

Emulsion Ozonization of Cycloolefins in Aqueous Alkaline Hydrogen Peroxide¹

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Cycloolefins reacted with ozone in emulsion with aqueous alkaline hydrogen peroxide to give α,ω -alkanedicarboxylic acids in a one-step process, generally in good yields. The scope of this method was explored with cyclic mono- and polyolefins and condensed, partially aromatic ring systems. Cyclic polyolefins by controlled ozonization gave olefinic dicarboxylic acids. Side reactions led to ω -hydroxy acids, lactones, and peroxy polymers; mechanisms for these reactions are presented.

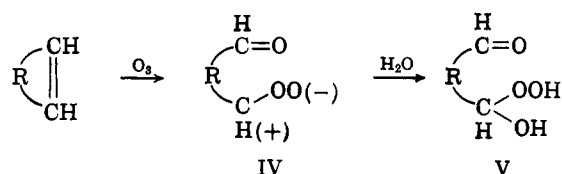
The ozonization of cycloolefins and subsequent oxidation of the ozonides to the corresponding terminal diacids have been reported in a few instances.²⁻⁴ In these cases the reaction involved two steps, namely the formation and accumulation of the ozonide in an inert solvent and the oxidation of the ozonide by peracids. Such ozonization of polyolefins could not be controlled short of complete destruction of all double bonds. The disadvantage of ozonide accumulation and a solvent change led to the question whether the ozonization can be conducted in such a way that the initially formed ozonolysis product would react immediately with the oxidizing reactant present.

In our laboratories, cyclic olefins in emulsions of aqueous, alkaline hydrogen peroxide reacted with ozone smoothly to give α,ω -dicarboxylic acids in one step, generally in good yields. Ozonization of cyclic polyolefins could be controlled to give olefinic dicarboxylic acids. This reaction was tested with nine cyclic olefins. Table I lists the results.

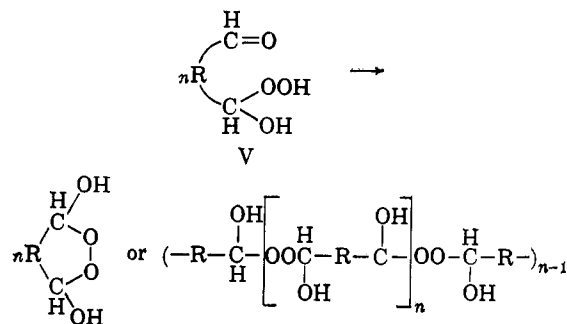
According to Criegee⁵ the stabilization of the ionic ozonolysis intermediate, I, is determined by the solvent used. In the case of aprotic solvents the stabilization proceeds by intermolecular polyaddition or by cyclic ozonide formation, while protonic solvents undergo a direct addition with the ionic intermediate. This gives, in addition to ketones or aldehydes, hydroperoxy

derivatives, II, and—in the case of cyclic olefins—terminal ω -carbonyl-hydroperoxy derivatives III.

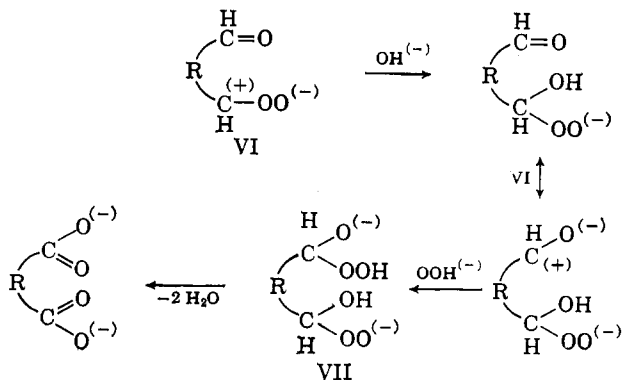
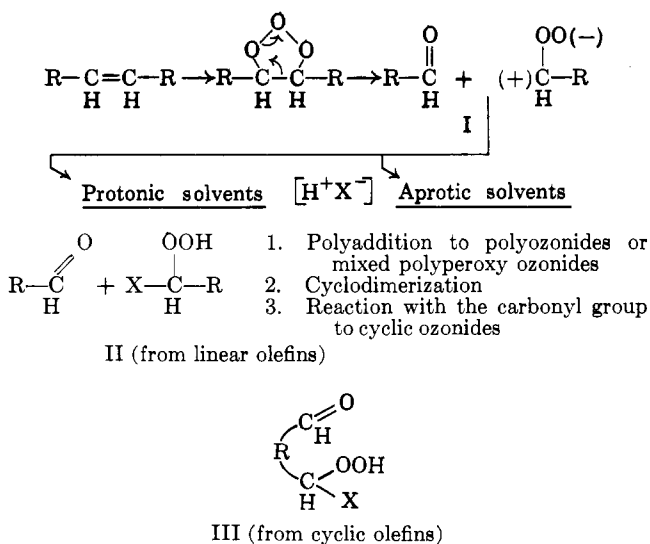
Although water is not miscible with the ozonized olefins, it reacts similarly when the intermediate ozonolefin adduct or zwitterion IV contacts sufficiently the aqueous phase.



The dialdehyde monohydroperoxide (V) is still highly reactive, and leads either to peroxy polymers of probable structure shown, by intermolecular polyaddition or to peroxy-bridged structures by intramolecular ring formation. Both reactions are attributed to hydroperoxide attack at the carbonyl double bond of the terminal aldehyde group.



For the formation of terminal dicarboxylic acids by the hydrolysis of the ozonolysis intermediate IV, additional oxidizing agents must be present. For this purpose the ozonization was carried out in alkaline hydrogen peroxide where both hydroxy and hydroperoxy anions were present as reactive components. They converted the terminal aldehyde group of IV to the



(1) Presented at the XIX International Congress of Pure and Applied Chemistry, London, July, 1963.

(2) P. S. Bailey, *Ind. Eng. Chem.*, **50**, 993 (1958); R. H. Callingham, M. F. Tarker, and M. H. Wilt, *J. Org. Chem.*, **26**, 1379 (1961).

(3) C. K. Ingold, *et al.*, *J. Chem. Soc.*, 142 (1936); A. Maggiolo, M. and A. L. Tumolo, U. S. Patent 3,023,233 (February 27, 1962).

(4) P. S. Bailey, *J. Org. Chem.*, **22**, 1548 (1957); A. Rieche, *Ber.*, **63**, 2642 (1930).

(5) R. Criegee, *Ann.*, **560**, 127 (1948); **564**, 9 (1949).

TABLE I
 EMULSION OZONIZATION OF CYCLOOLEFINS

(All runs were at 5° in a 1-l. Vibro-mix-glass reactor containing *ca.* 550 cc. of distilled water and 2 mole equiv. of sodium hydroxide for the ozonized olefin. One gram of Brij 30^a surfactant was dissolved in the olefin prior to the addition of the aqueous phase. One mole equivalent of ozone was introduced. Concentration of ozone in oxygen was between 2.8–3 wt. %.)

Olefin (g.)	30% H ₂ O ₂ , g. (mole equiv.)	Recovered starting material, g.	Carboxylic acid ^b	g.	(mole %)	Peroxy polymer, g.
Cyclohexene (30) + 50-g. excess	50 (1.4)	30	Adipic acid	21	(26)	19
Cyclooctene (60) + 20-g. excess	90 (1.5)	20	Suberic acid ^c	62	(63)	14
1,5-Cyclooctadiene (30) + 50-g. excess	48 (1.5)	45	1,6-Dicarboxyhexene-3 (XI)	25	(52)	5
1,5,9-Cyclododecatriene (55) + 45-g. excess	50 (1.2)	40	1,10-Dicarboxydecadiene-3,7 (XII)	42	(60)	5
Dicyclopentadiene (30) no excess	80 (1.5)	none	2,3,5-Tricarboxycyclopentylacetic acid (XIII)	39	(66)	0
Dicyclopentadiene (15) + 30-g. excess	20 (1.5)	26	6,8-Dicarboxybicyclo[3.3.0]-octene-4 and 1-carboxynorbornylene-2-acetic acid (XIV)	12	(55)	0
Indene (55) + 25-g. excess	80 (1.5)	16	Homophthalic acid	86	(83)	7
Acenaphthylene ^d (50) no excess	37 (1.0)	0.5–1	1,8-Naphthalic acid	51	(82)	5
Norbornylene ^d (30) + 10-g. excess	55 (1.5)	6	Cyclopentanedicarboxylic acid-1,3 (XVI)	34	(68)	8
4-Cyclohexene-1,2-di- carboxylic anhydride (50) no excess	54 (1.5)	none	1,2,3,4-Tetracarboxybutane (VII)	53	(73)	0

^a Trade-name for polyoxyethylated lauryl alcohol from Atlas Company. ^b For identification all esters were prepared by refluxing a solution of the crude acid in ethanol with a catalytic amount of concentrated sulfuric acid over a Soxhlet containing anhydrous magnesium sulfate. ^c The relatively water-soluble suberic acid was not quantitatively precipitated by acidification of the aqueous solution, requiring a total water evaporation for its complete isolation. ^d Acenaphthylene and norbornylene were dissolved in 30–50 cc. of chlorobenzene, and this solution was added together with Brij 30 to the aqueous phase.

hydroperoxide anion (VII) before it was able to undergo other reactions. This anion rearranged again to form the carboxylate anion with loss of water. A similar reaction proceeded with the anion VI which was formed by the addition of hydroxyl ion to the carbonium ion of the ozonide intermediate IV.

This reaction sequence demanded a narrow range of operating conditions, which were mainly determined by the degree of interfacial contact between the ozonized olefin and the aqueous solution, as well as the concentration of hydrogen peroxide and sodium hydroxide.

The degree of interfacial contact depended on the size of the suspended olefin droplets. When the droplet diameter was too large, the ozonide intermediate IV remained within the aprotic environment of the hydrocarbon, rapidly forming the insoluble polyozonide which gradually decomposed on contact with the aqueous phase to complex insoluble peroxy polymers. In addition, the polymerization of the aldohydroperoxide was favored to a considerable extent. Decrease of the droplet diameter permitted a faster hydrolysis of the zwitterionic ozonide intermediate IV and subsequent oxidation by OOH⁻ ions, which was best accomplished by using emulsions of the olefin in the aqueous reaction phase. This called for an effective emulsifier which had to be stable towards the oxidizing, alkaline reaction medium.

To form the dicarboxylic anion, the oxidation required stoichiometrically a minimum of a 2:1 mole ratio of alkali hydroxide as well as a 1:1 mole ratio of hydrogen peroxide to cycloolefin. In general, however, an excess of hydrogen peroxide was necessary due to its

accelerated decomposition in the alkaline solution. Without hydrogen peroxide the terminal aldehyde group of VI remains unoxidized so that such side reactions as polyadditions and OH⁻-catalyzed carbonyl reactions, namely aldol condensation of the aldehyde group or Canizzaro-type disproportionations, occur. A significant oxidation of the aldehyde group by oxygen present as carrier gas for ozone was not observed. Attempts to achieve this and avoid use of hydrogen peroxide by adding cobalt bromide to the system were unsuccessful. As expected, the Canizzaro reaction was noticed only on oxidation intermediates without α -hydrogen, while other intermediate products containing α -hydrogens underwent complex aldol condensations, leading to polymeric mixtures. Thus the Canizzaro reaction leads with acenaphthylene to naphthalic acid

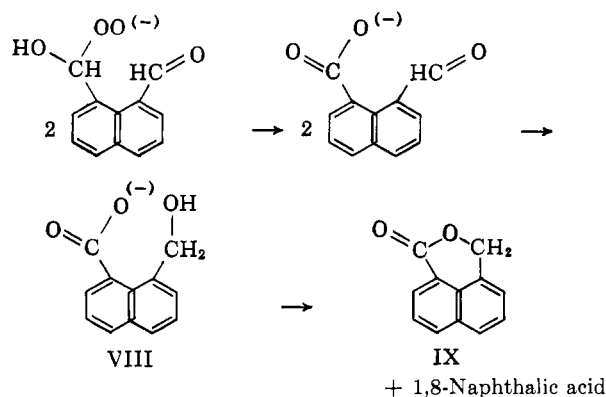


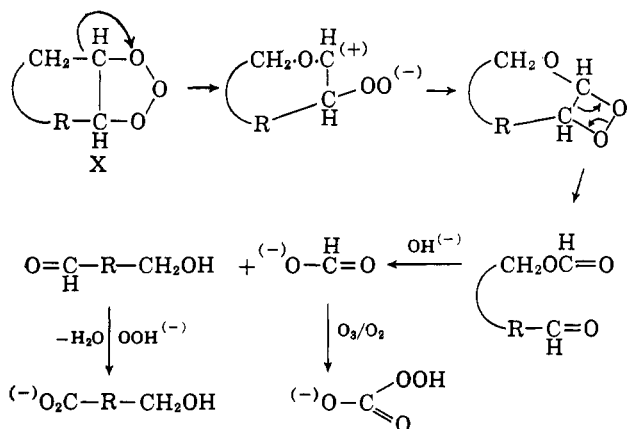
TABLE II
CHARACTERIZATION AND IDENTIFICATION OF THE DICARBOXYLIC ACIDS
(Identified products other than dicarboxylic acids and their esters are listed separately)

Dicarboxylic acids ^a		Anal. Calcd. for	Found:	Bromine no.:
XI as diethyl ester	B.p. 90° (0.1 mm.)	C ₁₂ H ₂₀ O ₄ :	C 62.79; H 8.92 Found: C 62.89; H 8.82	
XII	M.p. 161°	C ₁₂ H ₁₈ O ₄ :	C 63.36; H 8.10 Found: C 63.48; H 8.27	Calcd.: 140 Found: 138
XIII as tetraethyl ester	B.p. 150° (0.1 mm.)	C ₁₈ H ₂₈ O ₈ :	C 58.04; H 7.59 Found: C 58.11; H 7.63	
XIV as diethyl esters	B.p. 100° (0.1 mm.)	C ₁₄ H ₂₀ O ₄ :	C 66.63; H 7.92 Found: C 66.72; H 7.99	
XVI	M.p. 120°	C ₇ H ₁₀ O ₄ :	C 53.27; H 6.40 Found: C 53.10; H 6.55	
XVII as tetraethyl ester	b.p. 145° (0.04 mm.)	C ₁₆ H ₂₆ O ₈ :	C 55.47; H 7.58 Found: C 55.25; H 7.72	

^a Additionally the listed acids were identified by their infrared spectra and their mass spectra—except XII and XVI, which were identical with corresponding samples obtained by another synthetic route. Adipic acid, suberic acid, homophthalic acid and 1,8-naphthalic acid (as anhydride) were identified by mixture melting point with authentic samples as well as by their infrared spectra.

and to the hydroxy acid VIII, which readily formed the lactone IX.²

Besides the formation of dicarboxylic acids and lactones from IV, another reaction occurred during the emulsion ozonization, leading in low conversion to terminal hydroxy acids with cleavage of carbon dioxide. This side reaction, observed with cyclohexene and cyclooctene, suggested an abnormal stabilization of the molozonide X after its breakdown by insertion of one oxygen atom between the C—C bond adjacent to the original double bond, instead of forming the carbonyl group. Such reaction has been usually observed in ozonization of structures R—C=C—CHR'R'' where R' or R'' is O, N, or S, or for the system R—C=C—Ar.⁶ This insertion can be regarded as another way to compensate for the electron deficiency of the oxygen atom, caused by the molozonide cleavage.



The last phase represents ozone-catalyzed oxidation of the formate anion at the activated C—H and leads to a hydroperoxide that decomposed immediately on acidification to hydrogen peroxide and carbon dioxide. This side reaction resulted primarily in α -hydroxy- ω -aldehydes, which were finally oxidized to the corresponding ω -hydroxy acids.

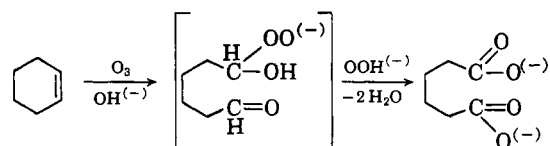
A further competitive side reaction was caused by oxygen. It reacted with the allylic hydrogen prior to the double-bond cleavage by ozone. This reaction is favored in alkaline media and is another example of the

known allylic oxidation of olefins.⁷ It gives olefin hydroperoxides that readily form unstable peroxy polymers of a low degree of polymerization in the alkaline aqueous solution. A steric effect influenced the oxidative attack on the allylic hydrogen. With increasing ring size (from cyclopentene to cyclohexene, cyclooctene and finally cyclododecatriene), this side reaction decreased significantly. The olefin hydroperoxide decomposes at pH < 7 with formation of ketones or secondary alcohols, a reaction that can be accelerated considerably by heavy metal ions, such as Co⁺² or Fe⁺².

This type of oxidation reduced the yield of dicarboxylic acids; it could be avoided by using nitrogen instead of oxygen as inert carrier gas for ozone.⁸ For this purpose the oxygen-ozone mixture was separated by adsorption on silicon dioxide or alumina from which the ozone was subsequently desorbed with nitrogen. The separated oxygen could be recycled for further ozone generation.

Cyclohexene gave most side reactions during the emulsion-ozonization. Thus, the allyl hydrogen was readily attacked in the aqueous alkaline medium by the oxygen and gave peroxides and peroxy polymers. Substitution of the oxygen by nitrogen as ozone carrier gas eliminated this side reaction.

The ozonization with ozone in oxygen gave adipic acid in 22–28% yield.



During the isolation of water-soluble diacid, a small amount of an oily product separated and was identified as α -hydroxyvaleric acid and its lactone; this explains the considerable amount of carbon dioxide evolved during the acidification of the alkaline reaction solution and is attributed to the abnormal ozonolysis. Cyclooctene, as a homolog of cyclohexene, exhibited nearly

(7) H. M. Stephens, *J. Am. Chem. Soc.*, **50**, 568 (1928); R. Criegee and H. Flygate, *Ber.*, **72**, 1799 (1939).

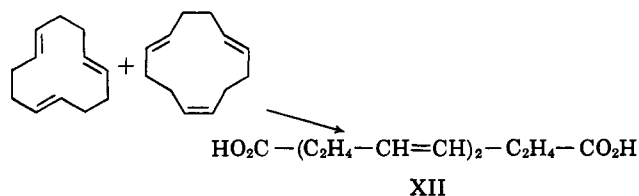
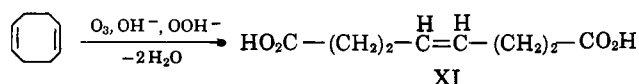
(8) G. A. Cook, L. A. Speuce, *Ozone Chemistry and Technology*, **44** (1959) (International Ozone Conference, Chicago, Ill., November, 1956).

(6) J. E. Leffer, *Chem. Rev.*, **45**, 385 (1949); P. S. Bailey, *ibid.*, **58**, 925 (1958).

the same properties during the emulsion-ozonization, except that the oxidative attack on the allylic hydrogen was considerably decreased. Here, also, a terminal hydroxy acid, the 7-hydroxyheptanoic acid, was formed in low yields. The main product of ozonization was succinic acid in 63% yield.

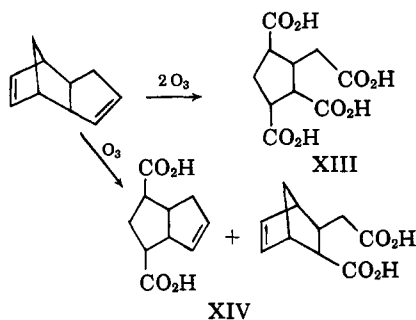
To obtain 1,6-dicarboxyhexene-3 (XI) by emulsion ozonization, cyclooctadiene was used in large excess for the oxidation so that the ozone attack on the second double bond would occur to a lesser degree. The reaction afforded the unsaturated diacid in a 52% yield; it was accompanied by peroxy polymer formation. Total ozonolysis led to succinic acid.

1,5,9-Cyclododecatriene, ozonized in the presence of a large excess of olefin, gave a 60% yield of 1,10-dicarboxydecadiene-3,7 (XII). This diacid was formed by cleavage of one double bond; minor amounts of higher cleavage-products, but no 1,6-dicarboxyhexene-3, were obtained. Carbon dioxide was evolved during the precipitation of the unsaturated diacid by acidification of the alkaline reaction solution. This indicated the occurrence of the abnormal molozonide stabilization forming terminal hydroxy acids which were, however, not identified.

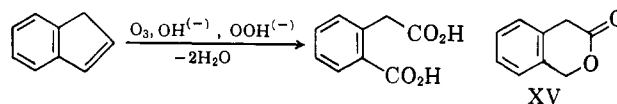


The cyclododecatriene was a mixture of the *cis*, *trans*, *trans*, and all-*trans* isomers. Comparison of the isomer ratio of the starting material with the excess hydrocarbon after ozonization showed that the ozone attacked both isomers to the same extent. This result was confirmed by a similar test with a 1:1 *cis/trans* 4-methylpentene-2 isomer mixture where both *cis* and *trans* olefin proved equally reactive.

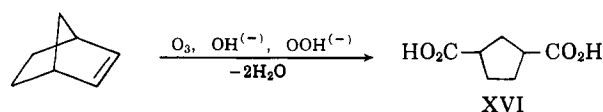
Ozonolysis of dicyclopentadiene gave (2,3,5-tricarboxycyclopentyl)acetic acid⁸ (XIII) in 66% yield. Partial ozonization, using an excess of dicyclopentadiene, resulted in a mixture of 6,8-dicarboxybicyclo[3.3.0]-octene-2 and 1-carboxynorbornylene-2-acetic acid in 55% yield (XIV). Elemental analysis was correct for either compound; the mass spectrum proved the molecular weight, but could not estimate the ratio of these compounds.



Ozonization of indene proceeded without significant allylic oxidation and led to homophthalic acid in yields averaging 80–85%. A minor amount of homophthalide (XV) could be isolated. Despite the presence of hydrogen peroxide, the aldehyde group of the ozonization intermediate in the alkaline solution gave some Cannizzaro product; absence of hydrogen peroxide increased the yield of homophthalide to 18% at the expense of homophthalic acid.

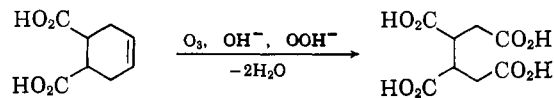


Acenaphthylene in chlorobenzene was ozonized without significant side reaction to yield 85% 1,8-naphthalic acid. Lower hydrogen peroxide concentrations resulted in more lactone formation, leading to 1-(hydroxymethyl)8-naphthoic acid and finally to the naphthalide (IX).



Similarly, norbornylene in chlorobenzene and alkaline hydrogen peroxide was ozonized, affording cyclopentane-1,3-dicarboxylic acid⁹ (XVI) in 68% yield.

The ozonization of 1,2-dicarboxycyclohexene-4 gave 1,2,3,4-tetracarboxybutane (XVII). The starting material was soluble in the alkaline aqueous reaction system and required no emulsifier. Ozone attacked the olefinic double bond of the dissolved dicarboxycyclohexene and gave the tetracarboxy acid anion without side reactions, although at a considerably smaller reaction rate due to the dissolved state of the cyclohexenedicarboxylic acid. This solution effect possibly caused the relative inertness of XI, XII, and XIV towards further ozonization of the unreacted double bonds while the unchanged olefins were still present in the emulsion.



Conclusion

This novel ozonization process offers a simple method for forming terminal dicarboxylic acids from cycloolefins in an aqueous reaction phase by one step. A number of acids—otherwise difficult to obtain—can be made in satisfactory yields. The emulsion ozonization is not limited to cyclic olefins but can be applied as well to open chain olefins to form two moles of carboxylic acid per mole olefin. Thus octene-1 in our system formed heptanoic acid in high yields.

Because the emulsion ozonization of cycloolefins results in the formation of two active terminal groups, new synthetic methods for polyfunctional compounds may be derived by use of reactive emulsion systems containing protonic—or more general ionic—reaction components of a wide variety. A subsequent paper

(9) R. H. Perry, U. S. Patent 2,963,487 (December 6, 1960).

will describe emulsion ozonization of cycloolefins in ammonia and amines.

Experimental

Cyclooctene and cyclooctadiene were obtained from Cities Service Chemical Co.; cyclododecatriene was prepared by trimerizing butadiene with chromyl chloride and aluminum triisobutyl as catalyst¹⁰; it is also now available from Enjay Chemical Co. and Cities Service Chemical Co. Cyclohexene, indene, and 4-cyclohexene-1,2-dicarboxylic anhydride were obtained from Eastman Chemical Co.; acenaphthylene from Rütgerswerke, A.G.

The ozone was generated by electric discharge in an oxygen stream, using a Welsbach T 23 ozonator. Its concentration in oxygen—which served also as carrier gas—averaged 2.8–3.0 wt. %. The ozone output of the generator was determined by percolation of the ozone–oxygen mixture through a 2% potassium iodide solution within a timed period, the amount of liberated iodine being titrated with 0.1 *N* thiosulfate solution. Thus the generator was calibrated for a fixed gas-flow rate, pressure, and discharge voltage for *n* g. of ozone/hr.

A typical ozonization is described for the formation of homophthalic acid from indene. An emulsion of 80 g. of indene in 600 cc. of distilled water was established by addition of the hydrocarbon and 1 g. of emulsifier to the well stirred aqueous phase in an indented three-necked 1500 ml. reaction flask. The reactor, provided with a high-speed stirrer, a gas-inlet tube, gas vent, and thermometer, was placed in an ice bath to maintain the reaction temperature at 10°. A saturated aqueous solution of 56 g. of sodium hydroxide (2 mole equiv.) and 142 g. of 30% hydrogen peroxide (1.5 mole equiv., 0.5 mole excess) was added and ozone was introduced into the vigorously stirred emulsion.

The reaction was interrupted after the absorption of 23 g. of ozone, leaving 25 g. of indene in excess as a safety margin for the prevention of over-ozonization. Addition of 15 g. of sodium chloride, after one additional hour of stirring, accelerated the demulsification, allowing some peroxy polymer and excess indene to separate from the aqueous phase. Acidification of the clear aqueous solution with hydrochloric acid precipitated the homophthalic acid, which was filtered, washed with water, and dried at 70° and 60 mm. Weight of the crude homophthalic acid was 80 g., (90%) m.p. 173°. Steam distillation of the peroxy polymer–indene mixture recovered 16 g. of indene. Acidification of the residual solution after filtration from polymeric products gave 6 g. more homophthalic acid and 5 g. of homophthalide.

In the absence of hydrogen peroxide (all other conditions being the same), yields of crude homophthalide and homophthalic acid were 38 g. and 42 g., respectively.

In case of the formation of water-soluble carboxylic acids, the acidified aqueous reaction phase was evaporated to dryness, and the residue—a mixture of sodium chloride and carboxylic acid—was extracted with anhydrous ethanol. Evaporation of the solvent left the crude acid, which was purified either by washing with ether, by recrystallization or by esterification and distillation.

The reaction data are summarized in Table I.

The choice of an emulsifying agent was limited by the strong oxidizing conditions during the reaction. Polyoxyethylated lauryl alcohol, Brij 30, proved stable enough to function satisfactorily.

Table II shows the characterization and identification of the dicarboxylic acids.

As products other than dicarboxylic acids from ring olefins, the following compounds were isolated from the ozonizations and identified. δ -Hydroxyvaleric acid as δ -valerolactone was separated from adipic acid by ether extraction of the concentrated aqueous reaction solution after acidification with 4 *N* sulfuric acid. Evaporation of ether and subsequent distillation gave 3 g. (8%) of δ -valerolactone, b.p. 85° (6 mm.), which was immediately treated with 10 cc. of 90% hydrazine at 80°, affording δ -hydroxyvaleric acid hydrazide, m.p. 105°, lit.¹¹ m.p. 106°. Another part of the valerolactone was oxidized with concentrated nitric acid at 95–110° to glutaric acid, identified by mixture melting point with an authentic sample.

7-Hydroxyheptanoic acid was separated from suberic acid by extraction with ether. Evaporation of the solvent left ca. 12 g. (15%) of crude hydroxy acid, which was heated with excess benzoyl chloride to 100° until no further hydrogen chloride evolved. Most of the excess benzoyl chloride was removed by vacuum distillation at 15 mm. Subsequent solution of the residue in anhydrous methanol and short refluxing gave methyl 7-benzoyloxyheptanoate, m.p. 130°.

Anal. Calcd. for C₁₅H₂₀O₄: C, 68.15; H, 7.64. Found: C, 68.42; H, 7.80.

The oxidation of 7-hydroxyheptanoic acid with nitric acid gave pimelic acid.

To determine a *cis* or *trans* selectivity of the ozonolysis, a mixture of 10 g. all-*trans*- and 10 g. of *cis*, *trans*, *trans*-cyclododecatriene was ozonized by the described technique. Two grams of the mixture was withdrawn from the reaction every 20 min. for the isomer ratio determination by gas chromatography. A similar method was applied for *cis*- and *trans*-4-methylpentene-2. In both cases no substantial isomer ratio shift in the unchanged olefin mixture was observed.

Homophthalide (18%) was separated from homophthalic acid by distillation *in vacuo*; it boiled at 140° (0.1 mm.), m.p. 79°. It was identified by mass and infrared spectroscopy.

Naphthalide, 13% crystallized from the hot aqueous filtrate of the naphthalic acid precipitation. Identification was by infrared spectroscopy; m.p. 153°, lit.⁴ m.p. 155–157°.

To confirm that the formate ion from the formation of the α -hydroxy acids would oxidize to carbon dioxide under the reaction conditions, a 10% aqueous sodium formate solution was prepared and 10% excess sodium hydroxide was added. Oxygen containing about 1.2% ozone was percolated through the formate solution for 3 hr. The alkaline solution was acidified; enough carbon dioxide evolved to account for 35% formate oxidation.

To determine the scope of the one-step process, a test was made with the emulsion ozonization of an open-chain olefin, octene-1, which reacted under the same conditions as described with cycloolefins. *n*-Heptanoic acid distilling at 114° (10 mm.) was obtained in 75% yield and was identified by infrared spectroscopy; formic acid also was formed (amount not determined). No peroxy polymer formed because of the monofunctional character of the products of cleavage.

(10) G. Wilke and H. Miller, German Provisional Patent 1,043,329 (November, 1958).

(11) R. M. Joyce, W. E. Hanford, and J. Harman, *J. Am. Chem. Soc.*, **70**, 2531 (1948).