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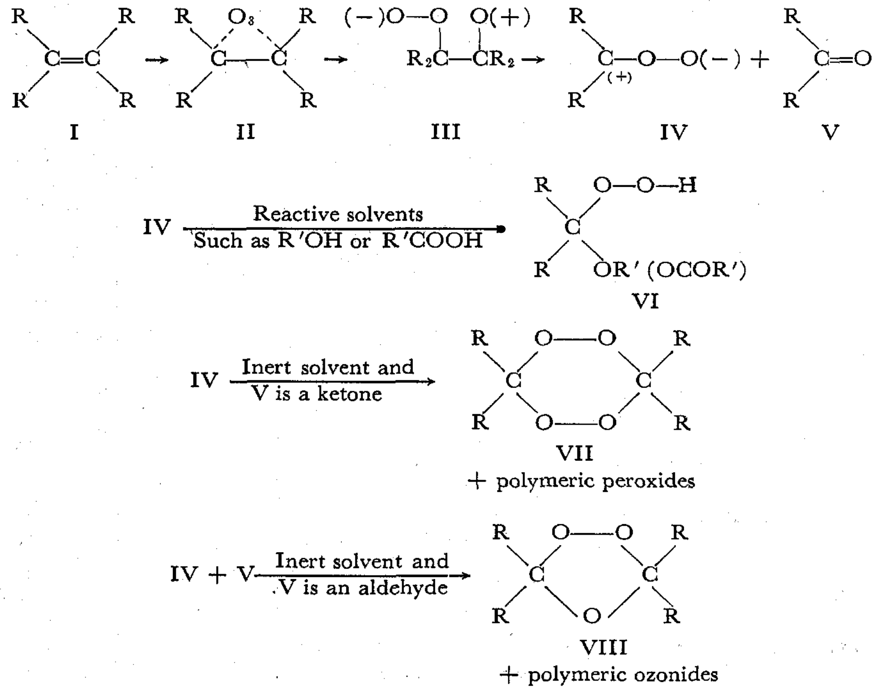
Adipic Acid by Ozonolysis of Cyclohexene

Oxidative decompositions in formic acid medium were the most satisfactory. The formic acid–acetic acid reaction medium obviates the need for solvent evaporation prior to oxidation and is superior to other media investigated for industrial use.

PREPARATION of adipic acid by ozonolysis of cyclohexene has been reported (*12, 16–20, 22–24*). In general, yields have been low, or the reagents used in the oxidative decomposition of the active oxygen-containing ozonolysis products have been expensive. The decreased cost of ozone production in recent years (*5*) has made it desirable to reinvestigate this synthesis from the viewpoint of possible commercial application.

Ozonolyses carried out in "reacting" solvents such as alcohols or carboxylic acids lead to higher yields of useful products (*2, 3*); the active oxygen-containing ozonolysis products are usually simple hydroperoxides (VI), produced, according to the Criegee mechanism (*1, 2, 6, 8–11, 21*), by addition of the solvent to a zwitterion intermediate (IV). These hydroperoxides are generally both obtained and converted to useful substances in high yield. Inert solvents, such as chloroform and hydrocarbons, lead to the formation of ozonides (VIII) or dimeric peroxides (VII), accompanied as a rule, by major or minor amounts of polymeric ozonides or peroxides. The dimeric and polymeric materials are frequently both dangerous and difficult to convert to useful products.

Outline of Criegee Mechanism



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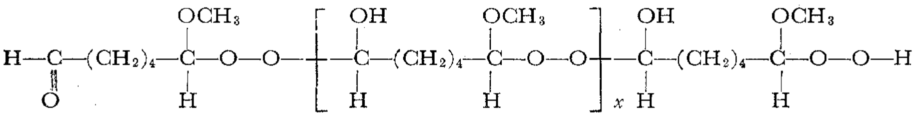
Methanol appears to be an especially good solvent for ozonolysis, in spite of the fact that it is reactive toward ozone (*15*). As long as reactive unsaturated molecules are present and the temperature is kept low, no appreciable reaction occurs between ozone and methanol.

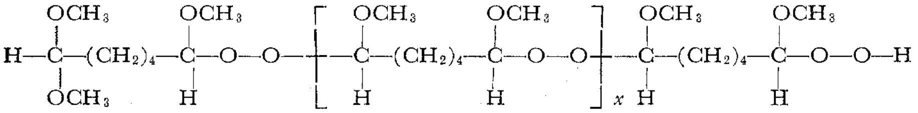
Two patents for the ozonolysis of cyclohexene, leading to the synthesis of hexamethylenediamine (*14*) and adipaldehyde (*13*), specify methanol as the preferred solvent.

In the present work the ozonolyses were carried out at low temperatures (−70° to −75° C.), to minimize the loss of cyclohexene through volatilization. The ozone was completely absorbed until one mole per mole of cyclohexene had reacted. Evaporation of excess methanol from the reaction mixture under reduced pressure gave a clear viscous peroxidic sirup, which was largely a mixture of the following polymeric materials, where the average value of *x* is 1.



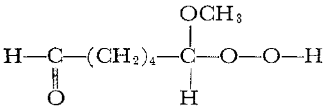
$$\mathrm{H{-}\underset{\underset{O}{\|}}{C}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O{-}\left[\overset{OH}{\underset{H}{C}}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O\right]_x{-}\overset{OH}{\underset{H}{C}}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O{-}H}$$

IX



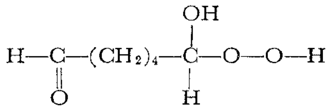
$$\mathrm{H{-}\overset{OCH_3}{\underset{OCH_3}{C}}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O{-}\left[\overset{OCH_3}{\underset{H}{C}}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O\right]_x{-}\overset{OCH_3}{\underset{H}{C}}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O{-}H}$$

X



$$\mathrm{H{-}\underset{\underset{O}{\|}}{C}{-}(CH_2)_4{-}\overset{OCH_3}{\underset{H}{C}}{-}O{-}O{-}H}$$

XI



$$\mathrm{H{-}\underset{\underset{O}{\|}}{C}{-}(CH_2)_4{-}\overset{OH}{\underset{H}{C}}{-}O{-}O{-}H}$$

XII

Structure IX is produced from the primary, expected hydroperoxide (XI) by addition of the hydroperoxy group of one molecule to the aldehyde group of another, thus forming hemiperacetal groupings. Structure X is produced by reaction of IX with methanol to convert the aldehyde group of IX to an acetal group and the hemiperacetal groups to peracetal groups (*4*).

Although these materials are polymeric, they are not of the type obtained in inert solvents. Having acetal, hemiperacetal, and peracetal linkages in their structures, they are easily hydrolyzed under acidic conditions (to XI or XII). Thus, oxidative decompositions in acidic media converted the material to adipic acid, whereas in basic media only intractable oils were obtained.

Oxidative decompositions in formic acid medium proved the most satisfactory. By using hydrogen peroxide, an 85% yield of nearly pure adipic acid was obtained. Only one mole of hydrogen peroxide per mole of peroxidic ozonolysis product was needed, showing that the alkoxy or hydroxy hydroperoxide end of the molecule being oxidized (probably monomeric compound XI or XII) needs no oxidizing agent, but is converted to a carboxyl group simply through decomposition and rearrangement.

Because hydrogen peroxide is too expensive for large scale use in this case, studies were made using oxygen in its place. Although the oxidation proceeded too slowly with oxygen alone, the use of catalytic amounts of ozone gave good results. It was necessary, however, to carry out oxidation of the aldehyde group below 70° C., after which the temperature was raised to the reflux point, where decomposition of the alkoxy (or hydroxy) hydroperoxide group was completed. If the temperature was raised too early, or if a formic acid solution of the peroxidic ozonolysis product was refluxed in the absence of an oxidant, tar formed, probably as the result of polymerization and/or condensation involving the aldehyde group. It was also necessary to use a vigorous flow of the oxygen-ozone stream through the system. Under the ideal conditions described, 70 to 75% yields of nearly pure adipic acid were obtained.

Acetic acid was not so good a solvent as formic acid, either in the hydrogen peroxide—or in the ozone-catalyzed oxygen oxidations. Apparently, oxidation of the aldehyde group was rapid enough, but the alkoxy (or hydroxy) hydroperoxide group decomposed too slowly. To determine whether or not this was due to the fact that formic acid is a stronger acid than acetic acid, acetic acid containing sulfuric acid was tested as a solvent. Although the alkoxy hydroperoxide group decomposed more rapidly than in acetic acid alone, it was neither so rapid nor so complete as in formic acid or a mixture of acetic and formic acids. The exceptional ability of formic acid to convert the alkoxy (or hydroxy) hydroperoxide group to a carboxyl group may lie in its easy oxidation to performic acid. The alkoxy (or hydroxy) hydroperoxide group, like hydrogen peroxide, may oxidize formic acid to performic acid which, in turn, oxidizes the resulting group [from reduction of the alkoxy (or hydroxy) hydroperoxide] to a carboxyl group.

The principal disadvantage in the process as described is the necessity of evaporating the methanol after the ozonolysis step and replacing it with formic acid for the oxygen oxidation step. Runs were made in which the ozonolysis was carried out in a formic acid–acetic acid mixture at −10° C., after which the temperature was raised and the oxygen oxidation was carried out. The yield of adipic acid was only 49 to 63%. The lower yield, however, appears to be due to loss of cyclohexene through volatilization during ozonolysis. On the basis of the amount of ozone absorbed, the yields would be 61 to 79%.

Experimental Procedures

The ozone source was a Welsbach T-23 laboratory ozonator. Oxygen was dried to a dew point of at least −60° C. The ozonolysis flask was essentially a tube with the gas inlet at the bottom, a sealed-in fritted disk just above the inlet, and the outlet near the top. When oxidations at higher temperature were carried out, a condenser was inserted. The cyclohexene, Phillips pure (99%) grade, was peroxide-free. All other reagents were of the highest grade commercially available.

Peroxidic Ozonolysis Products. A stream of oxygen containing approximately 6% ozone by weight was passed through a solution of 4.1 grams (0.05 mole) of cyclohexene and 50 ml. of anhydrous methanol at a rate of approximately −70° C. The ozone was completely absorbed until 1 mole per mole of cyclohexene had reacted. At this stage ozone passed through and released iodine in the adjoining potassium iodide trap. The reaction mixture was allowed to come to room temperature, after which the methanol was evaporated at 0.5-mm. pressure, in a Rinco rotary evaporator. The residue was a clear, viscous sirup weighing 9.5 grams. In acetic acid solution it strongly oxidized iodide to iodine and slowly released oxygen upon treatment with lead tetracetate. The latter is a positive test for hydroperoxides (*7*).

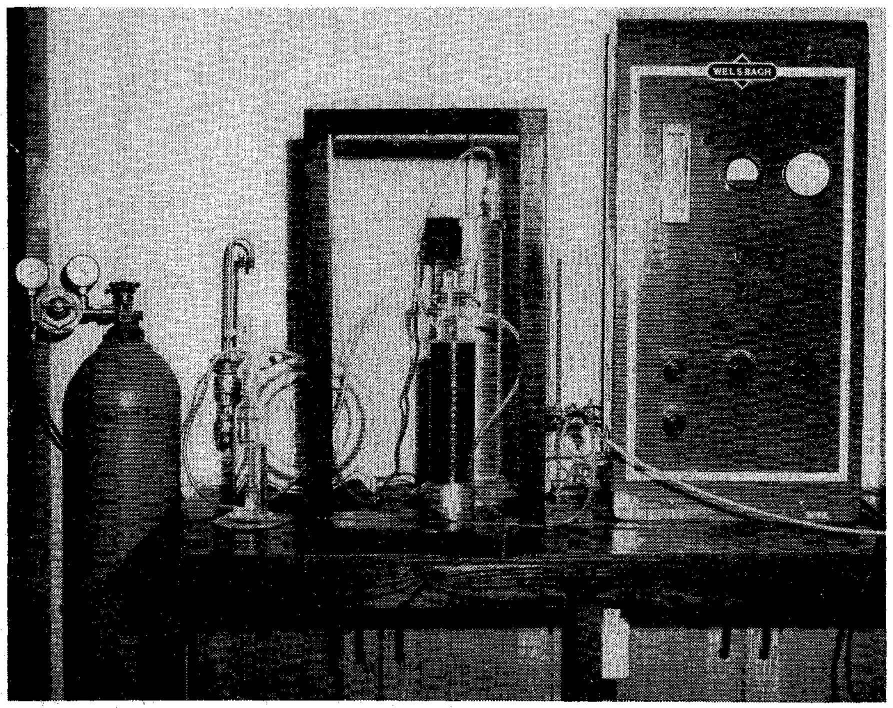
Ozonolysis in Methanol. Oxidation with Hydrogen Peroxide in Formic Acid. The ozonolysis was carried out on a 0.05-mole sample and the methanol evaporated as described in the preceding experiment. The peroxidic residue (9.1 grams) was dissolved in 35 ml. of 90% formic acid and 17 ml. of 30% hydrogen peroxide was added. Upon gentle warming a vigorous reaction set in (Caution!). After the spontaneous reaction had ceased (30 to 45 minutes), the reaction mixture was refluxed for 30 minutes, after which time it gave a negative peroxide test with sodium iodide. The mixture was cooled and the initial crop of adipic acid was filtered off. The filtrate was evaporated and the residue was washed with ether and separated by filtration. The total yield of adipic acid melting at 147–50° C. was 6.2 grams (85% based on cyclohexene). From the filtrates 0.3 gram of acidic material melting at 135° to 140° C. was obtained. The rest was an oil.

When this experiment was repeated, except that 50 ml. of formic acid and 6 grams of 30% hydrogen peroxide (1 mole per mole of cyclohexene ozonized) were employed in the second step, an 82% yield of adipic acid melting at 145–9° C. was obtained.

Hydrogen Peroxide Oxidation in Acetic Acid. The procedure described was followed, except that in the second step 30 ml. of glacial acetic acid and 15 ml. of 30% hydrogen peroxide were employed. No spontaneous reaction ensued and after refluxing for 13 hours the mixture still gave a peroxide test with sodium iodide. Evaporation of the mixture and trituration of the residue with ether gave only 4.1 grams of very impure material melting at 130° to 142° C.

Decomposition in Formic Acid. The ozonolysis was carried out and the methanol evaporated as described. The peroxidic residue was dissolved in 50 ml. of 90% formic acid and the resulting solution was refluxed for 1 hour. The mixture became dark brown. A peroxide test with sodium iodide after the first 30 minutes of reflux was very weak. The solution was evaporated and the residue was treated with ether. Filtration gave 1.1 grams of very impure material (melting point 133° to 142° C.). The rest was a tar.

Ozone-Catalyzed Oxygen Oxidation in Formic Acid. The ozonolysis was carried out on a 0.05-mole sample and the methanol evaporated as described. The sirupy residue was dissolved in 55 ml. of 80% formic acid (the remaining 20% was water). The reaction tube was heated with a tape heater. Oxygen containing approximately 0.9% ozone by weight was passed through at a rate of approximately 20 liters per hour. The temperature, measured at the heating tape, was allowed to rise quickly to 35° C. and then slowly to 70° C. over a period of 1.5 hours. Most of the ozone was absorbed, making a total of approximately only 0.15 mole per mole of peroxidic ozonolysis product. The ozonator was then shut off, but the oxygen stream containing traces of ozone was continued through the system while the temperature was raised to 105° C. (reflux) over a 15-minute period and kept there another 30 minutes. The solution was colorless, showing that oxidation of the aldehyde group had been complete at the time the temperature had been raised to the reflux point. It gave only a very weak sodium iodide test. The mixture was cooled in an ice bath and 4.3 grams of adipic acid (melting point 148–51° C.) was filtered off. Upon evaporation of the filtrate and recrystallization of the residue from a minimal amount of water, another 1 gram melting at 147–50° C. was obtained; total yield based on cyclohexene was 73%. When the same ozone-oxygen mixture was used, but at a much lower (about one tenth) rate of gas flow through the system, the yield of adipic acid (melting point 143–8° C.) dropped to 58%.



Entire laboratory setup used in carrying out ozonolysis experiments. List of equipment includes Welsbach ozonator, reaction vessel, shield, wet test meter, oxygen dryer, and KI trays following reaction vessel

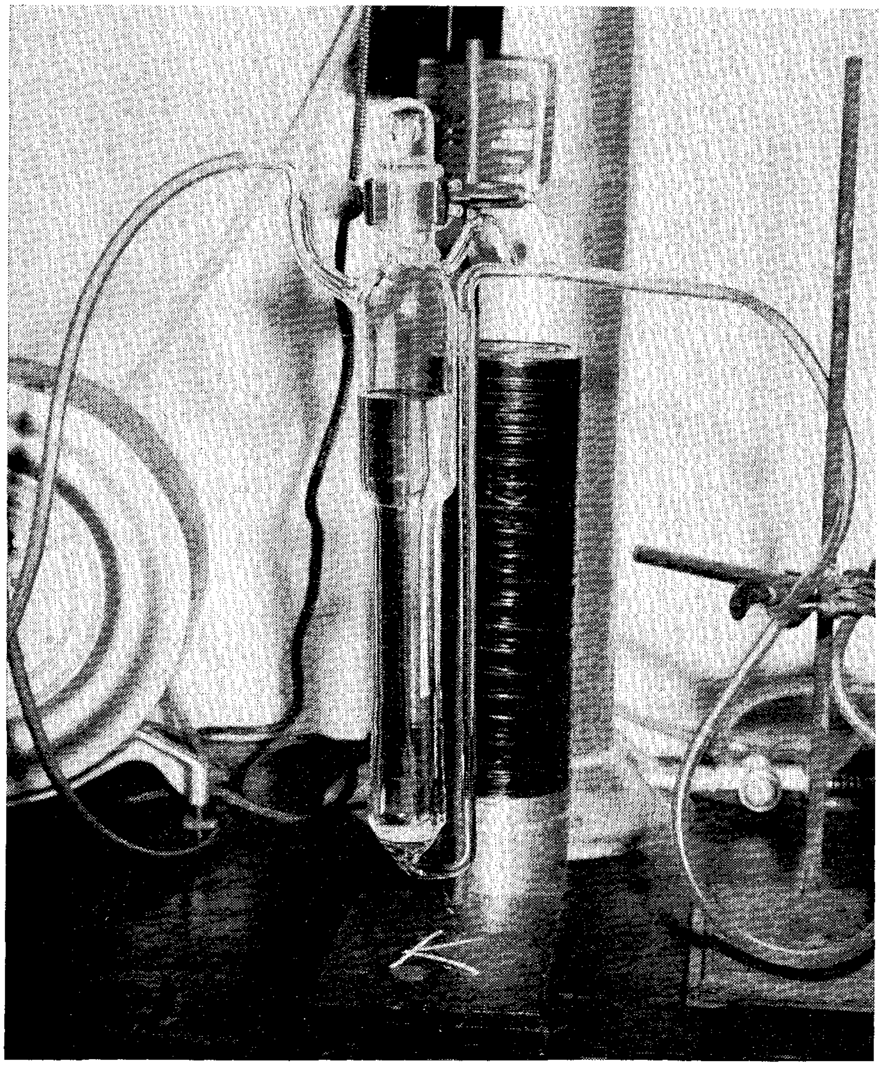
Oxidation in Formic Acid with Pure Oxygen. The procedure described was followed, except that pure oxygen was employed at approximately 20 liters per hour in the second step. The yield of impure adipic acid (1.9 grams, melting point 146–8° C. and 1.6 grams, melting point 133° to 142° C.) was 48%.

Ozone-Catalyzed Oxygen Oxidation in Acetic Acid. The ozonolysis and ozone-catalyzed oxygen oxidation were carried out as described, except that 90% acetic acid was used as the solvent in the second step. At the end of the normal reaction period the reaction mixture was strongly peroxidic. As this was analogous to the earlier described oxidation with hydrogen peroxide in acetic acid, the reaction mixture was not worked up.

Ozone-Catalyzed Oxygen Oxidation in Acetic Acid plus Sulfuric Acid. The procedure was repeated, except that in the second step 1 ml. of concentrated sulfuric acid was added to the reaction mixture. After the usual reaction period, the reaction mixture gave a moderately strong peroxide test with sodium iodide. It was cooled and 2.8 grams of adipic acid melting at 144–8° C. was obtained. Slow evaporation of the filtrate under a stream of air and trituration of the residue with ether gave 3.3 grams of material melting at 122° to 135° C. The oily residue from evaporation of the ether washings was still strongly peroxidic. Recrystallization of the low melting fraction from water resulted in low recovery and no improvement in melting point.

When the experiment was repeated using glacial acetic acid in place of 90% acetic acid, all other factors remaining the same, 4.4 grams of crystalline fractions were obtained ranging in melting point from 97° to 138° C.

Attempted Oxidation under Neutral or Alkaline Conditions. Ozonolysis was carried out in methanol as described. In one case excess 30%



Close-up of reaction vessel used for ozonolyses (in Dewar flask)

hydrogen peroxide and 10 to 20% sodium hydroxide was then added. After the spontaneous heat evolution had subsided the mixture was refluxed for 30 minutes, at which time it gave only a very weak peroxide test with sodium iodide. Acidification with sulfuric or hydrochloric acid, evaporation of the solution with a stream of air, extraction of the residue with methanol, and evaporation of the methanol extract gave only oily materials. Similar results were obtained when, in place of hydrogen peroxide, oxygen was passed through the neutral methanol solution for 6 to 8 hours at room temperature in the presence of ferrous phthalocyanine catalyst, after which the mixture was refluxed with excess sodium hydroxide solution and worked up as before.

Ozonolyses in Formic Acid–Acetic Acid Mixture. HYDROGEN PEROXIDE OXIDATION. A solution of 4.1 grams (0.05 mole) of cyclohexene in 30 ml. of glacial acetic acid and 15 ml. of 90% formic acid was ozonized at −5° C. by the procedure described for methanol solvent. Only about three fourths of the theoretical amount of ozone was absorbed before the reaction was complete. The mixture was then treated with 10 ml. of 30% hydrogen peroxide and refluxed for 2 hours (at which time only a weak peroxide test was given). Evaporation of the reaction mixture and trituration of the residue with ether gave 4.1 grams (56% yield) of adipic acid melting at 146–9° C. The cold trap placed after the ozonization flask contained cyclohexene. Based on the amount of ozone absorbed in the reaction, the yield of adipic acid was 75%.

Identical results were obtained when the ozonolysis was performed in acetic acid at about 0° C., after which formic acid was added and the hydrogen peroxide treatment was carried out. Without addition of formic acid, the reaction mixture gave a strong peroxide test even after 5 hours of reflux.

OZONE-CATALYZED OXYGEN OXIDATION. The ozonolysis was carried out at −10° C. as in the preceding experiment. A cold trap was placed immediately after the ozonization flask. Only about 80% of the theoretical amount of ozone was absorbed. The odor of cyclohexene was strong in the cold trap. The temperature of the reaction mixture was then increased and the ozone-catalyzed oxygen oxidation was carried out and worked up as described. The yield of crude adipic acid was 2.7 grams, melting at 145–9° C. and 1.9 grams melting at 133–43° C. (total crude yield, 63%). Recrystallization from 20 ml. of water gave 3.6 grams (49% yield) of pure adipic acid (melting point 150–2° C.). Based on the amount of ozone absorbed during ozonolysis, the crude and pure yields of adipic acid were 79 and 61%, respectively.

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