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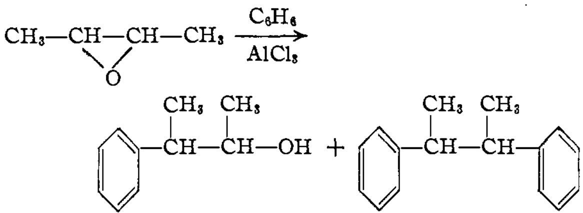
The Friedel-Crafts Reaction with Disubstituted Ethylene Oxides. I. Butylene and Isobutylene Oxides

BY WILLARD T. SOMERVILLE AND PAUL E. SPOERRI

Although the products of the Friedel-Crafts reaction with ethylene oxide and its mono substituted products have been described,[1] the nature of the products obtained from disubstituted oxides has not been characterized.[2] The reaction of 2,3-butylene oxide and isobutylene oxide with benzene in the presence of aluminum chloride has been investigated in order to determine the nature of the products formed, and elucidate the mechanism of the reaction.

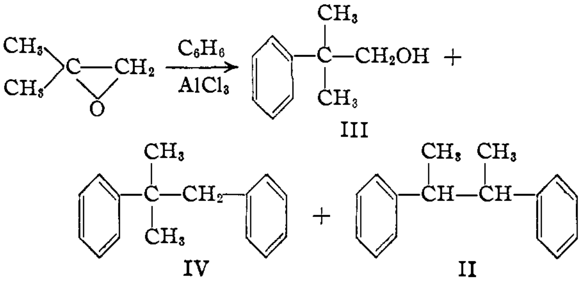
Although the yield of products is small with disubstituted oxides, it has been shown to be advisable, in the case of ethylene oxide, to employ twice the theoretical quantity of anydrous aluminum chloride and to operate with a large excess of benzene,[1] in order to obtain a maximum yield of product. A twenty-fold excess of benzene and the use of twice the theoretical quantity of aluminum chloride represses secondary reactions. The reaction apparently takes place on the surface of the aluminum chloride. 2,3-Butylene oxide reacts under the above conditions to form the previously unreported 3-phenyl-2-butanol (I) and *meso*-2,3-diphenylbutane (II).



I II

The 3-phenyl-2-butanol was oxidized with dichromate-sulfuric acid mixture to 3-phenylbutanone. The semicarbazone was shown to be identical with that derived from a synthetic sample. A mixed melting point of the solid hydrocarbon with an authentic specimen of *meso*-2,3-diphenylbutane showed their identity.

Theoretically, isobutylene oxide may react in two ways to produce 2-methyl-2-phenylpropanol (neophyl alcohol) or dimethylbenzylcarbinol, depending on the position of rupture of the oxide ring. Under the experimental conditions only the more stable neophyl alcohol (III) could be identified in the alcoholic portion of the reactants. The hydrocarbon fraction of the reactants was a mixture of α,α-dimethyldibenzyl IV together with *meso*-2,3-diphenylbutane, this latter product being formed by a rearrangement.

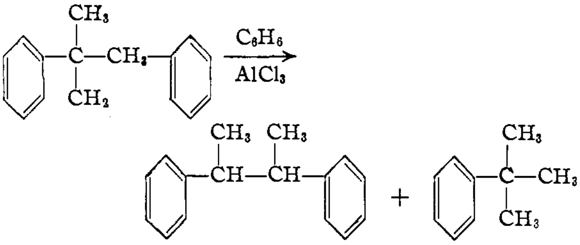


III

IV II

In this connection, it is interesting to note that a small amount of solid by-product was observed by Bodroux[3] in the products from the reaction of isobutylene dibromide with aluminum chloride and benzene. A repetition of this reaction has shown that this by-product is *meso*-2,3-diphenylbutane.

In order to determine at which step the formation of *meso*-2,3-diphenylbutane occurs in the Friedel-Crafts reaction with isobutylene oxide, pure α,α-dimethyldibenzyl was treated with benzene and aluminum chloride under the same experimental conditions. The α,α-dimethyldibenzyl was found to be partially rearranged to the more symmetrical *meso*-2,3-diphenylbutane. *t*-Butylbenzene was also isolated from the products of the reaction, indicating that rearrangement may occur through cleavage of the α,α-dimethyldibenzyl molecule. The tertiary alcohol, dimethylbenzylcarbinol, which would possibly be formed as one of the reaction products of isobutylene oxide could not be expected to survive in the presence of a strong Lewis acid such as aluminum chloride. This was demonstrated when dimethylbenzylcarbinol was allowed to react with aluminum chloride in benzene solution. The products consisted of a mixture of the expected α,α-dimethyldibenzyl together with the rearranged product *meso*-2,3-diphenylbutane. No unreacted carbinol was recovered.



Experimental Part

2,3-Butylene Chlorohydrin.—2,3-Butylene chlorohydrin was prepared by saturating 2,3-butanediol with anhy-

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(1) Theimer, U. S. Patent 2,047,396 (1936), and Abstracts A. C. S. Meeting, N. Y., 1935.

(2) Theimer, Abstracts 99th Meeting of A. C. S., Cincinnati, April, 1940.

(3) Bodroux, *Compt. rend.*, **132**, 1333 (1901).

drous hydrogen chloride. In a typical run, 2850 g. (*ca.* 41 moles) of 2,3-butanediol (b. p. 180–182°) contained in a three-necked flask fitted with an efficient condenser was vigorously stirred while anhydrous hydrogen chloride was bubbled in as rapidly as possible. The liquid temperature was kept at 80–90° until absorption ceased. The increase in weight amounted to approximately 1000 g. The crude mixture was distilled through an 18-inch packed column to yield 2865 g. of crude product, containing water, b. p. 95–102° and 130–137° (uncor.) containing 58.5% chlorohydrin by analysis and corresponding to a yield of 37.5%. The crude chlorohydrin was used as is for conversion to the oxide. The chlorohydrin boiling at 102° (763 mm.) was found to consist of an azeotrope containing 92% chlorohydrin; d^{20}_{15} 1.0937, $n^{20}\mathrm{D}$ 1.4290.

2,3-Butylene Oxide.—A yield of 88% of theory of mixed *cis* and *trans* oxides was obtained from the chlorohydrin,[4] having the physical constants: b. p. 57–59° (750 mm.), $n^{20}\mathrm{D}$ 1.3774.

Isobutylene Chlorohydrin.—Isobutylene chlorohydrin was prepared by the method[5] of Burgin, *et al.*, in a yield of 59% (63–66% reported).

Isobutylene Oxide.—Isobutylene oxide was prepared as indicated above for 2,3-butylene oxide; b. p. 57–58°; $n^{20}\mathrm{D}$ 1.3894; yield 76%.

Friedel–Crafts Reaction with Butylene Oxides.—The reactions were carried out in a three-necked flask fitted with a stirrer, condenser and drying tube, separatory funnel and thermometer. One mole of the oxide dissolved in 10 moles of dry benzene was slowly added during a two and one-half hour period to a vigorously agitated suspension of two moles of anhydrous aluminum chloride in 10 moles of benzene maintained at 10–12°. The reaction mixture was stirred for another fifteen-minute period after the addition was complete and was then decomposed by pouring onto a mixture of ice and water. The benzene layer was separated and washed free of acid. Unreacted benzene was removed by distillation at 50 mm. pressure followed by distillation of the reaction products at 2–3 mm. After a small forerun of chlorohydrin, the fractions boiling between *ca.* 65–85° (2–3 mm.) were examined for alcohols and the fractions b. p. *ca.* 100–125° (2–3 mm.) examined for hydrocarbons.

Isolation of 3-Phenyl-2-butanol.—Ninety-seven grams of the alcohol containing fractions (b. p. 69–79° (2 mm.)) obtained from 397 g. of 2,3-butylene oxide was carefully fractionated through a semi-micro still employing a 25 cm. Vigreux type column and reflux regulator. The fraction b. p. 73° (2 mm.) amounting to 23 g. was taken as pure alcohol. It had a refractive index of $n^{20}\mathrm{D}$ 1.5180; yield 3.0%. The phenylurethan was oily and for identification 0.9 g. was oxidized[6] to the ketone and the semicarbazone prepared. It had a m. p. 173–174°; a mixed melting point with an authentic specimen[7] showed no depression.

Anal. Calcd. for $C_{10}H_{14}O$: C, 79.80; H, 9.27. Found: C, 79.87; H, 9.27.

Isolation of 2,3-Diphenylbutane.—The hydrocarbon containing fractions (56 g.) were chilled to 0–5° for several hours and then filtered by suction. The crude crystalline material was washed with cold methanol and then recrystallized from the minimum amount of a boiling mixture of 3 parts methanol and one part benzene. The yield of white crystalline material after recrystallization was 40 g. (3.4%). It melted at 126°. It gave no depression when a mixed melting point with an authentic specimen was taken.

Anal. Calcd. for $C_{14}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.25; H, 8.58.

2-Methyl-2-phenylpropanol (Neophyl Alcohol).—The alcoholic fractions (63 g.) obtained from 392 g. of isobutylene oxide were carefully fractionated through the semi-micro fractionating column to obtain 8 g. of pure product b. p. 77° (3 mm.); $n^{20}\mathrm{D}$ 1.5224; α-naphthylurethan m. p. 91–92°; mixed melting point with an authentic specimen[8] gave no depression.

Hydrocarbon Fractions from Isobutylene Oxide Condensation. (a) **Separation of *meso*-2,3-Diphenylbutane.**—Ninety-six grams of the hydrocarbon fraction from 392 g. of isobutylene oxide was chilled to 0–5° and filtered by suction to remove the solid hydrocarbon. This was washed with cold methanol and recrystallized from a methanol–benzene mixture to constant melting point, m. p. 126°; mixed melting point with an authentic specimen of *meso*-2,3-diphenylbutane, 126°; yield 10 g. (1%).

Anal. Calcd. for $C_{14}H_{18}$: C, 91.37; H, 8.63. Found: C, 91.38; H, 8.86, 8.61.

(b) **Isolation of α,α-Dimethyldibenzyl.**—The filtrate from above was carefully fractionated through a 25 cm. column packed with small berl saddles. In this manner 50 g. of hydrocarbon was obtained (4%); b. p. 116° (2 mm.); $n^{20}\mathrm{D}$ 1.5589; d_{20} 0.9818.

Isobutylene Dibromide.—Isobutylene dibromide was prepared by the bromination of *t*-butanol.[9] It was found advantageous to keep the reaction mixture at 70–75° with external cooling. Its physical constants were b. p. 60–62° (45 mm.); d^{20}_{4} 1.7503; $n^{20}\mathrm{D}$ 1.5068; yield 64.8%.

α,α-Dimethyldibenzyl.—An attempt to prepare this compound from neophylmagnesium chloride and bromobenzene was not successful. It was prepared by a modification of the method of Bodroux.[3] For the condensation, 540 g. (2.5 moles) of isobutylene dibromide dissolved in 500 g. of benzene (6.4 moles) was added to a vigorously stirred mixture of 34 g. of anhydrous aluminum chloride (0.25 mole) and 1000 g. (12.8 moles) of benzene at 10–12°. It was stirred for three hours at this temperature until the evolution of hydrogen bromide ceased. The orange-red reaction mixture was decomposed by pouring on ice; the oily layer washed neutral and vacuum distilled through a 20-cm. packed column giving 292 g. of distillate boiling at 118–119° (3 mm.) and containing a crystalline solid. The solid was separated by chilling and filtration (30 g. crude) and recrystallized from methanol–benzene mixture to give 10.5 g. (2% yield) of crystalline hydrocarbon m. p. 127–128° (cor.). A mixed melting point with an authentic specimen of *meso*-2,3-diphenylbutane gave no depression, indicating a rearrangement had occurred. Redistillation of the liquid portion gave 232 g. (44%) of α,α-dimethyldibenzyl. Its physical constants are b. p. 114° (1 mm.); $n^{20}\mathrm{D}$ 1.5584 and d^{20}_{4} 0.9801.

Rearrangement of α,α-Dimethyldibenzyl.—One hundred grams (0.48 mole) of α,α-dimethyldibenzyl dissolved in 500 g. of benzene was added slowly over a two-hour period to a vigorously stirred suspension of 133 g. (1 mole) of aluminum chloride in 1000 g. of dry benzene at 10°. The mixture was stirred for an additional thirty minutes after the addition was completed before decomposing, washing and distilling. After a forerun of tertiary butylbenzene, the main portion of the distillate consisted of 59 g. of recovered hydrocarbons together with 11 g. of residue. The partly crystalline main portion was chilled and filtered cold to yield 3.0 g. of colorless crystalline hydrocarbon (after washing with methanol). This material after recrystallization showed no depression in melting point when mixed with an authentic specimen of *meso*-2,3-diphenylbutane. The liquid portion of the distillate consisted of 52 g. of recovered α,α-dimethyldibenzyl. The forerun was shown to consist of *t*-butylbenzene; melting point of diacetylamino derivative 212° (cor.); a mixed melting point with an authentic specimen showed no depression.[10]

Friedel–Crafts Reaction with Dimethylbenzylcarbinol.—Three moles (450 g.) of pure dimethylbenzylcarbinol dissolved in 30 moles of benzene was added during a two-hour

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(4) Norton and Haas, THIS JOURNAL, **58**, 2147 (1936); Wilson and Lucas, *ibid.*, **58**, 2396 (1936).

(5) Burgin, Hearne and Rust, *Ind. Eng. Chem.*, **33**, 385 (1941).

(6) "Organic Synthesis," John Wiley and Sons, Inc., New York, N. Y., 1941, Coll. Vol. I, second ed. p. 340.

(7) Darzens, *Compt. rend.*, **141**, 768 (1905).

(8) Whitmore, Weisgerber and Shabica, THIS JOURNAL, **65**, 1469 (1943).

(9) Evers, *et al.*, *ibid.*, **55**, 1136 (1933).

(10) Ipatieff and Schmeiling, *ibid.*, **59**, 1056 (1937).

period to 6 moles of aluminum chloride suspended in 30 moles benzene at 10°. After addition was completed, the mixture was stirred for an additional half-hour and then worked up in the normal manner. Distillation gave a main fraction of semi-solid hydrocarbons boiling at 115–135° (3 mm.), and amounting to 198 g. with 132 g. of residue. The solid hydrocarbon was separated in the usual manner, obtaining 36 g. of *meso*-2,3-diphenylbutane. The liquid portion (148.5 g.) was carefully refractionated obtaining 108 g. of pure α,α-dimethyldibenzyl.

Summary

1. The reaction of disubstituted ethylene oxides with aluminum chloride and benzene has been investigated.

2. The reaction with isobutylene oxide has been shown to yield neophyl alcohol together with two hydrocarbons, α,α-dimethyldibenzyl and *meso*-2,3-diphenylbutane, one the product of a rearrangement.

3. Both α,α-dimethyldibenzyl and dimethylbenzylcarbinol yield *meso*-2,3-diphenylbutane as the rearrangement product upon treatment with aluminum chloride and benzene.

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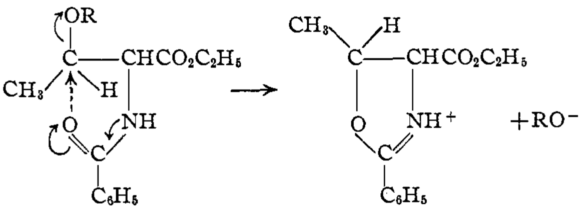
Ring Closure of the 2-Benzoylaminocyclohexanols. The Mechanism of Oxazoline Formation

BY WILLIAM S. JOHNSON AND ELLIOT N. SCHUBERT

In their recent studies on the interconversion of threonine and *allo*threonine *via* the oxazolines both Attenburrow, Elliott and Penny,[1] and Pfister, Robinson, Shabica and Tishler[2] have endorsed the mechanism suggested by Cornforth[3] which involves the postulation that the oxazoline ring is formed through a backside nucleophilic attack by the oxygen atom of the N-benzoyl group at the β-carbon atom with concomitant stereochemical inversion at this position and rupture of the β-C to O bond, *i. e.*



In our opinion this represents in essence a very reasonable *a priori* postulate particularly in view of the demonstration that the neighboring benzoylamino group can participate in nucleophilic displacements.[4] The cyclic intermediate postulated for such displacements is the oxazolinium ion, which in contrast with the oxygen analogs of Winstein, *et al.*,[4] would be expected to be quite stable. The isolation of the intermediary oxazoline III described in the present work, thus provides supporting evidence for the Winstein mechanism of participation of neighboring groups in such reactions. It occurred to us, moreover, that a convincing test of the inversion cyclization mechanism should evolve from a comparison of the behavior of the two stereoisomeric 2-aminocyclohexanols I and VI in these reactions, since the effect of the restricted rotation about the bond joining the two asymmetric carbon atoms, on the cyclization of the N-benzoyl derivatives should be to permit ring closure of the *trans*, but to inhibit cyclization of the *cis* form.

Both of the possible racemic 2-aminocyclohexanols are known; one melts at 68° and the other at 72°. The existing evidence, which is summarized and expanded by McCasland, Clark and Carter,[4] favors strongly the *trans* configuration (I) for the former and the *cis* (VI) for the latter. Of the two the *trans* isomer (I) is the more readily available, and for the present study was prepared by the ammonolysis of *trans*-2-chlorocyclohexanol.[5] When the crystalline N-benzoyl derivative (II) was treated with thionyl chloride and the resulting ether-insoluble hydrochloride (III) hydrolyzed with dilute hydrochloric acid according to the excellent procedure of Tishler, *et al.*,[2] the expected inversion product *cis*-2-aminocyclohexanol (VI) was isolated as the known hydrochloride, m. p. 187°, in about 19% over-all yield. When the thionyl chloride treatment was carried out at 52–54° instead of at room temperature, the yield of material of good quality was raised to 50%. This procedure thus constitutes the best method known to us for the preparation of the *cis* compound VI.[6] The intermediary oxazoline hydrochloride was not isolated in the pure form because on standing in air it was hydrolyzed to the *cis*-O-benzoyl derivative V.[7] However, if the oxazoline hydrochloride was immediately treated with dilute sodium hydroxide a crystalline base, m. p. 47°, was produced. Confirmation that

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[1] Attenburrow, Elliott and Penny, *J. Chem. Soc.*, 310 (1948).

[2] Pfister, Robinson, Shabica and Tishler, THIS JOURNAL, **71**, 1101 (1949).

[3] See footnote 1, p. 314, ref. 1.

[4] McCasland, Clark and Carter, THIS JOURNAL, **71**, 637 (1949); *cf.* Winstein and co-workers, *ibid.*, **70**, 812–846 (1948).

[5] Wilson and Read, *J. Chem. Soc.*, 1272 (1935).

[6] The method of McCasland, Clark and Carter ref. 4 gave the inverted N-benzoyl derivative in about 10% over-all yield, and the method described in Swiss Patent 194,642–5 [*Chem. Zentr.*, **108**, I, 2260 (1937)] involving the hydrogenation of 2-acetaminophenol gave *cis*-2-acetylaminocyclohexanol in 11% yield, ref. 4.

[7] *Cf.* the analogous behavior in the threonine series, ref. 1.