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

THE REACTION OF 1,2-EPOXY-2-METHYLPROPANE WITH AKLYLMAGNESIUM BROMIDES

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Olefin oxides have been found to react with both the alkylmagnesium and magnesium halide bonds of the Grignard reagent (1–4). A similarity also is marked in the formation of by-product carbonyl compounds. 1,2-epoxyethane, 1,2-epoxypropane, and 2,3-epoxybutane from ethanal (3), propanone (2), and 2-butanone (4) respectively. Rearrangement of the positive-negative fragment to form the carbonyl derivative takes place readily in alkaline media, (Grignard reagent). The shift of the hydrogen through the protonized double bond is therefore considered probable.

The reaction of 1,2-epoxy-2-methylpropane with an alkylmagnesium bromide may likewise involve either the alkylmagnesium bond (5) or the magnesium-bromide bond or both. The positive-negative fragment $CH_3\overset{O^-}{\underset{CH_3}{C}}CH_2^+$, which would result from the reaction of the magnesium-bromine bond, can not undergo a simple rearrangement by shifting a hydrogen from the oxygenated carbon to the positive end carbon as in the case of the fragment from 1,2-epoxypropane. However the shift of negative oxygen gives the fragment $CH_3\overset{+}{\underset{CH_3}{C}}CH_2O^-$ which may in turn undergo rearrangement by hydrogen shift to form 2-methylpropanal. Failure to isolate the 2-bromo-2-methyl-1-propanol from the reaction products and the formation of 2-methylpropanal from 1-bromo-2-methyl-2-propanol indicates that the fragment $CH_3\overset{+}{\underset{CH_3}{C}}CH_2O^-$ is not formed by the opening of the alternate carbon oxygen bond of the epoxide.

Henry (6) assumed that 2-methylpropanal was an intermediate in the formation of 3-methyl-2-butanol from 1,2-epoxy-2-methylpropane but proposed no mechanism for its formation.

The addition of 1,2-epoxy-2-methylpropane to molecular equivalents of ethylmagnesium bromide or *n*-propylmagnesium bromide shows no apparent reaction of the alkyl-magnesium bond. The secondary alcohol, 2-methyl-3-pentanol or 2-methyl-3-hexanol, was in each case the principal product. A slightly smaller yield of the bromohydrin, 1-bromo-2-methyl-2-propanol was formed. There was also some reduction of 2-methylpropanal as evidenced by the positive identification, in each case of 2-methyl-1-propanol.

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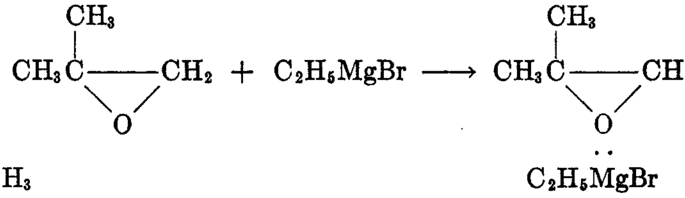

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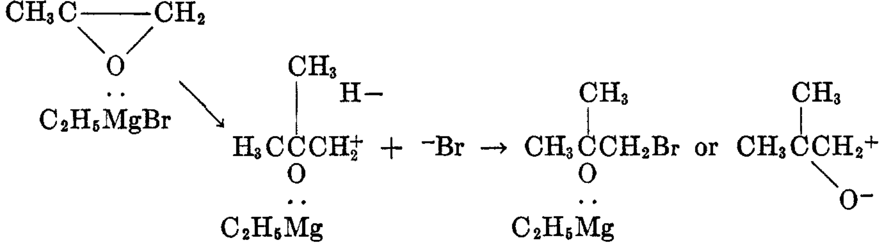

(It is obvious that the ring could be opened by $MgBr_2$ also).

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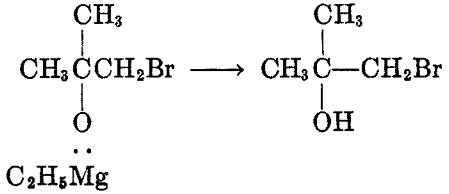
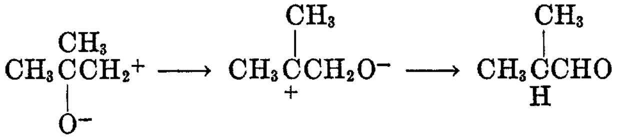


$$\underset{\substack{\mathrm{O}\\ \cdot\cdot \\ \mathrm{C_2H_5Mg}}}{\mathrm{CH_3\overset{CH_3}{C}CH_2Br}} \longrightarrow \mathrm{CH_3\overset{CH_3}{\underset{OH}{C}}{-}CH_2Br}$$

4.


$$\mathrm{CH_3\overset{CH_3}{\underset{O^-}{C}}CH_2^+} \longrightarrow \mathrm{CH_3\overset{CH_3}{\underset{+}{C}}CH_2O^-} \longrightarrow \mathrm{CH_3\overset{CH_3}{\underset{H}{C}}CHO}$$

When an excess of 1,2-epoxy-2-methylpropane (2 moles) was added to ethylmagnesium bromide or *n*-propylmagnesium bromide there was a marked *increase* in the yield of bromohydrin, and a marked *decrease* in the yield of secondary alcohol as compared with yields when molecular equivalents were used (Table I). Most of that portion of the 2-methylpropanal which was formed by rearrangement (equation 4) which did not react to form secondary alcohol was recovered as the trimer $C_{12}H_{24}O_3$ (7). The small amount of Grignard reagent available to react with 2-methylpropanal was decreased by the excess of 1,2-epoxy-2-methylpropane which apparently reacted with the alkylmagnesium bond.

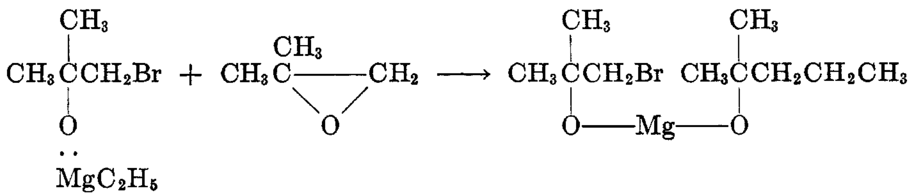
5.


TABLE I

PERCENTAGE YIELDS OF ALCOHOLS FROM 1,2-EPOXY-2-METHYLPROPANE AND GRIGNARD REAGENTS FROM ETHYL BROMIDE OR *n*-PROPYL BROMIDE

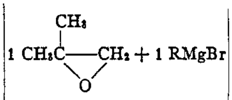
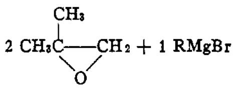
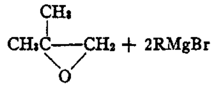
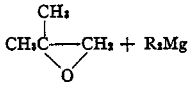
GRIGNARD REAGENT FROM						
	1 Bromo-2-methyl-2-propanol	Secondary alcohol	1 Bromo-2-methyl-2-propanol	Secondary alcohol	Tertiary alcohol	Polymer
Ethyl bromide	28.3	2-Methyl-3-pentanol 42.2	51.2	2-Methyl-3-pentanol 13.2	2-Methyl-2-pentanol 17.9	$(C_4H_8O)_3$ 14
n-Propyl bromide	30.5	2-Methyl-3-hexanol 39.4	57.2	2-Methyl-3-hexanol 12.8	2-Methyl-2-hexanol 15.2	$(C_4H_8O)_3$ 28

TABLE II

PERCENTAGE YIELDS OF ALCOHOLS FROM 1,2-EPOXY-2-METHYLPROPANE AND TWO MOLES OF GRIGNARD REAGENT OR ONE MOLE OF DIALKYLMAGNESIUM

REAGENT FROM			
	1-Bromo-2-methyl-2-propanol	Secondary alcohols	Tertiary alcohol
Methyl bromide	40.2	2-Methyl-3-butanol 40.8	2-Methyl-2-butanol —[a]
Ethyl bromide	40.4	2-Methyl-3-pentanol 51.4	2-Methyl-2-pentanol 35.0
n-Propyl bromide	23.0	2-Methyl-3-hexanol 44.5	2-Methyl-2-hexanol 25.5
sec-Propyl bromide	60.0	2,4-Dimethyl-3-pentanol 21.5	
n-Butyl bromide	41.0	2-Methyl-3-heptanol 20.1	2-Methyl-2-heptanol 11.5
tert-Butyl bromide	56.0	2,2,4-Trimethyl-3-pentanol 0.0	2,4,4-Trimethyl-2-pentanol 6.0

[a] The percentage yield was not determined.

Dialkylmagnesium resulting from the Schlenk equilibrium could also react directly with 1,2-epoxy-2-methylpropane to give intermediates which would yield, upon hydrolysis, 2-methyl-2-pentanol or 2-methyl-2-hexanol.

When 1,2-epoxy-2-methylpropane is added to an excess of ethylmagnesium bromide or *n*-propylmagnesium bromide (2 moles) there is a definite increase in the yields of secondary alcohol over those obtained when the reactants are used in molecular equivalents (Table II). This indicates a more efficient production of 2-methylpropanal (reactions 2 and 4) and a more complete conversion into the secondary alcohol. The yields of 1-bromo-2-methyl-2-propanol were definitely increased in the presence of excess ethylmagnesium bromide and decreased in the presence of excess *n*-propylmagnesium bromide.

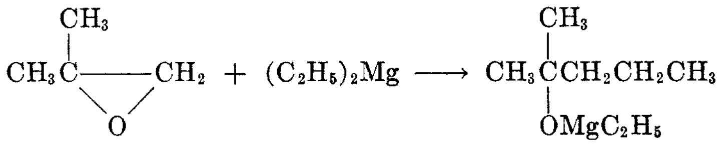
Since the best yields of secondary alcohols were obtained in these simple cases the epoxide was reacted with methylmagnesium bromide, *sec*-propylmagnesium bromide, *n*-butylmagnesium, and *tert*-butylmagnesium bromide under the same conditions.

Methylmagnesium bromide gave a yield of 1-bromo-2-methyl-2-propanol approximately equal to that given by ethylmagnesium bromide but the yield of secondary alcohol was somewhat smaller. The increased yield of 1-bromo-2-methyl-2-propanol resulting from the reaction between *sec*-propylmagnesium bromide indicates that secondary alkyls favor the formation of bromohydrin at the expense of 2-methylpropanal and alcohol.

A large yield of 1-bromo-2-methyl-2-propanol was also formed when *tert*-butylmagnesium bromide was used. In this case, the absence of secondary alcohol was attributed to the lack of ability of the *tert*-butylmagnesium bromide to react with 2-methylpropanal. The aldehyde was isolated as the trimer.

The addition of a mole of 1,2-epoxy-2-methylpropane to a mole of diethylmagnesium leads to the rupture of the ethylmagnesium bond and the formation of an intermediate which gives upon hydrolysis 2-methyl-2-pentanol (5).

6.



The reaction is quite slow and the yield of tertiary alcohol is small even when it is allowed to proceed until the Michler ketone test is negative (6 days). The time required to bring the reaction between di-*tert*-butylmagnesium and 1,2-epoxy-2-methylpropane to completion was from 30 to 40 days.

There was no evidence of the formation of 2-methylpropanal or its trimer in any of the reactions between dialkylmagnesium and 1,2-epoxy-2-methylpropane.

The 1-bromo-2-methyl-2-propanol which was formed in all reactions of 1,2-epoxy-2-methylpropane with Grignard reagents was prepared in quanity by adding 1,2-epoxy-2-methylpropane to a solution of magnesium bromide in ether. It was also synthesized from bromoacetone and methylmagnesium bromide (8). The identity of the compounds was proved by the melting points of the 3,5-dinitrobenzoates.

Attempts to prepare pure dibromo-di-*tert*-butoxymagnesium by dropping diethylmagnesium into 1-bromo-2-methyl-2-propanol gave precipitates which contained less bromine and more magnesium than the calculated amounts. Hydrolysis gave 1-bromo-2-methyl-2-propanol, 2-methylpropanal and its trimer, and some 2-methyl-1-propanol. When the reaction mixture was refluxed overnight and then hydrolyzed the only product isolated was the trimer of 2-methylpropanal.

Two experiments with ethylmagnesium bromide and 1,2-epoxy-2-methylpropane were performed under conditions which would provide an excess of the epoxide. When one mole of the Grignard reagent was dropped into one mole of the epoxide the products were: 1-bromo-2-methyl-2-propanol, 2-methyl-3-pentanol, and the trimer of 2-methylpropanal. A small amount of distillate came over at the boiling point of 2-methyl-2-pentanol, but it was not pure enough to be identified by its 3,5-dinitrobenzoate. When one mole of ethylmagnesium bromide was dropped into two moles of 1,2-epoxy-2-methylpropane the products were: 1-bromo-2-methyl-2-propanol, 2-methyl-1-propanol, 2-methyl-2-pentanol, and the trimer of 2-methylpropanal. The small fraction which came over at the boiling temperature of 2-methyl-3-pentanol was not pure enough to give a sharp-melting 3,5-dinitrobenzoate.

EXPERIMENTAL

Reactions of Grignard reagents with 1,2-epoxy-2-methylpropane. In the preparation of Grignard reagents and the reactions of these with 1,2-epoxy-2-methylpropane, the same techniques were used and the same precautions observed as in the study of 1,2-epoxypropane (2).

After the yield of 1-bromo-2-methyl-2-propanol had been determined by decomposition and titration, the ether solution was distilled at atmospheric pressure through a Fenske-type column to a temperature above the boiling point of 1,2-epoxy-2-methylpropane, and beyond that point at reduced pressure. In all cases a sufficient amount of 2-methylpropanal was isolated for identification by a mixed melting point (120°) of its 2,4-dinitrophenylhydrazone. The yield of 1,2-epoxy-2-methylpropane approximated in each case the yield of 1-bromo-2-methyl-2-propanol. In those reactions where two molecular equivalents of 1,2-epoxy-2-methylpropane reacted with one of Grignard reagent a small amount of 2-methyl-1-propanol was isolated and identified by its boiling point (106–108°) and the mixed melting point determination of its 3,5-dinitrobenzoate.

In these same reactions and in the reaction between one-half molecular equivalent of 1,2-epoxy-2-methylpropane and one of *tert*-butylmagnesium bromide the trimer of 2-methylpropanal was isolated. This was identified (7) by its boiling point (127° at 17 mm.), its refractive index (n_D^{30} 1.4370), and its depolymerization when treated with sulfuric acid.

Reactions of 1,2-epoxy-2-methylpropane with the dialkylmagnesiums. In the preparation of the dialkylmagnesium solutions the mixture was allowed to stand from 3 to 5 days before the dioxane precipitate was separated from the dialkylmagnesium by centrifuging. The concentration was determined by titrating with standard acid. In the preparation of dimethylmagnesium the dioxane precipitate was not centrifuged. The ether solution was decanted from the precipitate, and the latter was washed by shaking with ether and decanting. The dimethylmagnesium content of the combined ether solutions was not determined.

The reaction was carried out in the same manner and in the same apparatus as were the reactions with Grignard reagents except that refluxing with sodium hydroxide was omitted. Distillation of the dried ether solution gave no evidence of the presence of 2-methylpropanal or its trimer. Distillation of the tertiary alcohols was at reduced pressures.

Preparation of 1-bromo-2-methyl-2-propanol. One mole of 1,2-epoxy-2-methylpropane in 500 ml. of ether was slowly added to one mole of $MgBr_2$ in 500 ml. of ether (2). After standing one hour the solution was poured on cracked ice and the basic salts were dissolved in dilute hydrochloric acid. The ether layer was shaken with 5% sodium bicarbonate, washed with water, and dried over sodium sulfate. Distillation gave 1-bromo-2-methyl-2-propanol (56 g.), which was identified by its physical properties and the melting point of the 3,5-dinitrobenzoate as the same compound which was prepared from bromoacetone and methylmagnesium bromide (8).

The preparation of dibromodi-tert-butoxymagnesium. Two molecular equivalents of 1,2-epoxy-2-methylpropane in ether was slowly added to one mole of an ether solution of magnesium bromide. The precipitate was washed with anhydrous ether, centrifuged, and brought to constant weight in a vacuum desiccator.

Anal. Calc'd for $C_8H_{16}Br_2MgO_2$: Mg, 7.31; Br, 48.87.
Found: Mg, 7.67; Br, 42.3.

TABLE III

IDENTIFICATION OF ALCOHOLS

ALCOHOL	DERIVATIVE	M.P., °C.	NITROGEN	
			Calc'd	Found
1-Bromo-2-methyl-2-propanol (8)	3,5-dinitrobenzoate	120	8.04	8.11
B.p.$_{16\text{mm}}$49.5°; n_D^{20} 1.4710				
2-Methyl-3-butanol (9)	3,5-dinitrobenzoate	163	9.93	10.13
B.p.$_{745\text{mm}}$110–112°; n_D^{20} 1.3973				
2-Methyl-2-butanol (10)	3,5-dinitrobenzoate	116 (11)		
B.p.$_{740\text{mm}}$102°; n_D^{20} 1.4020				
2-Methyl-3-pentanol (12)	3,5-dinitrobenzoate	85 (11)		
B.p.$_{740\text{mm}}$127–128°; n_D^{20} 1.4168	3-nitrophthalate	150.5 (12		
2-Methyl-2-pentanol (11)	3,5-dinitrobenzoate	72 (11)		
B.p.$_{740\text{mm}}$117–118°; n_D^{20} 1.4125				
2-Methyl-3-hexanol (14)	3,5-dinitrobenzoate	59–60	9.80	9.60
B.p.$_{740\text{mm}}$142–145°; n_D^{20} 1.4178	acid phthalate	59–60 (9)		
2-Methyl-2-hexanol (15)	3,5-dinitrobenzoate	53–54°	9.03	9.10
B.p.$_{740\text{mm}}$139–140°; n_D^{20} 1.4175	phenylurethan	44–45 (16)		
2,4-Dimethyl-3-pentanol (12)	3,5-dinitrobenzoate	75	9.03	9.27
B.p.$_{740\text{mm}}$137–138°; n_D^{20} 1.4250	phenylurethan	94–94.5 (17)		
2-Methyl-3-heptanol (12)	3,0-dinitrobenzoate	53–54	8.64	8.44
B.p.$_{740\text{mm}}$165–167°; n_D^{20} 1.4259	acid phthalate	47–48 (9)		
2-Methyl-2-heptanol (18)	3,5-dinitrobenzoate	43–44	8.64	8.40
B.p.$_{15\text{mm}}$65°; n_D^{20} 1.4248				
2,2,4-Trimethyl-3-pentanol (18)				
B.p.$_{15\text{mm}}$55°; n_D^{20} 1.4038				

One molecular equivalent of diethylmagnesium in ether was added to two equivalents of 1-bromo-2-methyl-2-propanol in an equal volume of ether. After centrifuging and removing ether in a vacuum, the precipitate was analyzed.

Anal. Calc'd for $C_8H_{16}Br_2MgO_2$: Mg, 7.31; Br, 48.78.
Found: Mg, 9.4; Br. 42.9.

In one experiment the reaction mixture was hydrolyzed immediately after the addition of the diethylmagnesium. Distillation of the dried ether layer gave 1-bromo-2-methyl-2-propanol as the main product. Small amounts of the trimer of 2-methylpropanal, and 2-methyl-1-propanol were also identified.

In another experiment the reaction mixture was refluxed overnight and then hydrolyzed. The dried ether layer gave upon distillation only the trimer of 2-methylpropanal.

Addition of ethylmagnesium bromide to 1,2-epoxy-2-methylpropane. One mole of 1,2-epoxy-2-methylpropane in an equal volume of anhydrous ether was cooled with salt and ice. One mole of ethylmagnesium bromide was added slowly. The reaction mixture was stirred for two hours and allowed to stand overnight at room temperature. It was decomposed with ammonium bromide and the ether portion dried with sodium sulfate. The 1-bromo-2-methyl-2-propanol was decomposed and the distillation carried out as when the addition was made in the usual (reverse) manner. The following mole-% yields were obtained:

1-Bromo-2-methyl-2-propanol	27.3%
2-Methyl-3-pentanol	13.8%
Trimer of 2-methylpropanal	5.0%

About 5 ml. came over near the boiling point of 2-methyl-2-pentanol (116–121°) but a sharpmelting 3,5-dinitrobenzoate was not obtained.

When one mole of ethylmagnesium bromide was slowly added to a cooled ether solution of two moles of 1,2-epoxy-2-methylpropane and the reaction mixture treated as above the following yields were obtained:

2-Bromo-2-methyl-2-propanol	33.1%
2-Methyl-2-pentanol	8.5%
2-Methyl-1-propanol	6.0%
Trimer of 2-methylpropanal	16.0%

About 6 ml. which came over at 126–130° did not give a sharp melting 3,5-dinitrobenzoate of 2-methyl-3-pentanol.

Identification of alcohols. The boiling points and refractive indices were checked against those cited in the literature as were the melting points of known solid derivatives. (Table III). In those cases where the 3,5-dinitrobenzoates were not given in the literature these were prepared, analyzed, and checked by mixed melting points against those of alcohols prepared by methods cited in the literature.

SUMMARY

The addition of one or one-half molecular-equivalent of 1,2-epoxy-2-methylpropane to one equivalent of alkylmagnesium bromide leads to the opening of the oxirane ring and the reaction of the magnesium-bromine bond. The products formed are: 1-bromo-2-methyl-2-propanol, 2-methyl-1-propanal, and the secondary alcohol resulting from the reaction of 2-methylpropanal and excess Grignard reagent. When the Grignard reagent does not react with 2-methylpropanal, the trimer of the aldehyde is formed. When equimolecular quantities of reactants were used there was some reduction of the aldehyde to 2-methyl-1-propanol.

The addition of two molecular equivalents of 1,2-epoxy-2-methylpropane to one of ethylmagnesium bromide or of propylmagnesium bromide leads to the reaction of the magnesium-bromine bond with the formation of 1-bromo-2-methyl-2-propanol, 2-methylpropanal, and a relatively small yield of 2-methyl-3-pentanol or 2-methyl-3-hexanol. The trimer of 2-methylpropanal is formed in quantity. There is at the same time reaction of the alkylmagnesium bond with the formation of 2-methyl-2-pentanol or 2-methyl-2-hexanol.

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