flux temperature in a solution of 10 ml. of acetone, two drops of hydrochloric acid and enough water to make the solution turbid. Evaporation of the solvents left the product as white crystals. Recrystallization from an ether–petroleum ether mixture gave 0.55 g. (62%) of α-hydroxyheptaldehyde dimer, m.p. 120–122°.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.57; H, 10.84. Found: C, 64.09; H, 10.81.

Reaction of the Epoxyether XI with Organic Acids.—A solution of 4 g. (0.03 mole) of the epoxyether XI in 20 ml. of anhydrous ether was cooled in an ice-bath and 6 g. (0.03 mole) of 3,5-dinitrobenzoic acid added slowly. The reaction was allowed to stand overnight at room temperature. The ether solution was then quickly washed with 10% cold aqueous bicarbonate solution, dried with sodium sulfate and the ether removed with a water aspirator. The resulting solid was recrystallized from an ether–petroleum mixture to give 7.85 g. (79%) of white crystalline acylal, 1-methoxy-2-hydroxyheptyl 3,5-dinitrobenzoate (XIV), m.p. 86–87°.

Anal. Calcd. for $C_{15}H_{20}O_8N_2$: C, 50.56; *H*, 5.66. Found: C, 50.16; H, 5.60.

This pseudoester decomposed when heated above the melting point.

From 4 g. (0.03 mole) of epoxyether and 1.7 g. (0.03 mole) of acetic acid by a similar procedure was obtained 4.1 g. (73%) of the corresponding acylal, 1-methoxy-2-hydroxyheptyl acetate (XV), b.p. 73–77° (2 mm.), $n^{25}D$ 1.4282.

Anal. Calcd. for $C_{10}H_{10}O_4$: C, 58.79; H, 9.87; OCH_3, 15.2. Found: C, 58.23; H, 9.62; OCH_3, 14.8.

Acknowledgment.—The authors wish to thank Miss Phylis Tocco and Mr. Michael Papo for the microanalyses.

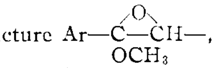
DETROIT 1, MICHIGAN

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE UNIVERSITY]

Epoxyethers. VIII. The Reaction of Epoxyethers with Grignard Reagents

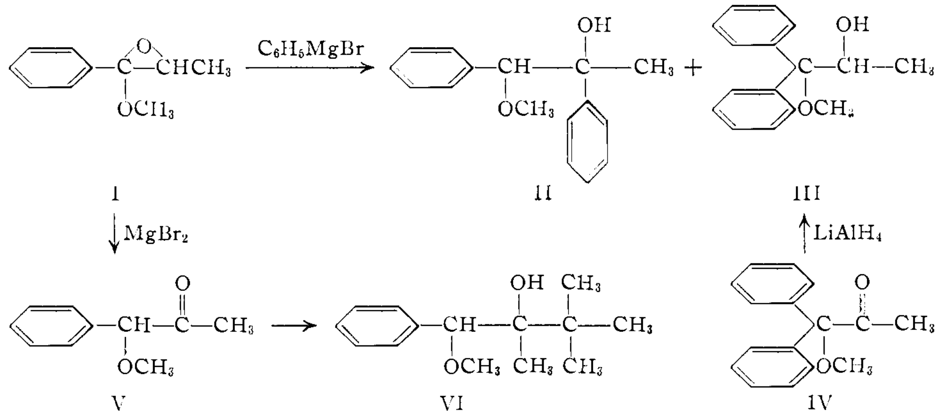
BY CALVIN L. STEVENS, MILTON L. WEINER[1] AND CARL T. LENK[2]

RECEIVED DECEMBER 8, 1953

The reaction of a Grignard reagent with certain epoxyethers, which have the characteristic structure  $\mathrm{Ar{-}\overset{\overset{O}{\diagup\;\;\diagdown}}{\underset{OCH_3}{C}{-}CH}{-}}$, has been shown to proceed to give two types of products. One product was a monomethyl ether of a substituted ethylene glycol that resulted from the attachment of the organic radical of the Grignard reagent to the carbon of the epoxide that contained the methoxyl group. The other product was an isomeric monomethyl ether of an ethylene glycol that resulted first from rearrangement of the epoxyether to the methoxyketone, Ar–$CHOCH_3$–CO–, followed by addition of the Grignard reagent to the carboxyl group of this ketone.

Ordinary 1,2-epoxides are known to undergo ring-opening reactions with Grignard reagents. These ethylene oxides react less readily than carbonyl compounds with the Grignard reagent, and in many instances the reaction must be heated above the reflux temperature of ether. The most important complication in this reaction is the rearrangement of the ethylene oxide prior to addition of the Grignard reagent.[3]

Epoxyethers have been shown in this investigation to react readily with Grignard reagents at the reflux temperature of ether or below, but in the examples studied the reactions are complicated by rearrangement of the epoxyether.



The epoxyether, 1-phenyl-1-methoxy-1,2-epoxypropane (I) reacted readily with phenylmagnesium bromide at room temperature to give 86% of a mixture of isomers from which a 24% yield of crystalline 1,2-diphenyl-1-methoxy-2-propanol (II) and a 42% yield of 1,1-diphenyl-1-methoxy-2-propanol (III) could be separated. The structure of III was proved by independent synthesis from 1,1-diphenyl-1-methoxy-2-propanone[4] (IV) by reduction with lithium aluminum hydride in 78% yield. The formation of III from the epoxyether and the Grignard reagent is comparable to the normal ring-opening reactions with ethylene oxides. In this instance the carbon of the epoxide that contains the methoxy group is most susceptible to attack by the nucleophilic reagent.

The structure of II was proved by synthesis from 1-methoxy-1-phenyl-2-propanone (V). V could be prepared by the alcoholysis of the corresponding

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(1) Atomic Energy Predoctoral Fellow, 1950–1952. Abstracted in part from the Doctoral thesis of M. L. Weiner, Wayne University, 1952.

(2) Parke, Davis and Company Fellow, 1951–1952.

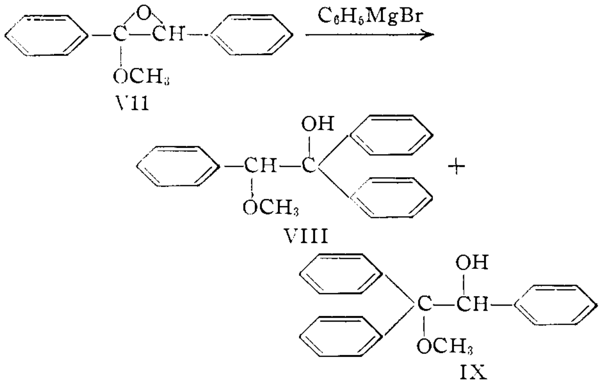
(3) Recently the literature concerned with the reaction of Grignard reagents with the oxirane ring has been exhaustively reviewed by N. G. Gaylord and E. I. Becker, *Chem. Revs.*, **49**, 113 (1951).

(4) The structure of IV has recently been proved in this Laboratory by synthesis from α-methoxydiphenylacetonitrile and methylmagnesium iodide and by alcoholysis of the corresponding bromoketone: C. L. Stevens and C. T. Lenk, *J. Org. Chem.*, in press.

bromoketone and when treated with phenylmagnesium bromide gave a 63% yield of II.[5]

The only reasonable route for the formation of II in the original reaction mixture involves rearrangement of the epoxyether I to V by the magnesium bromide of the Grignard reagent followed by conversion of V to II. The fact that the epoxyether I gave an 80% yield of the methoxyketone V when treated with an ethereal solution of magnesium bromide supports this view. Further, when the epoxyether was treated with a solution of diphenylmagnesium, only the normal product and none of II could be isolated.

When the epoxyether I was treated with a hindered Grignard reagent such as *t*-butylmagnesium chloride, only the product that resulted from rearrangement of the epoxyether followed by addition of the *t*-butylmagnesium chloride could be isolated. This product, 1-methoxy-2,3,3-trimethyl-1-phenyl-2-butanol (VI), was prepared independently by allowing the methoxyketone V to react with *t*-butylmagnesium chloride under the conditions of the initial reaction.



VII

VIII

IX

The epoxyether, 1,2-diphenyl-1-methoxyethylene oxide (VII), gave similar results when treated with Grignard reagents. VII reacted readily with phenylmagnesium bromide at room temperature and gave 63% of a crystalline mixture of isomers. The isomers were difficult to separate, but after repeated recrystallization 11% of pure 1,1,2-triphenyl-2-methoxyethanol (VIII) and 8% of pure 1,2,2-triphenyl-2-methoxyethanol (IX) could be isolated. The structure of IX was proved by independent synthesis from α,α-diphenyl-α-methoxyacetophenone (X). X was prepared from α-methoxydiphenylacetonitrile and phenylmagnesium bromide and when treated with lithium aluminum hydride gave IX in 69% yield. VIII could be prepared independently in 71% yield from the methyl ether of benzoin and phenylmagnesium bromide.

In this series, IX corresponds to the product formed from the epoxyether VII by normal opening of the epoxide ring with nucleophilic attack at the carbon atom bearing the methoxyl group. VIII results from rearrangement of the epoxyether[6] before addition. The rearrangement can be prevented by allowing the epoxyether VII to react with diphenylmagnesium, from which reaction pure IX can be isolated in 50% yield.

Experimental

Reaction of 1-Methoxy-1-phenyl-1,2-epoxypropane (I) **with Phenylmagnesium Bromide.**—A solution of 12.5 g. (0.076 mole) of the epoxyether[7] (I) in 30 ml. of dry ether was added slowly to the Grignard reagent prepared from 14.6 g. (0.093 mole) of bromobenzene, 2.2 g. (0.091 g. atom) of magnesium and 60 ml. of dry ether. The reaction mixture was stirred vigorously for three hours and then hydrolyzed with a saturated ammonium chloride solution. The ethereal layer was washed with water, dried and the ether evaporated. The residual oil was distilled to give 15.7 g. (86%) of a mixture of isomers, b.p. 128–136° (0.8 mm.). After the distillate had remained at room temperature overnight, partial solidification occurred. The solid was separated and recrystallized from petroleum ether to give 4.4 g. (24%) of 1,2-diphenyl-1-methoxy-2-propanol (II), m.p. 66–68°.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.44. Found: C, 79.01; H, 7.65.

The mother liquor gave no further solids and was distilled to yield 7.7 g. (42%) of 1,1-diphenyl-1-methoxy-2-propanol (III), b.p. 127–131° (0.7 mm.), $n^{31}\text{D}$ 1.5721.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.44. Found: C, 79.19; H, 7.52.

The benzoate derivative of III was prepared in 50% yield using benzoyl chloride and pyridine. The melting point was 104–106°.

Anal. Calcd. for $C_{23}H_{22}O_3$: C, 79.77; H, 6.36; CH_3O, 8.96. Found: C, 80.00; H, 6.50; CH_3O, 8.93.

In another experiment the Grignard reagent was prepared by 33.0 g. (0.21 mole) of bromobenzene and 5.3 g. (0.22 g. atom) of magnesium in 200 ml. of dry ether. A mixture of 80 ml. of purified dioxane and 50 ml. of dry ether was slowly added while the solution was heated to the reflux temperature. The mixture was stirred and heated for one-half hour and then allowed to cool to room temperature, after which 18.5 g. (0.113 mole) of epoxyether (I) in 50 ml. of dry ether was added. The mixture was then stirred and heated to the reflux temperature for one hour, after which the isolation procedure described above was used. After a low-boiling fraction of 1.85 g. was removed by distillation, 22.6 g. (83%) of III was collected, b.p. 122–126° (0.7 mm.), $n^{31}\text{D}$ 1.5714.

A mixture of 0.0248 g. of II, m.p. 66–68°, and 0.1640 g. of pure III, $n^{31}\text{D}$ 1.5743 (made by independent synthesis), corresponded to the percentage composition of 13.1% II, and 86.9% III, and was found to have $n^{31}\text{D}$ 1.5723.

Assuming that a change in the composition of the binary system II–III will cause the refractive index to change in a linear fashion, and that the III isolated above is contaminated only with II, the $n^{31}\text{D}$ value of 1.5714 corresponds to a mixture of 80.4% III and 19.6% II.

Rearrangement of the Epoxyether I.—Anhydrous magnesium bromide was prepared by the action of magnesium on propylene bromide. To a solution of 16.5 g. (0.09 mole) of anhydrous magnesium bromide in 150 ml. of anhydrous ether was added 15 g. (0.09 mole) of epoxyether I in 50 ml. of ether. After 15 minutes at the reflux temperature a thick brown insoluble paste formed, the character of which changed very little during 5.5 hours at the reflux temperature. After 23 g. (0.26 mole) of dioxane was added the character of the precipitate changed to a white granular solid. After the mixture had been heated to reflux overnight, the solid was filtered and the filtrate distilled to give 12 g. (80%) of 1-phenyl-1-methoxy-2-propanone (V)[8] b.p. 82–84° (0.8 mm.), $n^{25}\text{D}$ 1.5050. A semicarbazone de-

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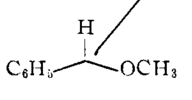
[5] According to the rules proposed by Curtin (THIS JOURNAL, **74**, 2901 (1952)) and Cram (*ibid.*, **74**, 5828 (1952)) II should have the following diastereomeric formula



[6] The rearrangement of this epoxyether in an ethereal solution of magnesium bromide has been reported previously in *ibid.*, **75**, 3977 (1953).

[7] C. L. Stevens, W. Malik and R. Pratt, *ibid.*, **72**, 4758 (1950).

[8] K. v. Auwers, H. Ludewig and A. Müller, *Ann.*, **526**, 143 (1936).

rivative,[8] m.p. 154–156°, was prepared in 52% yield. Recrystallization raised the melting point to 159–160°. The derivative contained 13.9% methoxy (calcd. 14.0).

The methoxyketone V was prepared independently by alcoholysis of 1-bromo-1-phenyl-2-propanone[9] with a large excess of methyl alcohol and three equivalents of calcium carbonate at the reflux temperature for 30 days, b.p. 68–69° (1 mm.), $n^{25}\mathrm{D}$ 1.5055. A semicarbazone, m.p. 154–156°, did not depress the melting point of the derivative prepared from V from the rearrangement of the epoxyether.

The semicarbazone of α-methoxypropiophenone,[7] which melted at 161–162°, caused a large depression of melting point when mixed with the semicarbazone of V.

1,2-Diphenyl-1-methoxy-2-propanol (II).—An ethereal solution of 4.65 g. (0.028 mole) of V was added slowly to a slight excess of phenylmagnesium bromide. After the usual isolation procedure, 4.25 g. (63%) of II, m.p. 67–70°, was obtained. The mixture melting point with II from the epoxyether was not depressed.

1,1-Diphenyl-1-methoxy-2-propanol (III).—An ethereal solution of 13.8 g. (0.057 mole) of 1,1-diphenyl-1-methoxy-2-propanone[4] (IV) was slowly added to a suspension of 1.14 g. (0.03 mole) of lithium aluminum hydride in ether and the mixture stirred and heated at the reflux temperature for six hours. After the reaction had been hydrolyzed with 5% hydrochloric acid, the ether layer was washed, dried and the ether evaporated. Distillation gave 3.7 g. of forerun, b.p. 134–138°, and 7.0 g. of 1,1-diphenyl-1-methoxy-2-propanol, b.p. 138–139° (1 mm.), $n^{31}\mathrm{D}$ 1.5743. The total yield of III was 78%.

Anal. Calcd. for $C_{16}H_{18}O_2$: C, 79.34; H, 7.44. Found: C, 79.13; H, 7.48.

A benzoate derivative, m.p. 104–106°, was prepared in 66% yield and was identical with the benzoate of III obtained from the epoxyether I as determined by mixture melting point determination.

Reaction of the Epoxyether I with *t*-Butylmagnesium Chloride.—An ethereal solution of the Grignard reagent was prepared from 2.43 g. (0.1 g. atom) of magnesium and 9.26 g. (0.1 mole) of *t*-butyl chloride. The solution was cooled to 0° and 8.2 g. (0.05 mole) of the epoxyether I slowly added. After 15 minutes of 0°, 30 minutes at 25° and 15 minutes at the reflux temperature, the reaction was hydrolyzed with saturated ammonium chloride solution. The ether layer was decanted, dried and the ether removed. The residue, 9.7 g., was dissolved in petroleum ether and cooled to −60°, at which temperature 1 g. of product crystallized, m.p. 40–43°. The remainder was distilled to give a fraction, 2.0 g., b.p. 58–68° (0.5 mm.), $n^{25}\mathrm{D}$ 1.5058. This fraction was composed mostly of V since the semicarbazone of V could be prepared in 50% yield.

The second fraction, 2.65 g., b.p. 68–77° (0.5 mm.), solidified. After this material was dissolved in petroleum ether and the solution cooled to −80°, 1.8 g. of crystalline material was obtained. The total yield of solid was 35%. Recrystallization from a mixture of methanol and water gave pure 1-methoxy-2,3,3-trimethyl-1-phenyl-2-butanol (VI), m.p. 48.5–49°.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97; CH_3O, 14.0. Found: C, 75.90; H, 9.95; CH_3O, 14.2.

VI also was prepared from 6.1 g. (0.037 mole) of V and 0.07 mole of *t*-butylmagnesium chloride by the same procedure as used for the epoxyether. Distillation gave a forerun of 0.9 g., b.p. 68–84° (1 mm.), $n^{25}\mathrm{D}$ 1.5058, and then 3.7 g. (45%) of VI, b.p. 84–89° (1 mm.), which solidified. Recrystallization of this fraction gave 2.75 g. of pure VI, m.p. 47–48°. A mixture melting point with VI from the epoxyether was not depressed.

Reaction of 1,2-Diphenyl-1-methoxyethylene Oxide (VII) with Phenylmagnesium Bromide.—A solution of 4.7 g. of the epoxyether[10] VII, m.p. 56–58°, in 30 ml. of dry ether was added to an ethereal solution of phenylmagnesium bromide made from 3.6 g. (0.023 mole) of bromobenzene and 0.55 g. (0.023 g. atom) of magnesium. Heavy salt formation occurred during addition of the last 10% of the epoxyether. After the reaction was stirred for an additional one-half hour, hydrolysis was effected with 5% hydrochloric acid solution. The ether layer was washed, dried and the ether evaporated. Heptane (10 ml.) was added to the residual oil and crystallization was induced. The crude solid mixture of isomers was filtered and amounted to 4.0 g. (63%). Recrystallization of the solid from heptane gave 2 g. of material, m.p. 112–119°. The filtrate from this solid gave 1.5 g. of material, m.p. 81–85°, after concentration.

Repeated recrystallization of the former material gave 0.7 g. (11%) of 1,1,2-triphenyl-2-methoxyethanol (VIII), m.p. 138.5–139.5°.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.57; H, 6.58. Found: C, 82.78; H, 6.91.

Repeated recrystallization of the lower melting component from a mixture of benzene and petroleum ether gave 0.50 g. (8%) of 1,2,2-triphenyl-2-methoxyethanol (IX), m.p. 84.5–86.5°.

Anal. Calcd. for $C_{21}H_{20}O_2$: C, 82.57; H, 6.58. Found: C, 82.62; H, 6.70.

In another experiment, 30 ml. of purified dioxane in dry ether was slowly added to an ethereal solution of phenylmagnesium bromide (from 0.075 mole of bromobenzene) which had been heated to the reflux temperature. After the addition, the mixture was heated an additional hour and then cooled. A solution of 6.3 g. (0.028 mole) of the epoxyether VII in dry ether was then added and the stirring continued for one-half hour. From the same isolation procedure described above was isolated 4.25 g. (50%) of IX, m.p. 83–85°. A mixture melting point with authentic IX was not depressed. None of the more insoluble isomer VIII was found in this experiment.

1,1,2-Triphenyl-2-methoxyethanol (VIII).—Phenylmagnesium bromide was made from 4.86 g. (0.031 mole) of bromobenzene and allowed to react with 6.40 g. (0.028 mole) of the methyl ether of benzoin. After hydrolysis and evaporation of the ether from the ether layer, the residue solidified and amounted to 6.6 g. Recrystallization from a benzene–heptane mixture gave 6.1 g. (71%) of VIII, m.p. 138.5–139.5°. A mixture melting point with VIII obtained from the epoxyether was not depressed.

1,2,2-Triphenyl-2-methoxyethanol (IX).—α-Methoxydiphenylacetonitrile, m.p. 52–53.5°, was prepared from diphenylacetonitrile by chlorination with phosphorus chloride to give α-chlorodiphenylacetonitrile and then alcoholysis of the chloronitrile to the methoxynitrile.[11]

A solution of 13.0 g. (0.058 mole) of α-methoxydiphenylacetonitrile in 40 ml. of ether was added to an ethereal solution of phenylmagnesium bromide made from 11.6 g. (0.074 mole) of bromobenzene. The mixture was stirred and heated to the reflux temperature for 18 hours, after which time 100 ml. of 20% hydrochloric acid was added and the mixture stirred an additional three hours. The ether layer was separated and the aqueous layer stirred an additional 20 hours and then extracted with ether. The combined ether extracts were washed with water, dried and the ether solution concentrated to give an oil which slowly crystallized. The solid was recrystallized from a methylcyclohexane–petroleum ether mixture to give 4.6 g. (26%) of α,α-diphenyl-α-methoxyacetophenone[12] (X), m.p. 90–92°.

X was reduced with lithium aluminum hydride following the procedure described for the reduction of IV. From 4.6 g. of X was obtained 3.2 g. (69%) of 1,2,2-triphenyl-2-methoxyethanol (IX), m.p. 85–87°. A mixture melting point with IX from the epoxyether showed no depression.

DETROIT 1, MICHIGAN

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[9] E. M. Schultz and S. Mickey, *Org. Syntheses*, **29**, 38 (1949).

[10] C. L. Stevens, M. L. Weiner and R. C. Freeman, THIS JOURNAL, **75**, 3977 (1953).

[11] This procedure is described in the article given in ref. 4.

[12] The melting point of X was not depressed when mixed with the α,α-diphenyl-α-methoxyacetophenone made previously in this Laboratory by alcoholysis of the corresponding chloroketone or bromoketone, or by rearrangement of the epoxyether, 1,2,2-triphenyl-1-methoxyethylene oxide (THIS JOURNAL, **76**, 718 (1954)). This independent synthesis further confirms the structure of X and the latter three compounds.