isomeric secondary chlorides (Table I).

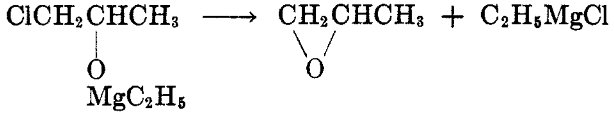
We were unable to detect the presence of acetone in any of the reaction mixtures from equimolecular quantities of alkylmagnesium chloride and 1,2-epoxypropane and concluded that (if formed at all) the positive-negative group  $—O\overset{\overset{CH_3}{|}}{C}H\ CH_2^+$ was formed to a much smaller extent than in the case of the alkylmagnesium bromides (2). The absence of appreciable amounts of this intermediate fragment suggested that the yields of secondary alcohols might be increased by refluxing the reaction mixture with benzene (4).

As shown in Table I, heating gave in all cases an increase in the yield of alcohol. These increases may be ascribed either to a more complete reaction of the alkyl-magnesium bond (equation 1), or to a Wurtz type of reaction between alkylmagnesium chloride (or dialkylmagnesium) with chloropropoxy ethylmagnesium (or chloropropoxymagnesium chloride or dichlorodipropoxymagnesium).

3.


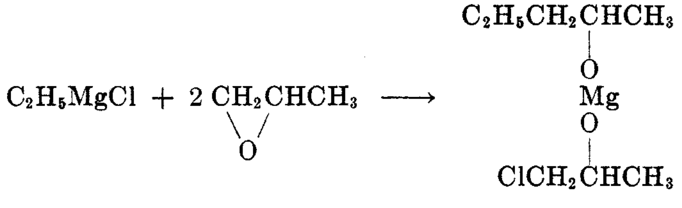
$$C_2H_5\boxed{MgCl + Cl}CH_2\underset{\substack{|\\ O\\ MgC_2H_5}}{C}HCH_3 \longrightarrow C_2H_5CH_2\underset{\substack{|\\ O\\ MgC_2H_5}}{C}HCH_3 + MgCl_2$$

In all cases but one (ethylmagnesium chloride), heating gave a decreased yield of 1-chloro-2-propanol. There appears to be no correlation between the decrease in yield of the chlorohydrin and increase in yield of alcohol. In most cases the percentage decrease in yield of chlorohydrin is much greater than the percentage increase in yield of alcohol. This indicates some decomposition of chloropropoxy ethylmagnesium (or chloropropoxymagnesium chloride) of the type indicated in equation 4. In no case was there evidence that heating of the reaction mixture caused the formation of acetone or propionaldehyde (2).

4.


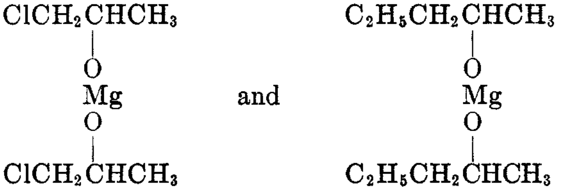
$$ClCH_2\underset{\substack{|\\ O\\ MgC_2H_5}}{C}HCH_3 \longrightarrow \underset{\substack{\diagdown\,\diagup\\ O}}{CH_2CH}CH_3 + C_2H_5MgCl$$

When one molecular equivalent of alkylmagnesium chloride was treated with two equivalents of propylene oxide (Table I) and the reaction mixture was allowed to stand until a negative test was obtained with Michler's ketone, the yields of both secondary alcohol and 1-chloro-2-propanol were such that, in some molecules of Grignard reagent, both alkyl-magnesium and magnesium-chlorine bonds reacted with propylene oxide

5.


$$C_2H_5MgCl + 2\,\underset{\substack{\diagdown\,\diagup\\ O}}{CH_2CH}CH_3 \longrightarrow \begin{array}{c} C_2H_5CH_2CHCH_3\\ |\\ O\\ Mg\\ O\\ |\\ ClCH_2CHCH_3 \end{array}$$

The Schlenk equilibrium would lead to the formation of such intermediates as

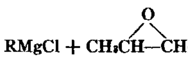
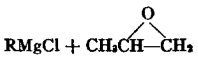
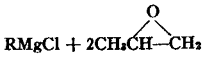


$$\begin{array}{c} ClCH_2CHCH_3\\ |\\ O\\ Mg\\ O\\ |\\ ClCH_2CHCH_3 \end{array} \quad \text{and} \quad \begin{array}{c} C_2H_5CH_2CHCH_3\\ |\\ O\\ Mg\\ O\\ |\\ C_2H_5CH_2CHCH_3 \end{array}$$

In all cases, except when *tert*-butylmagnesium chloride was used, this reaction ratio gave maximum yields of both 1-chloro-2-propanol and secondary alcohols.

TABLE I

Percentage Yields of Alcohols and 1-Chloro-2-propanol from 1,2-Epoxypropane and Alkylmagnesium Chlorides

GRIGNARD REAGENT Prepared from	 $RMgCl + CH_3\overset{O}{CH-CH_2}$		 $RMgCl + CH_3\overset{O}{CH-CH_2}$		 $RMgCl + 2CH_3\overset{O}{CH-CH_2}$		
	Not heated		Heated		Not heated		
	1-Chloro-2-propanol yield, %	Alcohol yield, %	1-Chloro-2-propanol yield, %	Alcohol yield, %	Time (days)	1-Chloro-2-propanol yield, %	Alcohol yield, %
Ethyl chloride (1-chloroethane)	35	2-Pentanol 37	40	2-Pentanol 42	3	73	2-Pentanol 56
Propyl chloride (1-chloropropane)	50	2-Hexanol 28	35	2-Hexanol 31	9	64	2-Hexanol 63
Isopropyl chloride (2-chloropropane)	55	4-Methyl-2-pentanol 23	53	4-Methyl-2-pentanol 30	9	81	4-Methyl-2-pentanol 46
Butyl chloride (1-chlorobutane)	52	2-Heptanol 41	28	2-Heptanol 58	8	77	2-Heptanol 59
sec-Butyl chloride (2-chlorobutane)	54	4-Methyl-2-hexanol 10	24	4-Methyl-2-hexanol 16	10	69	4-Methyl-2-hexanol 30
Isobutyl chloride (2-methyl-1-chloropropane)	58	5-Methyl-2-hexanol 19	19	5-Methyl-2-hexanol 40	17	73	5-Methyl-2-hexanol 62
tert-Butyl chloride (2-methyl-2-chloropropane)	65	4,4-Dimethyl-2-pentanol 0	3	4,4-Dimethyl-2-pentanol 25	23	61	4,4-Dimethyl-2-pentanol 15

Yields of 1-chloro-2-propanol varied between 60% and 80%. Yields of secondary alcohols from primary alkylmagnesium chlorides approximated 60%, yields from secondary alkylmagnesium chlorides were from 30 to 45%, and yields from *tert*-butylmagnesium chloride averaged 15%. With the exception of that from isobutylmagnesium chloride these yields were of the same order as those obtained from the corresponding alkylmagnesium bromides and propylene oxide under the same conditions (2).

EXPERIMENTAL

Preparation of alkylmagnesium chlorides. Ethylmagnesium chloride and the higher alkylmagnesium chloride were prepared in approximately three-mole quantities by using the same techniques that were used in the preparation of these reagents for reaction with ethylene oxide (4). The concentrations were carefully determined by titration (5) of aliquots. Each Grignard reagent was divided into three equal parts and each part was treated in a different way. A typical run of each of the three procedures is described below.

Reaction of one mole of 1,2-epoxypropane with one mole of Grignard reagent. One-third of the total Grignard solution was placed in a one-liter, three-necked, round-bottomed flask. The flask was fitted with a bulb condenser, a glycerol-sealed stirrer, and a dropping-funnel. The condenser and the funnel were fitted with calcium chloride: soda-lime tubes. The required amount of 1,2-epoxypropane was placed in the dropping-funnel along with an equal volume of anhydrous ether. This solution was added dropwise, with stirring, as fast as possible while still maintaining a gentle reflux. After the addition had been completed, the mixture was stirred for an hour and allowed to stand overnight.

The mixture was hydrolyzed, without external cooling, by adding a saturated solution of ammonium chloride dropwise, with stirring, at a rate sufficient to maintain gentle reflux. About 100 ml. were required to reach a point where a clear separation occurred. The ether solution was decanted from the precipitated magnesium salts and the dense precipitate was washed with one or two portions of ether.

The combined ether solutions were placed over 40 g. of sodium hydroxide pellets and 150 ml. of water was added slowly, with stirring. This mixture was refluxed, with stirring, for seven hours to convert the 1-chloro-2-propanol to 1,2-epoxypropane and sodium chloride. The mixture stood overnight, the layers were separated, and the water layer extracted with ether. The combined ether solutions were dried with potassium carbonate, and the water layer was diluted to one liter. Two-milliliter portions were titrated for chloride ion by the Volhard method to give an accurate measure of the yield of 1-chloro-2-propanol.

The dried ether solution of the products was distilled at atmospheric pressure through either a 9.0″ or a 16.5″ Fenske-type column packed with glass helices and fitted with a total reflux, partial take-off type head. All like runs were combined after one fractionation and a refractionation made before physical constants were determined and derivatives made.

Reaction of one mole of 1,2-epoxypropane with one mole of Grignard reagent followed by refluxing with benzene. The addition of 1,2-epoxypropane was carried out as described above and the mixture allowed to stand overnight. The condenser was set for distillation, approximately one-half of the ether was removed, and twice the amount of anhydrous benzene was added. This solution was distilled until the temperature of the liquid reached 75°. The mixture was refluxed, with stirring, for seven hours and allowed to stand overnight. It was hydrolyzed, and the yields of products were determined by titration and distillation as before.

Reaction of two moles of 1,2-epoxypropane with one mole of Grignard reagent. The ether solution of 1,2-epoxypropane was added to the Grignard reagent. The reaction mixture was stirred for an hour after addition was completed and then allowed to stand until the test with Michler's ketone was faint or negative. By this time the reaction mixture had set to a gel. Hydrolysis and analysis were carried out as in the other two experiments.

In all experiments, tests for acetone and propionaldehyde were made with 2,4-dinitrophenylhydrazine on those fractions which came over at 48–60°. The results were uniformly negative.

The alkanols were also prepared by allowing the dialkylmagnesium to react at room temperature with 1,2-epoxypropane.

All figures given in Table I are averages of at least three experiments.

Identification of products. The alcohols were identified by the boiling points, refractive indices, and the mixed melting points of their 3,5-dinitrobenzoates. These identifications are summarized in Table II.

TABLE II

CHARACTERIZATION OF ALCOHOLS

ALCOHOL	B.P., °C./MM.	n_D^{20}	3,5-DINITROBENZOATE
			M.P. °C.
1-Chloro-2-propanol	125–126/745 (6)	1.4392 (7)	—
2-Pentanol	120.1/743 (2, 8)	1.4068 (2, 8)	60–61 (2, 8)
2-Hexanol	139.2/743 (2, 10)	1.4140 (2, 10)	36–37.5 (2, 9)
4-Methyl-2-pentanol	131.4/745 (2, 11)	1.4132 (2, 11)	60.5–61.5 (2, 9
2-Heptanol	158.8/745 (2, 10, 12)	1.4218 (2, 10, 12)	47.5–48.5 (2, 10, 12)
4-Methyl-2-hexanol	152.2/744 (2, 13)	1.4236 (2, 13)	62–63 (2, 13)
5-Methyl-2-hexanol	150.4/744 (14, 15)	1.4194 (14, 15)	34.5–35.5 (2)
4,4-Dimethyl-2-pentanol	135.4/742 (16)	1.4241 (16)	48–50 (2)

SUMMARY

1. Treatment of alkylmagnesium chlorides with equimolecular quantities of 1,2-epoxypropane gives a much larger yield of alcohol than does the treatment of alkylmagnesium bromides with the epoxide.

2. The yields of alcohols are increased when the reaction mixtures from alkylmagnesium chlorides and 1,2-epoxypropane are heated, in the presence of benzene.

3. Excellent yields of both 1-chloro-2-propanol and secondary alcohols were obtained when alkylmagnesium chlorides were treated with two molecular equivalents of 1,2-epoxypropane.

4. We found, in this group of reactions, no evidence of rearrangement of 1,2-epoxypropane with the formation of acetone or propionaldehyde.

EAST LANSING, MICHIGAN

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