

[CONTRIBUTION FROM THE NORTHERN REGIONAL RESEARCH LABORATORY¹]

The Ozonization of Methyl Oleate²

E. H. PRYDE, D. E. ANDERS, H. M. TEETER, AND J. C. COWAN

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The effect of solvent on the ozonization of methyl oleate and on the reductive decomposition of the ozonolysis products has been studied. The use of a reactive solvent such as methanol or acetic acid resulted in isolated product yields of 87%. Carbonyl yields before isolation of product were on the order of 90–92%. The use of a nonreactive solvent such as ethyl acetate or heptane resulted in low yield and impure products. The results are explained on the basis of the Criegee zwitterion mechanism for ozonization.

The ozonide of oleic acid and the cleavage products obtained by treatment with water azelaic semialdehyde, azelaic acid, pelargonaldehyde, and pelargonic acid were first described by Harries and Thieme.³ This original work was carried out without the use of solvent. Subsequently, hexane,⁴ chloroform,⁵ carbon tetrachloride,⁶ glacial acetic acid,^{7,8} ethyl chloride,⁹ ethyl acetate,¹⁰ and ethyl alcohol¹¹ have been used as solvents. The highest yields of isolated product (60% of pure or 75% of crude methyl azelaaldehyde) were obtained by ozonization in glacial acetic acid followed by reduction with zinc.⁸ Azelaic semialdehyde has been isolated in 80% yield as the semicarbazone by ozonization in ethyl chloride followed by catalytic hydrogenation in methanol.⁹ Sodium oleate has also been ozonized in aqueous solution, but the apparent yield of product, isolated as the oxime, was only 53%.¹²

Recent studies on the ozonization of various unsaturated compounds have shown not only methanol^{13–16} but also ethanol¹⁷ to be a superior

reaction medium. Methanol reacts to a considerable extent with ozone at -15° ,¹⁸ but in the presence of an unsaturated compound little reaction occurs between the ozone and methanol, and the products of such a reaction do not interfere in the analysis or isolation of carbonyl compounds.¹⁶

Application of methanol to the ozonization of methyl oleate in the present work resulted in a significant improvement in the yield of isolated carbonyl compounds. Thus, when chemical reduction with zinc and acetic acid was used, the total carbonyl yield as determined by the hydroxylamine hydrochloride method was 92%. The isolated yield of methyl azelaaldehyde with a two degree boiling range and purity of 92% was 88%. Redistillation gave a product of 96% purity. The hydroxylamine analyses were confirmed by gas chromatography.

Because methanol is not a satisfactory solvent for glycerides at ozonization temperatures, other solvents and solvent combinations were investigated. Furthermore, a solvent system was sought which would obviate the washing step required to remove the dissolved zinc salts. Methylene chloride and propionic acid were tried (Table I). Methylene chloride precipitated the zinc salts as they were formed, but an unsatisfactory yield was obtained. Reduction in propionic acid could not be carried out with zinc in the absence of water.

Catalytic hydrogenation was then investigated. Hydrogenation with 5% palladium on calcium carbonate to give an 80% yield of azelaic semialdehyde isolated as the semicarbazone has been reported.⁹ Hydrogenation was carried out in methanol after removal of the ethyl chloride used for the ozonolysis. Ethyl oleate ozonized and hydrogenated in ethyl acetate gave a 57% yield of the desired aldehydic products.¹⁰ A British patent describes the use of ethanol in the ozonization of oleic acid with subsequent hydrogenation in the same solvent, the product being isolated as the aldoxime.¹¹ No yield is stated.

The use of methanol as a common solvent for both ozonization and hydrogenation has been described in the preparation of adipaldehyde from

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(2) Presented in part before the Division of Organic Chemistry at the 136th meeting of the American Chemical Society at Atlantic City, N. J., September 16, 1959.

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(6) C. Harries, *Ber.*, **39**, 3728 (1906).

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TABLE I
 OZONIZATION OF METHYL OLEATE

| Solvent (Volume, %) | Ozone, % of Theory | | Tempera- ture of Reduction | Yield, % | | | Methyl Azela- alde- hydate Purity ^a |
|--|--------------------|----------------------|----------------------------------|--|-----------------------|--------------------------------------|--|
| | Con- sumed | Not Con- sumed | | Total Car- bonyl | Pelargon- aldehyde | Methyl- azela- alde- hydate | |
| A. Chemical Reduction (Zinc + Acetic Acid) | | | | | | | |
| Methanol | 101 | 1.6 | 30 to 35 | 92 | 77 | 88 | 92 |
| Methylene chloride | 105 | 1.7 | 30 to 35 | 72 | 75 | 76 | 87 |
| Methylene chloride | 132 | 1.0 | 30 to 35 | — | 72 | 66 ^b | — |
| Propionic acid | 124 | 2.1 | — | (No reduction occurred in absence of water) | | | |
| B. Catalytic Hydrogenation (10% Palladium on Charcoal) | | | | | | | |
| Methanol ^c | 115 | 3 | -10 to 0 | 78 | 83 ^d | 85 ^d | 84 |
| <i>n</i> -Butanol | 98 | 4.8 | <0 | 63 | — | — | — |
| Propionic acid | 113 | 4.7 | <8 | 81 | — | 44 ^b | — |
| Ethyl acetate | 107 | 3.0 | 25 | — | 70 | 87 | 75 |
| Ethyl acetate | 118 | 5.0 | 25 | — | — | 81 ^b | — |
| Ethyl acetate + 20% methanol | 110 | 4.4 | <13 | — | 69 ^e | 76 ^e | — |
| Ethyl acetate + 20% acetic acid | 114 | 4.0 | 25 | — | 76 | 83 ^f | 87 |
| Methyl acetate + 20% methanol | 105 | 2.7 | 20 | — | 82 ^d | 87 ^d | — |
| <i>n</i> -Heptane + 50% ethanol | 120 | 2.2 | >20 | 68 | — | 60 ^e | — |
| <i>n</i> -Heptane + 20% <i>t</i> -butanol | 141 | 4.4 | 50 | — | 60 | 67 ^b | — |

^a Purity determined by the hydroxylamine hydrochloride method. ^b An impure product was obtained, as indicated by the refractive index. ^c Average of seven runs. ^d Product was isolated as the dimethyl acetal. ^e Product was isolated as the diethyl acetal. ^f On basis of methyl oleate consumed in ozonization, calculated from methyl stearate recovered, yield was 93%.

cyclohexene.^{19,20} A yield of about 50% of the aldehyde was reported in this patented work.

When methanol was used as the common solvent for the ozonization and subsequent hydrogenation of methyl oleate, fair yields (78%) of carbonyl compounds were obtained (Table I). Hydrogenation was carried out at atmospheric pressure with 10% palladium on charcoal. Direct distillation of the reaction product, however, resulted in an apparent mixture of aldehyde and acetal compounds. Conversion of the carbonyl products to the dimethyl acetals resulted in the isolation by distillation of the acetal of pelargonaldehyde in 83% yield and of the acetal of methyl azelaaldehyde in 85% yield. Conversion to the acetal was accomplished by treatment with 2,2-dimethoxypropane in the presence of ammonium chloride. The purity of the product was 84%, as determined by the hydroxylamine method, although the refractive index ($n_D^{30} = 1.4301$) was close to that of a sample analyzing over 95% ($n_D^{30} = 1.4297$).

The use of catalytic hydrogenation in a number of other solvents was then investigated. The best results were obtained when methanol or acetic acid was used in combination with methyl or ethyl acetate. Here again, the use of an alcohol resulted in the formation of a mixture of aldehydes and acetals. However, conversion of the product to the acetals gave 82% yield of pelargonaldehyde dimethyl

acetal and 87% yield of methyl azelaaldehyde dimethyl acetal. Conversion to the acetals could be obviated by using acetic acid, which made possible the isolation of methyl azelaaldehyde in 83% yield by direct distillation. The purity of the product obtained by this method was 87% and redistillation was not effective in improving the purity. The refractive index of the product was not a criterion for purity, as was true for the acetal.

The following single solvents were tried but found to be unsatisfactory: *n*-butanol, propionic acid, and ethyl acetate. The solvent combinations 50% ethanol in heptane and 20% *t*-butanol in heptane were also found to be unsatisfactory. Note that the temperature at which hydrogenation could be carried out depended upon the solvent used (Table I). Hydrogenation in the alcohols or the acids, or combinations of these in ethyl acetate, readily occurred below room temperature. On the other hand, hydrogenation in ethyl acetate alone or in *n*-heptane with either ethanol or *t*-butanol present took place only above room temperature. The presence of peroxidic oxygen in the latter solvents could be detected only with potassium iodide in glacial acetic acid, whereas it could be readily detected in the other solvents by means of aqueous potassium iodide.

These differences in behavior are explained by the Criegee mechanism for ozonization.^{21,22} It is

(19) E. I. du Pont de Nemours and Co., Inc., Brit. Patent 709,450, May 26, 1954.

(20) E. E. Fisher, U. S. Patent 2,733,270 (to Du Pont), Jan. 31, 1956.

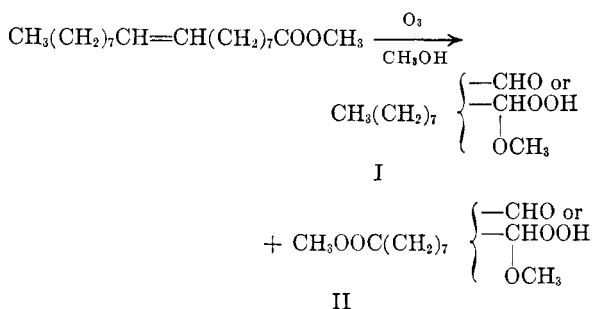
(21) P. S. Bailey, *Chem. Revs.*, **58**, 925 (1958).

(22) R. Criegee, G. Blust, and H. Zinke, *Ber.*, **87**, 766-768 (1954).

postulated that the addition of ozone to a double bond results in a primary ozonide which breaks down to a zwitterion and a carbonyl compound. The zwitterion may react in any one of several different ways: with itself to form a dimeric or polymeric peroxide, with a carbonyl compound to form an ozonide with the classical five-membered cyclic structure, with a compound having an active hydrogen; or it may undergo rearrangement. The zwitterion reacts with methanol to form a methoxy hydroperoxide,²³ and with glacial acetic acid to give a mixture of acetoxy hydroperoxides and polymeric peroxides.¹⁴

It is apparent that polymeric peroxides were formed in the solvents in which hydrogenation occurred only above room temperature, and that these entered into a number of side reactions which resulted in impure products and low yields. On the other hand, the alkoxy or acetoxy peroxides formed in the solvents in which hydrogenation occurred below room temperature resulted in high yields of pure products. The presence of ethanol or *t*-butanol apparently was not sufficient to prevent polymeric peroxide formation in heptane.

Since methoxy hydroperoxide compounds described in the literature appear to be unusually stable, the mixture of those which would be formed from methyl oleate according to the following equation was isolated:



Analyses for carbon, hydrogen, and methoxyl showed the resultant product to be a mixture of the methoxy hydroperoxides and the hemiacetals formed by reaction with an additional molecular amount of methanol. This material, when ignited, burned gently for several seconds before more vigorous oxidation occurred.

EXPERIMENTAL

Ozonization procedure. The reactor vessel consisted of a cylindrical flask with a $\frac{1}{2}$ 55/50 outer joint, which was attached to a reactor head containing fittings for a stirrer, a thermometer, a condenser, a dropping funnel, and a gas inlet, all passing through a $\frac{1}{2}$ 55/50 inner joint. Pure oxygen was passed through a 1 in. \times 3 ft. column packed with indicating Drierite²⁴ to remove traces of moisture, then into

(23) G. Lohaus, *Ann.*, **583**, 6 (1953).

(24) The mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.

a Welsbach Model T-23 laboratory ozonator.²⁴ The oxygen, containing 2–3% ozone, was passed through a gas dispersing bulb into the bottom of the reaction medium at a rate of from 1 to 2 l. of oxygen per min. The exit gases from the reactor were passed through a potassium iodide absorber, then a wet test meter. During the course of the reaction a small side-stream of the ozonized oxygen was also passed through a potassium iodide absorber, then through a wet test meter. Titration of the iodine liberated made it possible to calculate the rate of ozone produced in mmoles per liter of oxygen. By this means the total amount of ozone introduced to the system and also the amount absorbed by the system were calculated. Less than 1% of the ozone was not absorbed by the system until near the end point of the reaction.

Examples of the preferred procedures for both chemical reduction and catalytic hydrogenation follow.

Chemical reduction. Methyl oleate having an iodine value of 84.3 and a refractive index of 1.4481 (30.2°) was obtained from Applied Science Laboratories, State College, Pa.²⁴ No polyunsaturated compounds were detected by alkali isomerization, and no impurities were detected by gas chromatography. The methyl oleate (120.4 g., 0.40 g. mole of unsaturation) was dissolved in 1800 ml. of reagent grade methanol in a 2-l. round bottom reactor and cooled to –20°. Oxygen containing 1.092 mmoles of ozone per liter was passed through the solution at the rate of 1.94 l. per minute. At the end of 195 min., the potassium iodide solution at the exit of the reactor became strongly colored indicating that ozone was no longer being absorbed. The total amount of ozone consumed was 101% of theory, and 1.6% of theory was not absorbed in the reactor but was absorbed by the potassium iodide solution. Glacial acetic acid (150 ml.) was added, and the solution was warmed to 30°. Zinc dust was added, a small pinch at a time, until a total of 60 g. had been added, while maintaining the temperature at 30–35° with cooling. The mixture was filtered and distilled on a steam bath until about one half of the methanol had been removed. Methylene chloride (500 ml.) and water (500 ml.) were added, and the layers separated. The methylene chloride layer was washed with water (each wash was back-washed with a small amount of methylene chloride) until free of acid. It was then dried over anhydrous calcium sulfate. Analysis of this solution by the hydroxylamine hydrochloride method showed that a 92% yield of carbonyl products was obtained. It should be noted that the washing step should be carried out as soon as possible and as thoroughly as possible, otherwise varying amounts of the dimethyl acetal will form.

Methylene chloride was removed from the solution by distillation on the steam bath. The residue was distilled under vacuum through a small Vigreux column using a nitrogen capillary ebullator. There was obtained 43.9 g. of pelargonaldehyde boiling at 37–47° (0.35 mm.), n_D^{20} 1.4193 (lit., n_D 1.4245). An additional 2.27 g. was recovered from the solid carbon dioxide trap for a total yield of 81%. Methyl azelaaldehyde (65.3 g.) was obtained as a fraction boiling 94–96° (0.75 mm.) n_D^{20} 1.4348 (lit., n_D^{20} 1.4384) and purity of 92%. Redistillation of this fraction gave a product purity of 96%. Another fraction (4.87 g.) was obtained boiling at 96–120° (0.30 mm.) n_D^{20} 1.4349, and having a purity of 74.7%. The total yield of crude methyl azelaaldehyde was 94% or 85.4% of pure methyl azelaaldehyde.

The use of methylene chloride for the ozonization and reduction solvent (Table I) resulted in precipitation of the zinc salts. However, poor carbonyl yields and impure products were obtained, even with consumption of ozone at nearly the theoretical level. Reduction in propionic acid did not proceed until water was added. Since an extraction step would then be necessary, the experiment was not carried to completion.

Methyl azelaaldehyde has been reported to have a tendency to polymerize.⁸ However, it was found that after storage under nitrogen at 0° for 4 weeks, methyl azelaaldehyde

hydrate could be recovered quantitatively with no evidence of polymer formation.

Catalytic hydrogenation. Methyl oleate (15.0 g., 0.05 g. mole) having an iodine value of 84.8 and n_D 1.4481 (30.2°) was dissolved in 210 ml. of methyl acetate and 40 ml. of methanol. The ozonization was carried out as before. The amount of ozone consumed was 118% of the theoretical, and 2.9% of theory was found to have been absorbed by the potassium iodide solution. At the end of the ozonization the solution was purged with nitrogen, then hydrogen. The catalyst (0.1 g. of 10% palladium on charcoal) was dispersed in a small amount of methyl acetate and added to the solution through a dropping funnel. The solution was allowed to warm to 22° gradually as hydrogen was passed through the solution, and at the end of 1.5 hr. a negative test for peroxide (carried out with potassium iodide in glacial acetic acid) was obtained. Analysis of this solution by the hydroxylamine hydrochloride method gave misleading results because of hydrolysis of the ester to acetic acid. Distillation of this solution gave a product of indefinite composition.

In a similar experiment the product was converted to the dimethyl acetal. To the product solution was added 25 ml. of 2,2-dimethoxypropane and 0.1 g. of ammonium chloride. The mixture was distilled at atmospheric pressure to a pot temperature of 95° to remove the methyl acetate. An additional 50 ml. of methanol and 15 ml. of 2,2-dimethoxypropane were added and the distillation continued to a pot temperature of 105°, at which point the vapor temperature was 64.5°. The total heating period was about 6 hr. The residue was cooled, filtered, transferred to a similar distillation flask equipped with a nitrogen capillary ebullator, and distilled under reduced pressure through a 1 in. \times 6 in. glass helices packed column. There was recovered from 15.0 g. of methyl oleate, 7.69 g. (82%) of a fraction boiling 56.5–70° (0.35 mm.) $n_D^{30.2}$ 1.4166, and a fraction (10.13 g., 87%) boiling 95–103° (0.35 mm.) $n_D^{30.2}$ 1.4302. Since the

latter value did not agree with that recorded in the literature⁷ ($n_D^{30.2}$ 1.4312) for the dimethyl acetal of methyl azelaaldehyde, elemental analyses were carried out on a redistilled fraction having a boiling point of 88° (0.25 mm.), $n_D^{30.2}$ 1.4301.

Anal. Calcd. for $C_{12}H_{24}O_4$: C, 62.04; H, 10.41; sapon. equiv. 232.3. Found: C, 61.89; H, 10.29; sapon. equiv. 231.

A more convenient procedure involved ozonization in the ethyl acetate–acetic acid solvent mixture followed by catalytic hydrogenation. Direct distillation of the product solution resulted in the isolation of methyl azelaaldehyde, $n_D^{30.2}$ 1.4347, in 83% yield. Analysis by the hydroxylamine hydrochloride method indicated a purity of 87%. Apparently, a relatively low proportion polymeric peroxides, which are reported to be found as well as the acetoxy peroxides,¹⁴ were present.

The other solvents which were tried (Table I) resulted in low yields of impure products.

Isolation of the methoxy hydroperoxides. Methyl oleate (6.0 g., 0.020 g. mole) was ozonized in 150 ml. of methanol in the manner described. The amount of ozone consumed was 107% of theory and the amount absorbed in the potassium iodide trap was 6.0% theory. The solution was filtered, and methanol was removed in a rotary evaporator at a temperature of 21° first under vacuum from a water aspirator and then finally at a pressure of 0.2 mm. for a total time of about 18 hr. under vacuum. The colorless oil which remained weighed 7.8 g.

Anal. Calcd. for $C_{20}H_{40}O_6$: (an equimolar mixture of I and II) C, 63.80; H, 10.71; methoxyl, 16.48. Found: C, 63.3; H, 10.8; methoxyl, 19.5.

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PEORIA, ILL.

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AND BACTERIOLOGY, STATE UNIVERSITY OF IOWA]

Preparation of Long Chain Alkyl Hydroperoxides¹

S. WAWZONEK, P. D. KLIMSTRA,^{2,3} AND R. E. KALLIO

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Dodecyl, tetradecyl, hexadecyl, and octadecyl hydroperoxides have been prepared for testing as intermediates in the biological oxidation of saturated hydrocarbons. The hydroperoxides were prepared in a state of purity varying from 92–100 per cent by the alkylation of hydrogen peroxide in basic medium with the corresponding alkyl methanesulfonate.

In the study of the oxidation of saturated hydrocarbons by certain microorganisms, recent data indicate that biological oxidation of paraffins occurred at one terminal carbon and did not involve the formation of an olefin, epoxide, or 1,2-glycol.⁴

In this work a series of hydroperoxides containing twelve, fourteen, sixteen, and eighteen carbon atoms

have been synthesized for testing as possible intermediates in this oxidation.

Of the methods available the reaction of a Grignard reagent with oxygen⁵ and the alkylation of hydrogen peroxide with alkyl methanesulfonates⁶ were studied as possible sources of these compounds.

Treatment of dodecylmagnesium bromide with oxygen at –75° gave a peroxidic product which could not be separated by distillation under reduced pressure from the tetracosane formed. In contrast to the stability reported for decyl hydroperoxide towards distillation,⁶ dodecyl hydroper-

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(3) American Chemical Society–Petroleum Research Fund Predoctoral Fellow.

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(6) H. R. Williams and H. S. Mosher, *J. Am. Chem. Soc.*, **76**, 2984 (1954).