[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF TUFTS COLLEGE]

STUDIES IN OZONOLYSIS. III. CLEAVAGE OF ALKENE OZONIDES WITH LITHIUM ALUMINUM HYDRIDE

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Received February 28, 1955

The reductive cleavage of ozonides has been inferior to the oxidative decomposition of these substances so far as the yield of products is concerned. The most widely employed reductive procedure has been the use of zinc and acetic acid (1). Catalytic reduction which was originally introduced by Fischer, Düll, and Ertel (2) has been used less widely. Cook and Whitmore (3) decomposed ozonides with a large quantity of Raney nickel, but this procedure appears to have been rarely employed. More recently, two instances of the use of lithium aluminum hydride as a reducing agent for ozonides have appeared in the literature. Hinder and Stoll (4) treated the ozonide of an unsaturated tricyclic compound with the hydride and obtained the corresponding dialcohol. Witkop and Patrick (5) have reduced the ozonide of 2-phenylskatole with lithium aluminum hydride and obtained *o*-benzylaminophenylmethylcarbinol which was isolated as its dibenzoyl derivative. The above procedures rarely gave cleavage products in yields in excess of 70% of theory.

Some years ago a study of the ozonide-lithium aluminum hydride reaction was undertaken in this laboratory. This work showed that the reaction was a vigorous one, but with proper cooling and cautious admixture of the reactants the reaction could be satisfactorily controlled. The ozonide was cleaved at the original position of the carbon-carbon unsaturation of the alkene, and the reduction products were the corresponding alcohols which were obtained in excellent yield. An excess of hydride was used, and under these conditions one mole of the ozonide reacted with the equivalent of one mole of the hydride. During the reaction one mole of hydrogen was evolved per mole of ozonide. These facts can be expressed by the following equation,

$$\mathrm{RCHO_3CHR + LiAlH_4 \rightarrow LiAlO(OCH_2R)_2 + H_2}$$

By ozonation and treatment of the ozonide with lithium aluminum hydride, 3-octene has been converted to *n*-propyl and *n*-amyl alcohols in 87% yields. In the same way 2-heptene gave rise to an 89% yield of *n*-amyl alcohol. In this case ether extraction of the aqueous layer permitted the isolation of ethyl alcohol in an amount equal to 21% of theory. During the fractional distillation of the alcohols from 3-octene and 2-heptene difficulty was experienced in getting from the lower-boiling to the higher-boiling alcohol. Apparently, this was due to the association of the alcohols and resulted in a rather large intermediate fraction which decreased the yields of the individual alcohols. With 1-octene there was no evidence of methyl alcohol in the ether extract of the aqueous layer. *n*-Heptyl alcohol, however, was obtained in a yield of 93% of theory.

The reduction of alkene ozonides with lithium aluminum hydride is an excellent method for the reductive cleavage of these substances. The reaction appears to be a quantitative one, and the cleavage products can be isolated in nearly theoretical yields.

Acknowledgments. The author wishes to express his gratitude to the Welsbach Corporation of Philadelphia for financial assistance. Thanks are due Dr. A. C Cope for the use of the spinning-band column in his laboratory. I am also indebted to Sidney Cohen and Ernest Comeau who did the original experiments which showed that ozonides were reduced by lithium aluminum hydride.

EXPERIMENTAL

Ozonizer. The ozonizer used in these experiments has been described elsewhere (6). The voltage on the transformer primary was constant at 114. The flow of oxygen through the apparatus was kept constant at 11.6 liters per hour. Under these conditions the ozone concentration for different experiments varied from 1.6 to 2.0% (vol.) (419–487 mg. ozone per hour); however, during any one experiment the ozone concentration was checked every two or three hours and it remained constant.

Ozonation apparatus. The apparatus has been described previously (7).

Chemicals. n-Pentane was the solvent employed for all ozonations. The purification of the *n*-pentane (Phillips Petroleum Company, pure grade) has been described (7).

3-Octene was prepared by a Boord synthesis essentially as described by Wibaut and Gitsels (8). The 3-octene was distilled through an 18-plate, Fenske column; the material had b.p. 121.4°/770 mm. and n_D^{25} 1.4115.

The *1-octene* (Phillips Petroleum Company, pure grade) was distilled through an 18-plate, Fenske column and had b.p. 119.5°/756 mm. and n_D^{25} 1.4070.

The *2-heptene* (Phillips Petroleum Company, pure grade) was distilled through an 18-plate, Fenske column and had b.p. 98°/761 mm. and n_D^{25} 1.4039.

n-Propyl alcohol (Distillation Products) was distilled through the Fenske column; the material used had b.p. 97°/756 mm. and n_D^{25} 1.3839.

n-Amyl alcohol (Distillation Products) was distilled through the Fenske column; the material used had b.p. 136°/768 mm. and n_D^{25} 1.4085.

n-Heptyl alcohol (Distillation Products) was distilled through a spinning-band column; the material accepted had b.p. 72°/9 mm. and n_D^{25} 1.4230.

Lithium aluminum hydride (Metal Hydrides) was dissolved in anhydrous ether. Just before using, the solution was filtered under nitrogen pressure through a sintered glass disc, and the filtrate was standardized by evaporating a 10-ml. sample *in vacuo* and heating the residue *in vacuo* at 80° for 45 minutes. The gas evolved on addition of moist dioxane and then dilute sulfuric acid to the residue was measured.

Reaction of 3-octene ozonide with lithium aluminum hydride. The ozonide was prepared by passing ozonized oxygen (452 mg. ozone per hour) through a solution of 11.22 g. (100 mM.) of 3-octene in 150 ml. of purified *n*-pentane for 10.61 hours. At the conclusion of the ozonation dry nitrogen was passed through the solution for one hour at a rate of 11.6 liters per hour to remove dissolved oxygen. During the passage of the gases the temperature of the solution was −42 to −38°.

The solution of the ozonide was transferred to a one-liter three-necked flask which was immersed in an ice-salt bath and which had been thoroughly flushed with nitrogen. The flask was fitted with a mercury-seal stirrer, dropping-funnel, reflux condenser, thermometer, and gas collecting bottle which was filled with saturated calcium chloride solution. The addition of the lithium aluminum hydride solution (150 ml. of solution containing 149.4 mM. of hydride) was controlled such that the temperature of the reaction mixture did not rise above −10°; the addition required two hours. The addition of the hydride must be cautious for the reaction is vigorous. The reaction mixture was allowed to warm slowly and finally was refluxed for 15 minutes. No gas was evolved after the first few minutes of refluxing. The reaction mixture which was homogeneous was cooled to room temperature and allowed to stand overnight.

To remove ether and pentane from the gas which was evolved during the ozonide-hydride reaction, the gas was passed twice through a spiral condenser which was immersed in Dry Ice-alcohol. The gas had a volume of 3151 ml. (S. T. P.). This gas burned with a blue flame and was assumed to be hydrogen. The reaction mixture was initially at a temperature of −15°, and final equilibration of the reaction mixture with the gas evolved during the reaction occurred at room temperature (24°). In order to determine the amount of gas which was dissolved in the solvents, the proper amounts of *n*-pentane and dry ether were carried through the above reaction procedure in the same apparatus. The dissolved gas had a volume of 726 ml. (S. T. P.). Thus, the volume of gas evolved from the ozonide-hydride reaction was 2425 ml. or 108.3 mM.

During the decomposition of the reaction mixture with a solution of 20 ml. of concentrated sulfuric acid and 125 ml. of water, the temperature of the reaction mixture was not allowed to rise above −7°. The reaction mixture was warmed to room temperature. The gas which was evolved during the decomposition was led twice through the spiral condenser which was immersed in Dry Ice-alcohol. This gas burned with a blue flame and was assumed to be hydrogen. After subtracting the amount of nitrogen which was absorbed on cooling the reaction mixture, the gas evolved during the decomposition was equivalent to 43.9 mM. of lithium aluminum hydride. Thus 105.5 mM. of hydride underwent reaction with the 100 mM. of ozonide.

The layers of the reaction mixture were separated and the organic layer was extracted with two 10-ml. portions of water. The combined aqueous solutions were extracted with alcohol-free ether in a continuous extractor for 72 hours. The ether extract was combined with the original organic layer and the solution was dried with sodium sulfate. After standing overnight the sodium sulfate was removed and extracted several times with dry ether. The ether-pentane was removed from the combined ether solutions by distillation through the Fenske column until the pot temperature rose to 45°. The residue was transferred to a smaller flask and distilled through a spinning-band column.

The fractional distillation gave six fractions weighing 5.25 g. and having n_D^{25} 1.3818 to 1.3870. Of this 5.25 g. of material, 4.88 had n_D^{25} 1.3835. The 5.25 g. of material represented an 87.4% yield of *n*-propyl alcohol. Two intermediate fractions (0.44 g.) of n_D^{25} 1.3964 and 1.4041 were obtained. Finally, six fractions (7.67 g.) of n_D^{25} 1.4064 to 1.4082 were obtained. Of this 7.67 g. of material, 7.44 g. had n_D^{25} 1.4082. The 7.67 g. of material represented an 87.0% yield of *n*-amyl alcohol. A residue of 0.43 g. remained in the distilling flask. The identity of the *n*-propyl and *n*-amyl alcohols was verified by the preparation of α-naphthylurethans. Urethan of above-mentioned *n*-propyl alcohol, m.p. 78.7–79.0°; authentic urethan, m.p. 78.2–78.6°; mixture m.p. 78.2–78.8°. Urethan of above-mentioned *n*-amyl alcohol, m.p. 67.0–67.5°; authentic urethan, m.p. 65.7–66.2°; mixture m.p. 66.0–66.8°.

In order to check the distillation of the alcohols a mixture of 100 mM. of *n*-propyl alcohol and 100 mM. of *n*-amyl alcohol was distilled through the spinning-band column. A sizeable intermediate fraction (0.53 g.) could not be avoided in getting from the *n*-propyl alcohol to the *n*-amyl alcohol. The recovery of the alcohols was slightly better than in the case of the alcohols from the ozonide; 96% of the *n*-propyl alcohol and 90% of the amyl alcohol was recovered as good material.

The reaction of 3-octene ozonide with lithium aluminum hydride was carried out several times in order to establish the amount of gas evolved during the reaction and to establish the ozonide-hydride reaction ratio. For these experiments 50 mM. of 3-octene was used, and the procedure followed was the same as that described above, except that the alcohols were not isolated. Table I gives the results of these experiments.

Reaction of lithium aluminum hydride with ozonized n-pentane. Earlier work (7) had indicated that purified *n*-pentane is resistant to attack by ozone at −40°. To rule out any possibility of interference in the ozonide-hydride reaction by reaction of the hydride with ozonized *n*-pentane or with residual dissolved oxygen, the following experiment was carried

TABLE I

REACTION OF 3-OCTENE OZONIDE WITH $LiAlH_4$

Ozonide, mM.	Hydride Used, mM.	Temp. of Ozonide-Hydride Rx. Mixt., °C.	Gas Evolved During Reaction, mM.	Hydride Reacted with Ozonide, mM.
50.0	75.6	−10	51.3	52.3
50.0	76.0	−10	50.3	52.3
50.0	92.0	−30	51.8	53.2

out. Purified *n*-pentane (100 ml.) was cooled to −40° and ozonized oxygen (419 mg. ozone per hour) was led through the solution for 3.89 hours. Then nitrogen was passed through the solution for one hour at a rate of 11.6 liters per hour. The *n*-pentane was transferred to the apparatus for treatment with lithium aluminum hydride. The reaction flask had been cooled with a salt-ice bath; the temperature of the *n*-pentane was −14°. An ether solution of the hydride containing 22.0 mM. of hydride was added to the pentane. No gas was evolved and the temperature of the pentane did not rise. The unreacted hydride was decomposed as described above, and hydrogen equivalent to 23.6 mM. of hydride was liberated. The experiment shows that there is nothing in ozonized pentane which is reacting with the hydride.

Reaction of 2-heptene ozonide with lithium aluminum hydride. The experimental procedure was the same as that described for the reaction of the hydride with 3-octene ozonide. The ozonide was prepared by treatment of a solution of 9.82 g. (100 mM.) of 2-heptene in 150 ml. of purified *n*-pentane with ozonized oxygen (487 mg. ozone per hour) for 9.86 hours. The ozonide was treated with 125 ml. (pipet) of hydride-ether solution containing 146.0 mM. of lithium aluminum hydride. During the reaction 112.7 mM. of gas was evolved. This gas burned with a blue flame and was assumed to be hydrogen. Decomposition of the reaction mixture gave a volume of gas which was equivalent to 44.7 mM. of lithium aluminum hydride. Thus 101.3 mM. of hydride had reacted with the 100 mM. of ozonide.

The aqueous layer of the reaction mixture was extracted with alcohol-free ether in the continuous extractor for 91 hours.

Distillation of the reaction products through the spinning-band column gave three fractions (0.97 g.) of n_D^{25} 1.3640 to 1.3607 which were identified as ethyl alcohol. Commercial absolute ethyl alcohol had n_D^{25} 1.3600 and 95% ethyl alcohol had n_D^{25} 1.3620. The 0.97 g. of material corresponds to a 21.0% yield of ethyl alcohol. Four intermediate fractions (0.66 g.) of n_D^{25} 1.3689 to 1.4040 were obtained. The odor of *n*-amyl alcohol could be detected in the second of these intermediate fractions. Finally, five fractions (7.81 g.) of n_D^{25} 1.4060 to 1.4085 were obtained. These were identified as *n*-amyl alcohol and corresponded to a yield of 88.6% of amyl alcohol. The identity of the alcohols was verified by the preparation of α-naphthylurethans. Urethan of above-mentioned ethyl alcohol, m.p. 80.0–80.3°; authentic urethan, m.p. 80.0–80.3°; mixture m.p. 80.0–80.3°. Urethan of above-mentioned *n*-amyl alcohol, m.p. 66.2–66.7°; authentic urethan, m.p. 65.7–66.2°; mixture m.p. 66.0–66.3°.

Reaction of 1-octene ozonide with lithium aluminum hydride. The experimental procedure was the same as that described for the reaction of the hydride with 3-octene ozonide. The ozonide was prepared by treating a solution of 11.22 g. (100 mM.) of 1-octene in 150 ml. of purified *n*-pentane with ozonized oxygen (440 mg. ozone per hour) for 10.91 hours. The ozonide was treated with 150 ml. (pipet) of hydride-ether solution containing 147.2 mM. of lithium aluminum hydride. During the reaction 102.3 mM. of gas which was assumed to be hydrogen was evolved. Decomposition of the reaction mixture gave a volume of gas which was equivalent to 46.7 mM. of lithium aluminum hydride. Thus, 100.5 mM. of hydride reacted with the 100 mM. of ozonide.

The aqueous layer of the reaction mixture was extracted with alcohol-free ether in the continuous extractor for 92 hours.

Distillation of the reaction product through the spinning-band column gave no evidence of methyl alcohol. When it was clear that no methyl alcohol was present, the distillation was carried out at 12 mm. Five fractions (10.81 g.) of n_D^{25} 1.4214 to 1.4228 were obtained. This material was identified as *n*-heptyl alcohol and represented a yield of 93.0% of theory. The identity of the material as *n*-heptyl alcohol was verified by the preparation of the α-naphthylurethan. Urethan of the above-mentioned *n*-heptyl alcohol, m.p. 58.0–58.6°; authentic urethan, m.p. 58.3–58.9°; mixture m.p. 58.2–58.9°.

SUMMARY

Alkene ozonides react with lithium aluminum hydride in equimolar quantities to give the corresponding alcohols in excellent yields. During the reaction one mole of hydrogen per mole of ozonide is evolved.

3-Octene, 2-heptene and 1-octene have been found to yield *n*-propyl and *n*-amyl alcohols, *n*-amyl and ethyl alcohols, and *n*-heptyl alcohol, respectively.

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REFERENCES

(1) WHITMORE AND CHURCH, *J. Am. Chem. Soc.*, **54,** 3710 (1932); HENNE AND HILL, *J. Am. Chem. Soc.*, **65,** 752 (1943); HENNE and PERILSTEIN, *J. Am. Chem. Soc.*, **65,** 2183 (1943).

(2) FISCHER, DÜLL, AND ERTEL, *Ber.*, **65,** 1467 (1932).

(3) COOK AND WHITMORE, *J. Am. Chem. Soc.*, **63,** 3540 (1941).

(4) HINDER AND STOLL, *Helv. Chim. Acta*, **33,** 1308 (1950).

(5) WITKOP AND PATRICK, *J. Am. Chem. Soc.*, **74,** 3855 (1952).

(6) GREENWOOD, *Ind. Eng. Chem., Anal. Ed.*, **17,** 446 (1945).

(7) GREENWOOD AND WOLKOWICH, *J. Org. Chem.*, **17,** 1551 (1952).

(8) WIBAUT AND GITSELS, *Rec. trav. chim.*, **59,** 947 (1940).