[A CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Action of Diethylmagnesium upon the Methyl Substituted Derivatives of Epoxyethane[1,2]

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Recently, Bartlett and Berry[3] have shown that dimethyl- and diethylmagnesium react with 1,2-epoxycyclohexane to form when hydrolyzed the products *trans*-2-methyl- and *trans*-2-ethylcyclohexanol. The present paper presents the results obtained by extending the use of dialkylmagnesium as a reagent into the field of epoxyalkanes.

The reactions of epoxyalkanes with Grignard reagents may be summarized as follows. Epoxyethane and 1,2-epoxypropane are known to react by simple splitting of the oxygen-to-carbon linkage; but the more highly substituted epoxyalkanes rearrange to produce alcohols which can be obtained from the corresponding aldehyde or ketone by use of the same alkylmagnesium halide.[4]

The authors have allowed diethylmagnesium to react with the methyl substituted derivatives of epoxyethane. Their purpose was to discover whether or not there is rearrangement when a dialkylmagnesium is allowed to react with epoxyalkanes and to determine the difference in activity of the two carbon to oxygen valences in the epoxyalkane. To ensure identification of the alcohols synthesized by this method, the authors allowed ethylmagnesium bromide to react with the same epoxyalkanes. Reference alcohols also were prepared by other Grignard reagents.

Quite accidentally, the authors discovered and separated *cis* and *trans* 2,3-epoxybutane. The identification was performed before the authors ascertained through a private communication that Lucas and Wilson[5] had synthesized these compounds in order to prove Lucas' identification of *cis* and *trans* 2-butenes.

Experimental

Purification of Organic Liquids.—All organic liquids were carefully rectified at atmospheric or reduced pressure in a Podbielniak column or in a rectifying column[6] packed with Penn State glass spirals. A reflux ratio of 20 to 1 or higher was maintained in all distillations.

Cis and trans 2,3-epoxybutane were synthesized from 2-butanol. Eight hundred and fourteen grams of 2-butanol was converted to *cis* and *trans* 2-butene.[7] The mixture of butenes was allowed to react with a cold solution of hypochlorous acid to form 3-chloro-2-butanol, 245 g., b. p. 76–79° at 100 mm.;[8,9] yield 20.6%. The crude 2,3-epoxybutanes were prepared by treatment with solid potassium hydroxide,[10] and were separated by rectification. Sixty-one and one-half grams of *trans*-2,3-epoxybutane distilled from 52–53° at 741 mm., and 43.5 g. of *cis*-2,3-epoxybutane boiled from 58–59° at 745 mm. (yield of combined *cis* and *trans* isomers, 66% based on chlorohydrin).

2,3-Epoxy-2-methylbutane was prepared from 2-methyl-2-butanol by pyrolysis[11] to 2-methyl-2-butene which was converted to the epoxyalkane as described above. Ninety-six grams of 2,3-epoxy-2-methylbutane distilled from 73.0–74.2° at 753 mm.; yield, 8.6% based on alcohol; 74% based on chlorohydrin.

2,3-Dimethyl-2,3-epoxybutane was prepared from acetone. The following reactions were carried out: the conversion of acetone to pinacol hydrate,[12] the dehydration of pinacol hydrate by a benzene distillation,[13] the treatment of 909 g. of anhydrous pinacol with molar proportions of anhydrous hydrogen chloride,[14] crystallization and filtration of the resulting chlorohydrin, 3-chloro-2,3-dimethyl-2-butanol[15] and treatment as above with potassium hydroxide to produce the corresponding epoxyalkane. One hundred and fifteen grams of 2,3-dimethyl-2,3-epoxybutane distilled from 90.2–91.4° at 753 mm. Yield of oxide was 15% based on anhydrous pinacol.

Preparation of Diethylmagnesium.—An ether solution of diethylmagnesium was prepared from ethylmagnesium bromide made from 109 g. of bromoethane, 24.5 g. of magnesium and 150 ml. of ether. The Grignard reagent was treated while refluxing with 110 g. of 1,4-dioxane in 300 ml. of ether.[16, 17] The mixture was centrifuged, the clear ether layer decanted and analyzed for diethylmagnesium[18] and for bromide ion. The solution was concentrated by distillation of about 60% of the ether.

Reactions of Diethylmagnesium upon Epoxyalkanes (Table I).—A general procedure was used in this reaction, typified by the case of 1,2-epoxypropane. The sample of epoxypropane in an equal volume of ether was added

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(1) Presented at the Kansas City Meeting of the American Chemical Society, April, 1936.

(2) This paper is an abstract of a thesis submitted by F. H. Norton to the Faculty of Purdue University in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1936.

(3) Bartlett and Berry, THIS JOURNAL, **56**, 2683 (1934).

(4) Schlenk, "Houben-Weyl," 2d Ed., Vol. IV, 1924, p. 781.

(5) Private communication with Dr. H. J. Lucas, California Institute of Technology, March 23, 1936.

(6) Hass, McBee and Weber, *Ind. Eng. Chem.*, **27**, 1195 (1935).

(7) Lucas and Young, THIS JOURNAL, **52**, 1964 (1930).

(8) Beilstein, Vol. I, 1918, p. 373.

(9) Fourneau and Puyal, *Bull. soc. chim.*, **31**, 424 (1922).

(10) Beilstein, Vol. XVII, Part II, 1933, p. 11.

(11) Matignon, Moureu and Dode, *Compt. rend.*, **196**, 973 (1933).

(12) "Organic Syntheses," Coll. Vol. I, 1932, p. 448.

(13) King and Stewart, *C. A.*, **25**, 1799 (1931).

(14) Delacre, *Bull. soc. chim.*, [4] **3**, 203-12 (1908).

(15) Nilsson and Smith, *Z. physik. Chem.*, **166**, 145 (1933).

(16) Noller and Hilmer, THIS JOURNAL, **54**, 2506 (1932).

(17) Cope, *ibid.*, **57**, 2238 (1935).

(18) Gilman, *ibid.*, **45**, 150 (1923).

TABLE I

REACTIONS OF DIETHYLMAGNESIUM UPON EPOXYALKANES

Epoxyalkane	G.	Di-Et-Mg, eq.	Product				
				G.	Yield, % on oxide	B. p. °C.	Mm.
1,2-Epoxypropane[a]	25.2	0.47	2-Pentanol	9	23	118.0–119.5	763.4
1,2-Epoxy-2-methylpropane	29	.37	2-Methyl-2-pentanol	11.3	27.5	64.8–65.6	70
cis-2,3-Epoxybutane	19	.4	3-Methyl-2-pentanol	16.5	61	75.4–75.8	70
trans-2,3-Epoxybutane	21	.4	3-Methyl-2-pentanol	6.5	21.8	73.0–74.0	70
2,3-Epoxy-2-methylbutane	25.8	.4	2,3-Dimethyl-2-pentanol	7	21	71–73	50
2,3-Dimethyl-2,3-epoxybutane	20	.4	2,3,3-Trimethyl-2-pentanol	9	34.6	81.8–83.2	50

[a] B. p. 34.1–34.6°.

TABLE II

REACTION OF ETHYLMAGNESIUM BROMIDE UPON THE EPOXYALKANES

EtMgBr + reactant	G.	Product				
			G.	Yield, % on oxide	B. p. °C.	Mm.
1,2-Epoxypropane[a]	45	2-Pentanol	8	11.7	117–118	756
1,2-Epoxy-2-methylpropane	135	2-Methyl-3-pentanol	39	21	67.0–67.2	70
cis-2,3-Epoxybutane	14	3-Methyl-3-pentanol	3.5	17.5	62.6–64.6	70
trans-2,3-Epoxybutane	15	3-Methyl-3-pentanol	10.5	49	63.7–64.9	70
2,3-Epoxy-2-methylbutane	40	2,3-Dimethyl-3-pentanol	27	50	67.8–68.6	50
2,3-Dimethyl-2,3-epoxybutane	50	2,2,3-Trimethyl-3-pentanol	25	38	76.6–77.2	50

[a] This fraction was obtained from the third rectification and its 3,5-dinitrobenzoate indicated that it was still impure. The impurity probably was 3-pentanol.

TABLE III

PREPARATION OF REFERENCE ALCOHOLS

Prepared from Grignard reagents and aldehydes or ketones in the usual manner

Reactants					Product				
I	G.	II	G.	Mg., G.	Pentanol	G.	% on I	B. p. °C.	Mm.
Acetone	36.5	1-Bromopropane	86.1	17.1	2-Methyl-2-	37.3	72	64.8–65.3	70
2-Methylpropanal	33	Bromoethane	56	12.5	2-Methyl-3-	28	68	67.4–68.2	70
Acetaldehyde	79	2-Bromopropane	362	63	3-Methyl-2-	31	16.9	74.0–75.8	70
2-Butanol	68	Bromoethane	109	24.5	3-Methyl-3-	43	44.5	63.6–64.1	70
Acetone	113	2-Bromobutane	378	65.7	2,3-Dimethyl-2-	17.4	7.7	70.0–70.8	50
2-Butanone	61	2-Bromopropane	123	24.5	2,3-Dimethyl-3-	26	26.4	68.0–68.6	50
Acetone	130	2-Chloro-2-methylbutane	542	120	2,2,3-Trimethyl-2-	17.5	6	78.9–80.1	50
3,3-Dimethyl-2-butanone	93	Bromoethane	109	24.5	2,2,3-Trimethyl-3-	41	34	76.9–77.1	50

slowly to the diethylmagnesium which had been prepared from bromoethane. The mixture was refluxed for twenty minutes, cooled, poured into ice, treated with only enough dilute sulfuric acid to dissolve the precipitate and then separated. The water layer was extracted with ether. The combined ether solutions were dried with anhydrous potassium carbonate for twelve hours. The ether was distilled off slowly in a packed column and the residue then rectified in a Podbielniak column, the fraction distilling from 113–120° being again distilled.

Reaction of Ethylmagnesium Bromide upon the Epoxyalkanes.—The epoxyalkanes (Table I) were allowed to react with ethylmagnesium bromide. The products were treated in the same manner as for those formed with diethylmagnesium (Table II).

Determination of Physical Constants.—The boiling point at atmospheric pressure,[19] the density at 25° (Ostwald pycnometer, vol. 1.1134 ml.), and the refractive index (Abbé) at 25° of all the alcohols were determined in a ten-day period. The reaction rate with zinc chloride-hydrochloric acid was determined at 27.4° in a three-hour period. The reagent was prepared as described in the literature.[10]

It is very evident from this table that diethylmagnesium reacts with the epoxyalkane to produce 2-pentanol. In the case of the corresponding Grignard reagent there is evidence that two products are formed. The alcohol prepared from ethylmagnesium bromide was rectified repeatedly and still gave a 3,5-dinitrobenzoate melting at 72°. A mixture of this derivative and the 3,5-dinitrobenzoate of 3-pentanol melted from 69–71°, which is very nearly the melting point of both derivatives. The 3-pentanol was a commercial product prepared by a distillation of a mixture of pentanols. It probably contained 2-pentanol.

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[19] Willard and Crabtree, *Ind. Eng. Chem., Anal. Ed.*, **8**, 79 (1936).

It is apparent from Table V that diethylmagnesium and ethylmagnesium bromide form different alcohols when they react with 1,2-epoxy-2-methylpropane.

TABLE IV

ALCOHOLS FROM 1,2-EPOXYPROPANE

Source	B. p. °C.	B. p. Mm.	n^{25}_D	d^{25}_4	R_L	$ZnCl_2$–HCl sec.	Derivative M. p., °C.	Derivative Mixed m. p., °C.
2-Pentanol								
Lit.	118.9	760	1.4127^{20}	0.811^{19}			61	60
Ref. cpd.	117.8	750	1.4051	.8082	26.72	210	*a* 59	60 *a* + *b*
Et_2Mg	118.0	749	1.4042	.8085	26.66	285	*b* 61	59 *b* + *e*
EtMgBr	116.1		1.4061	.8121	28.64	65	*c* 72	59–66 *a* + *c*
3-Pentanol								
Lit.	116		1.4057	0.8157			*d* 97	
Ref. cpd.							*e* 71	69–71 *c* + *e*

TABLE V

ALCOHOLS FROM 1,2-EPOXY-2-METHYLPROPANE

Source	B. p. °C.	B. p. Mm.	B. p. 70 mm.	n^{25}_D	d^{25}_4	R_L	$ZnCl_2$–HCl sec.	Derivative M. p., °C.	Derivative Mixed m. p., °C.
2-Methyl-2-pentanol									
Lit.	122.0	758			0.8194				
Ref. cpd.	119.3	748	65.0	1.4089	.8051	31.39	0		
Et_2Mg	119.4	748	65.2	1.4089	.8071	31.27	0		
2-Methyl-3-pentanol									
Lit.	127.2	721		1.4134	0.8243				
Ref. cpd.	124.6	747	67.8	1.4151	.8193	31.22	50	*a* 79	80 *a* + *b*
EtMgBr	124.5	747	67.1	1.4150	.8207	31.16	10	*b* 80	

TABLE VI

ALCOHOLS FROM *cis* AND *trans*-2,3-EPOXYBUTANE[a]

Source	B. p. °C.	B. p. Mm.	B. p. 50 mm.	n^{25}_D	d^{25}_4	R_L	$ZnCl_2$–HCl sec.	Derivative M. p., °C.	Derivative Mixed m. p., °C.
3-Methyl-2-pentanol									
Lit.	134	760		1.4205	0.8307				
Ref. cpd.	134.2	749	74.9	1.4178	.8264	31.13	65	*a* 41	40 *a* + *b*
Et_2Mg *cis*	134.4	749	75.6	1.4179	.8235	31.24	55	*b* 45	41 *b* + *c*
Et_2Mg *trans*	133	749	73	1.4180	.8240	31.23	10	*c* 51	40–44 *a* + *c*
3-Methyl-3-pentanol									
Lit.	121.8	758			0.8494				
Ref. cpd.	120.0	749	63.8	1.4165	.8240	31.13	0		
EtMgBr *cis*	117.5	751	63.6	1.4161	.8245	31.09	0		
EtMgBr *trans*	121.3	749	64.3	1.4161	.8234	31.13			

[a] *Trans* is the lower boiling oxide.

TABLE VII

ALCOHOLS FROM 2,3-EPOXY-2-METHYLBUTANE

Source	B. p. °C.	B. p. Mm.	B. p. 70 mm.	n^{25}_D	d^{25}_4	R_L	$ZnCl_2$–HCl sec.
2,3-Dimethyl-2-pentanol							
Lit.	Not reported in the literature						
Ref. cpd.	139.0	744	70.4	1.4234	0.8285	35.72	0
Et_2Mg	139.7	744	72	1.4231	.8276	35.74	0
2,3-Dimethyl-3-pentanol							
Lit.	139	750			0.8329^{21}		
Ref. cpd.	138.5	743	68.3	1.4263	.8366	35.59	0
EtMgBr	137.7		68.2	1.4262	.8382	35.51	0

Anal. Calcd. for $C_7H_{16}O$: C, 72.34; H, 13.88. Found: C, 72.01; H, 13.86.

TABLE VIII

ALCOHOLS FROM 2,3-DIMETHYL-2,3-EPOXYBUTANE

	Boiling point,						$ZnCl_2$–HCl
Source	°C.	mm.	50 mm.	n^{25}_D	d^{25}_4	RL	sec.
			2,3,3-Trimethyl-2-pentanol				
Lit.			79	1.4410^{20}			
Ref. cpd.	159.4	750	78.5	1.4360	0.8151	41.75	0
			2,2,3-Trimethyl-3-pentanol				
Lit.	151	760	76^{40}	1.4353^{20}			
Ref. cpd.	152.4	743	77.0	1.4330	0.8423	40.16	0
EtMgBr	151.8	743	76.9	1.4330	.8434	40.10	0

Table VI is the basis for the following discussion. 3-Methyl-2-pentanol is the only alcohol obtained from *cis* or *trans* 2,3-epoxybutane and diethylmagnesium. There are four possible isomers: the *cis* should give one set of racemic forms while the *trans* yields the other set. The reference compound should be a mixture of the four isomers. The physical properties of the 3-methyl-2-pentanols check each other closely. The melting points and mixed melting points of their derivatives also tend to show that they are 3-methyl-2-pentanols.

3-Methyl-2-pentanol is obtained from ethylmagnesium bromide. All of the physical properties are very nearly identical with the exception of the boiling point of the alcohol produced from the *cis* form. In this case only 3.5 g. of the alcohol was obtained from the distillation at reduced pressure. This quantity was insufficient for an accurate determination of the boiling point.

The alcohols listed in Table VIII are identified entirely by their physical properties. All the alcohols which were isolated were tertiary derivatives, as shown by the zinc chloride–hydrochloric acid method.

It is evident from the data compiled in Table V that diethylmagnesium reacts with 2,3-dimethyl-2,3-epoxybutane to produce 2,3,3-trimethyl-2-pentanol. Ethylmagnesium bromide, on the other hand, forms 2,2,3-trimethyl-3-pentanol.

In the reaction of diethylmagnesium upon the unsymmetrical expoxyalkanes only one product was isolated. In every case there is a possibility of two products. The alcohol formed by the reaction is tertiary if possible, and secondary if there is a choice and tertiary is impossible.

Summary

1. Dialkylmagnesiums react with epoxyalkanes to form addition products which yield alcohols when hydrolyzed. These alcohols are the result of the splitting of the oxide linkage and not of rearrangement such as occurs with alkylmagnesium halides.

2. Diethylmagnesium reacts with 1,2-epoxypropane to give 2-pentanol, 1,2-epoxy-2-methylpropane to form 2-methyl-2-pentanol, *cis*-2,3-epoxybutane to produce a stereoisomeric mixture of 3-methyl-2-pentanols, *trans*-2,3-epoxybutane to yield a different racemic mixture of 3-methyl-2-pentanols, 2,3-epoxy-2-methylbutane to make 2,3-dimethyl-2-pentanol, and 2,3-dimethyl-2,3-epoxybutane to engender 2,3,3-trimethyl-2-pentanol.

3. When there is a difference between the two carbon valences holding the epoxy oxygen atom, the primary valence breaks rather than the secondary or tertiary and the secondary rather than the tertiary.

4. Ethylmagnesium bromide reacts with 2,3-dimethyl-2,3-epoxybutane to produce 2,2,3-trimethyl-3-pentanol.

5. Certain physical properties of ten alcohols have been determined.

6. A new alcohol, 2,3-dimethyl-2-pentanol, has been synthesized for the first time.

7. The synthesis of Bartlett and Berry, namely, the reaction of dialkylmagnesium upon an alpha epoxy compound has been extended to the epoxyalkanes and has been shown to be widely applicable as a method of synthesizing secondary and tertiary alcohols free from isomers.

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