THE REACTIONS OF OZONE WITH ORGANIC COMPOUNDS

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CONTENTS

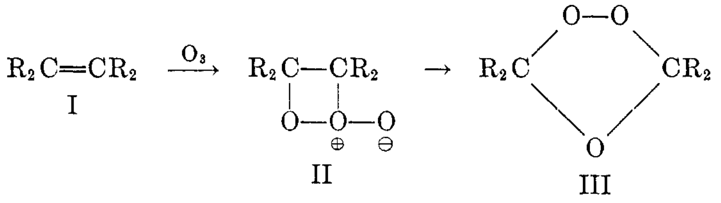
I. INTRODUCTION

There have been many new developments concerning the reactions of ozone with organic compounds since the review by Long (380) in 1940. These include a better understanding of the theory of the reactions, new industrial applications brought about by a decreased cost of production of ozone, and new reactions and techniques. A number of summaries have been written covering special aspects of this work (29, 31, 100, 196, 198, 201, 230, 267, 289, 364, 386, 388, 468, 480, 481, 542, 543, 544, 567, 569, 570, 571, 573, 574), but no comprehensive review has appeared. The present review will deal only with developments since 1939, unless prior investigations have not been covered adequately elsewhere.

Three terms are commonly used in regard to the reactions of ozone with organic substances. In this review the terms *ozonization* and *ozonation* are considered synonymous and will refer to the action of ozone on any substance. *Ozonolysis* will refer to cleavage by ozone of molecules at unsaturated linkages. The products may or may not contain active oxygen. By *active oxygen* is meant a peroxidic functional group which will oxidize iodide ion to iodine. Except where specifically stated to the contrary, the ozonolysis procedure under discussion will be the attack of gaseous ozone diluted with oxygen or air (1–10 per cent ozone by volume) upon an unsaturated substance in the liquid phase (pure or in solution).

II. MECHANISM OF OZONOLYSIS OF THE DOUBLE BOND

Since the classical work of Staudinger (529), most organic chemists have assumed that ozone reacts with a double bond to form initially an unstable "molozonide" (II), which then rearranges to the more stable ozonide (or "isoozonide") (III).



Mechanisms for this rearrangement have been proposed by Criegee (195), Leffler (364), and Milas (406, 407). Although Staudinger (529) suggested other possible fates for the molozonide (II), these often have been overlooked and an ozonide (III) has been an assumed intermediate in all ozonolysis reactions.

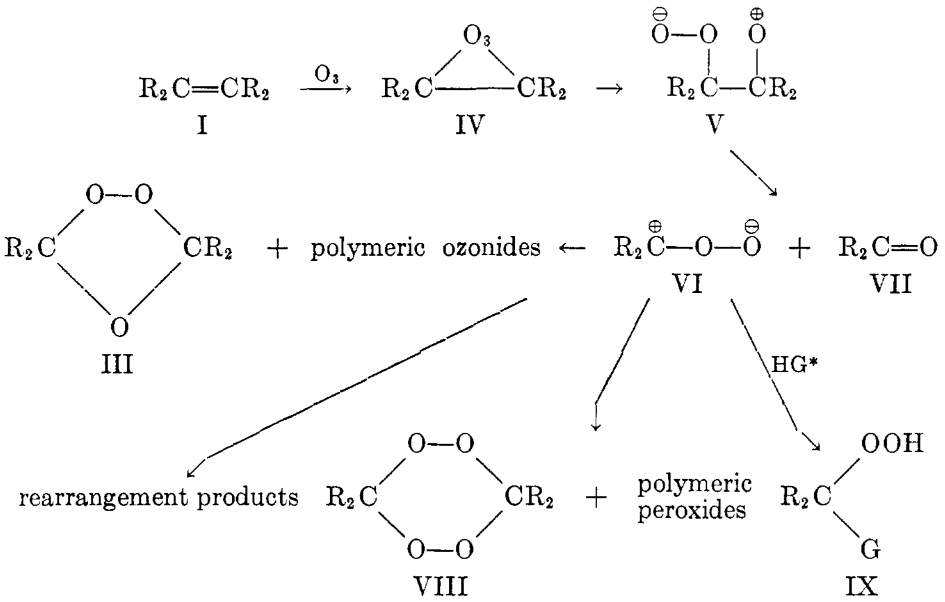
Answers to the following questions are necessary for an understanding of the ozonolysis reaction: (*1*) What is the structure of the ozone molecule? (*2*) What is the nature of the initial attack of ozone on an unsaturated system? (*3*) What is the route from the initial attack to the formation of the active oxygen-containing ozonolysis products? (*4*) What are the active oxygen-containing ozonolysis products? (*5*) What is the course of the conversion of the active oxygen-containing ozonolysis products to acids, aldehydes, ketones, and other nonperoxidic products?

Criegee and coworkers (36, 37, 199, 201, 205, 207, 209, 214, 379) have made great progress toward answering questions 3 and 4. The other questions can best be discussed after their work is described.

A. CRIEGEE MECHANISM: NATURE OF PEROXIDIC OZONOLYSIS PRODUCTS

1. Criegee mechanism

An extensive study of the active oxygen-containing products of ozonolysis of a wide variety of unsaturated substances in different types of solvents led to the following mechanism (201, 205, 207, 210, 214):



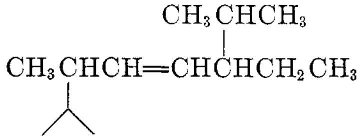
*G = OH, OR, or OCOR.

The first intermediate (IV), the structure of which Criegee leaves in doubt, is very unstable and cleaves to a zwitterion (VI) and an aldehyde or ketone (VII), presumably through the unstable intermediate V. The fate of VI depends partly on its structure, but largely on its environment. There are at least four ways in which it may stabilize itself (199, 201, 205, 207, 214): (*a*) polymerization, (*b*) reaction with a solvent of type HG, (*c*) reaction with an aldehyde or ketone, (*d*) rearrangement.

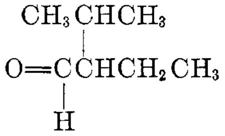
The reactions of zwitterion VI are competitive and no one of them is likely to be the sole reaction. Interaction with a reactive solvent generally occurs to give IX in high yield, since the concentration of the solvent far exceeds that of any other substance with which the zwitterion may react. Ozonides (III) and dimeric (VIII) or polymeric peroxides may be by-products. When the solvent is inert, the zwitterion must react either with itself or with VII. Reaction with VII to form a monomeric ozonide (III) as the major product and polymeric ozonides as minor products usually predominates if VII is an aldehyde. Since the carbonyl group of most ketones is less susceptible to nucleophilic attack than that of most aldehydes, zwitterion VI generally dimerizes (to VIII) and/or polymerizes when VII is a ketone.

Dimeric and polymeric peroxides often are by-products when VII is an aldehyde (205, 207, 334, 335, 378, 391, 392). The isolation of considerable amounts of benzaldehyde, formaldehyde, and acetaldehyde during ozonolyses of stilbene, styrene, anethole, and *O*-methylisoeugenol (112, 113, 114, 221) is indicative that these moieties are left as products when zwitterion VI polymerizes. This also may be the explanation for many of the reports in the literature concerning spontaneous decompositions of "ozonides" to aldehydes, ketones, and acids during ozonolysis (e.g., 297, 333).

Steric hindrance apparently can cause polymerization of VI to predominate even if VII is an aldehyde. Ozonolysis of the side-chain double bond of 4,22-stigmastadien-3-one (X) yielded approximately one mole of an aldehyde and one mole of peroxidic material per mole of compound (516, 517). The moiety from the right-hand side of the double bond of X (i.e., XI or the corresponding zwitterion) would be sterically hindered, and interaction with the moiety from the other side would be difficult. For example, there are nine hydrogen atoms in the "six position" of XI (429).



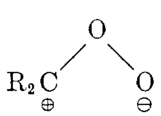
X



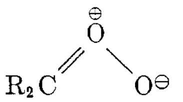
$O{=}\underset{H}{C}\overset{CH_3CHCH_3}{C}HCH_2CH_3$

XI

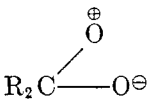
Zwitterion VI, the key intermediate in the Criegee mechanism, is a modernization of Staudinger's (380, 529) proposal of a minor fate for his molozonide (II). Criegee (200, 201) formulated the zwitterion as ionic rather than radical, because of its reactions and because it does not initiate the polymerization of olefins (such as styrene to polystyrene) during ozonolyses at low temperatures. He suggested that it is a hybrid of structures VI, XII, and, possibly, XIII, since its reactions indicate an actual, though short, lifetime (201). Such a hybrid might be represented conveniently by structure XIV.



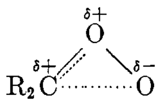
VI



XII



XIII



XIV

2. The peroxidic ozonolysis products

Ozonides frequently have been described as unstable viscous liquids or amorphous solids, too dangerous to purify and characterize. This unwarranted generalization is a result of a lack of distinction among the various types of peroxidic ozonolysis products. Many polymeric peroxides do have these properties (470).

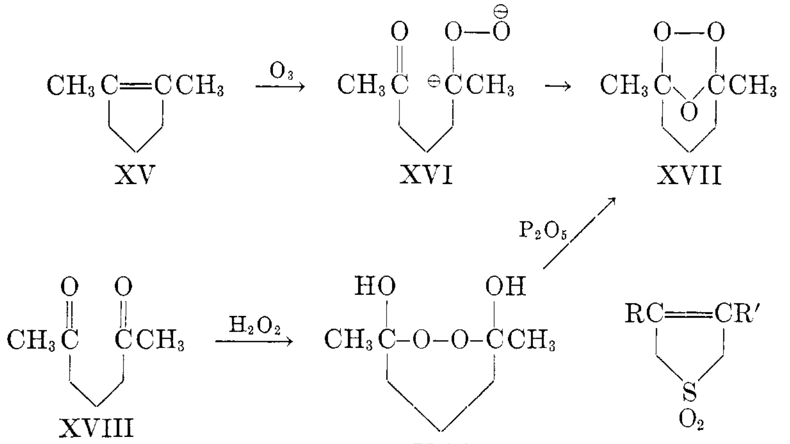
The term "ozonide" should refer only to a substance with a five-membered ring of type III. This structure has been established satisfactorily by Rieche and coworkers (380, 469, 470). Some examples of olefins which yield simple ozonides in inert solvents are 1-pentene, 1-hexene, 2-hexene, 3-hexene, 2-octene, 4-octene, 3,3-dimethyl-1-butene, styrene, and stilbene (207). These ozonides have sharp boiling or melting points.

There are at least two exceptions to the generalization that ozonides are not produced from compounds which yield a ketone (VII) along with zwitterion VI. One involves cyclic olefins in which the double bond is part of a five-membered ring or, in certain instances, a four-membered ring. The other concerns olefins which yield as VII a ketone with an activated carbonyl group (e.g., an α-keto ester).

Some examples of the first type are 1,2-dimethylcyclopentene (XV) (204, 207, 209, 210), the cyclic sulfone (XXa) of 2,3-dimethyl-1,3-butadiene (211), some maleic acid imides (XXI) (207, 466), the isomeric 1,2,3,4-tetramethylcyclobutenes (202), and certain indenes (Section IV,D), indenones (Section IV,D), indoles (Section V,D), and steroids (405, 473, 487). The very stable peroxide formed as a by-product during the ozonolysis of XXIII (477) is probably ozonide XXIV. The ozonides of five-membered unsaturated rings usually are quite stable. That of XXa melts at 154°C. and is stable to shock, heat (100°C. for 5 hr.), refluxing with alcohols or water, and refluxing with 1 *N* sulfuric acid at 100°C. for 2 hr. (211).

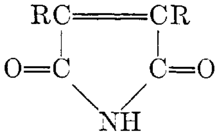
That these substances actually are ozonides has been established in the case of 1,2-dimethylcyclopentene ozonide (209). The substance was synthesized from the corresponding diketone (XVIII → XIX → XVII) by the same method used in the proof of the structure of 2-butene ozonide (380, 469, 470).

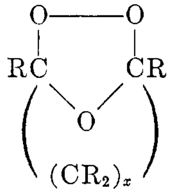
Apparently the driving force for intramolecular cyclizations of zwitterions of type XVI is the formation of systems containing, besides the five-membered trioxalan ring, six- and seven-membered rings (e.g., XVII) or five- and six-membered rings (e.g., XXIIa), all of which are classical rings (207). The tendency to form such systems would be much greater than the tendency to form



XV XVI XVII
XVIII XIX XX

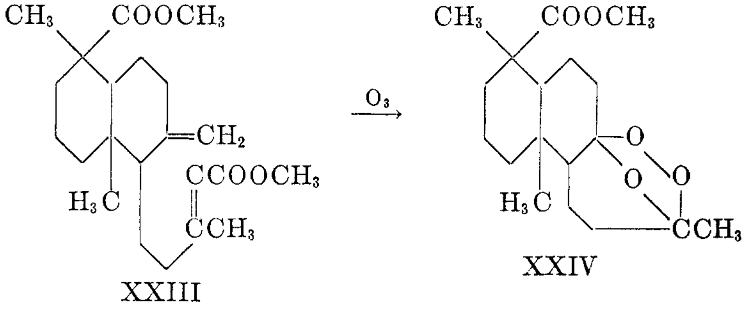
a: R = R′ = CH_3
b: R = *tert*-butyl; R ′ = H


XXI


XXII

a: $x = 2$

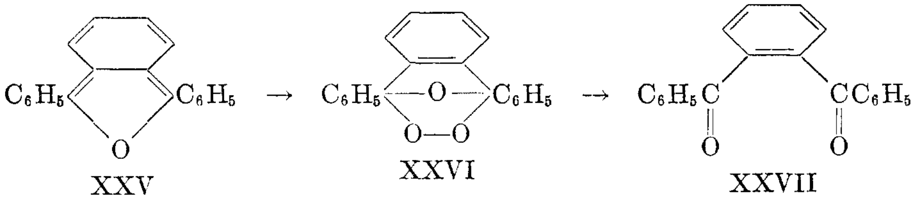
b: $x = 4$


XXIII XXIV

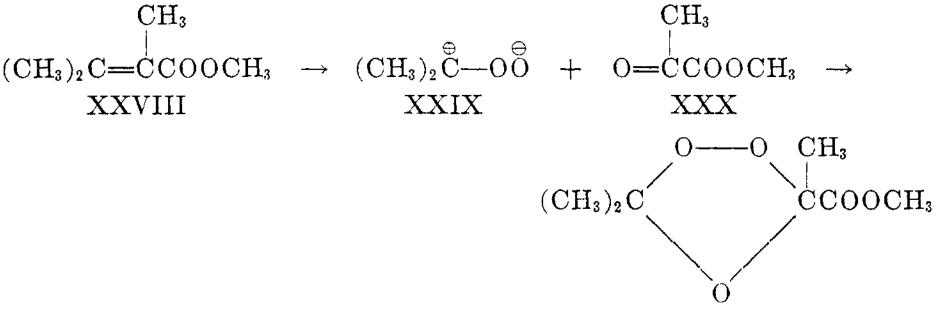
an ozonide of a cyclohexene derivative, which would have seven- and eight-membered rings (e.g., XXIIb). Cyclohexene, 1-methylcyclohexene, 1,2-dimethylcyclohexene, cycloheptene, cyclooöctene, and cholesterol yield largely polymeric ozonides and/or peroxides (72, 73, 204, 207, 209).

The yields of monoözonides from unsaturated five-membered ring systems in which there is only one or no substituent on the atoms of the double bond are much lower than the yields of monoözonides from the corresponding systems with substituents on both atoms of the double bond (204, 207). The lack of substituents around the zwitterion at one end and/or the carbonyl group at the other end of the cleavage product apparently allows intermolecular reaction to polymeric ozonides (or peroxides) to compete successfully with intramolecular cyclization. The cyclic sulfone (XXb) of 1-*tert*-butyl-1,3-butadiene is an exception, for it gave an 85 per cent yield of an ozonide (211, 378). The earlier reports that the sulfone formed an open-chain aldehyde peroxide upon ozonolysis in moist carbon tetrachloride (23, 24, 25) were shown to be erroneous (211).

Ozonides of type XXIIa reportedly have been produced by light-catalyzed autoxidation of certain furans (e.g., 2-methyl- and 2,5-dimethylfurans) (482, 483, 484) and of diphenylisobenzofuran (XXV) (241). The materials were very unstable and were characterized only by their reactions, such as reduction of XXVI to XXVII.


XXV XXVI XXVII

Compound XXXI is an example of an ozonide produced by the interaction of zwitterion VI and an activated ketone (XXX) (200, 201). The ozonolysis of XXVIII must have proceeded as shown, since the other possible ketone moiety, acetone, does not undergo zwitterion addition (210). The ability of methyl pyruvate (XXX) to react with zwitterion XXIX is analogous to the ability of such substances to form stable hydrates.

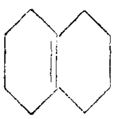

XXVIII XXIX XXX

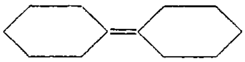
XXXI

Several structures have been suggested for polymeric ozonides (380, 470). A structure seems to have been reasonably well established, however, only for the polymeric ozonide of phenanthrene (51, 52) (Section IV,C).

Tetramethylethylene (210), tetraphenylethylene (392), 9,10-octalin (XXXII) (214), bicyclohexylidene (XXXIII) (210), and bicyclopentylidene (210) are examples of substances which yield a ketone and a mixture of dimeric and polymeric peroxides upon ozonolysis. Simple dimeric ketone peroxides, such as XXXIV (from tetramethylethylene), also have been obtained by treatment of the corresponding ketone with Caro's acid (H_2SO_5) or hydrogen peroxide (198). In general, they are stable, high-melting solids. No effort has been made to purify and characterize polymeric peroxides. They generally are described as explosive, viscous oils or amorphous solids (210, 470). The ones of high molecular weight probably are linear polymers of VI.

The literature before the work of Criegee spoke of "perozonides" and "oxozonides" (380, 423, 424, 425, 470). Probably most of these substances with greater oxygen contents than that of ozonides were dimeric (242) and polymeric peroxides (470). Some may have been peroxidic ozonolysis products in which further oxidation had occurred at some vulnerable part of the molecule (Section VII,C).


XXXII


XXXIII

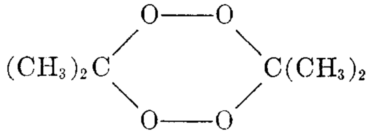
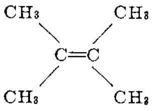
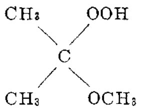
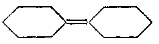
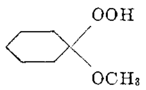
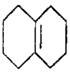
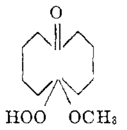
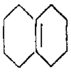
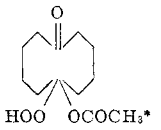
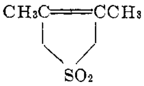
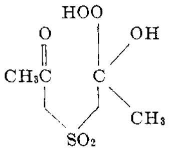
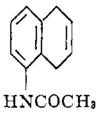
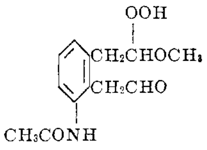
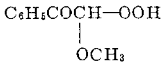
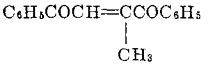
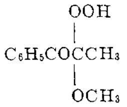

XXXIV

Table 1 lists some alkoxy, acyloxy, and hydroxy hydroperoxides obtained from ozonolyses in "reactive" solvents. Many of these substances are quite stable and some have relatively high melting points (hydroperoxide No. 5 melts at

TABLE 1

Hydroperoxides produced by ozonolysis

No.	Substance	Solvent	Product	Yield	Reference
				per cent	
1		CH_3OH		77	(210)
2		$CCl_4 + CH_3OH$		68	(210)
3		CH_3OH		88	(214)
4		Acetone + CH_3COOH			(214)
5		Acetone + water		57	(211)
6		CH_3OH		42	(456)
7	$C_6H_5COCH{=}CHCOC_6H_5$	Acetone + CH_3OH	 $C_6H_5COCH(OCH_3){-}OOH$	60	(44, 45)
8	 $C_6H_5COCH{=}C(CH_3)COC_6H_5$	Acetone + CH_3OH	 $C_6H_5COC(OOH)(OCH_3)CH_3$	74	(44, 45)

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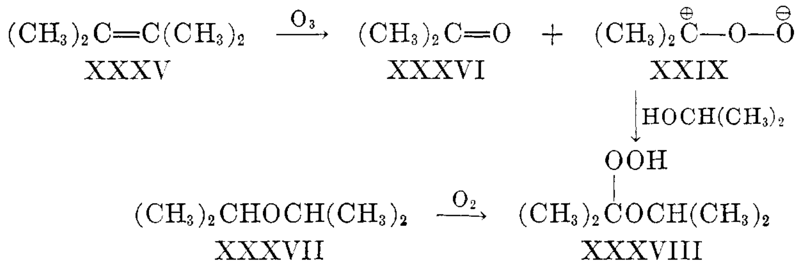
* Unstable; isolated as the benzoate (benzoperoxy derivative).

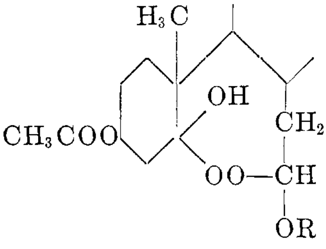
94–95°C.) (211). One alkoxy hydroperoxide (XXXVIII) has been obtained both by the ozonolysis of an alkene (XXXV) and by the autoxidation of an ether (XXXVII) (200, 201). Similar alkoxy hydroperoxides have been prepared by the addition of hydrogen peroxide to vinyl ethers (410).



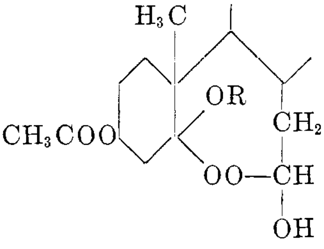
$$\underset{\text{XXXV}}{(CH_3)_2C{=}C(CH_3)_2} \xrightarrow{O_3} \underset{\text{XXXVI}}{(CH_3)_2C{=}O} + \underset{\text{XXIX}}{(CH_3)_2\overset{\oplus}{C}{-}O{-}\overset{\ominus}{O}} \xrightarrow{HOCH(CH_3)_2} \underset{\text{XXXVIII}}{(CH_3)_2\overset{OOH}{\overset{|}{C}}OCH(CH_3)_2} \xleftarrow{O_2} \underset{\text{XXXVII}}{(CH_3)_2CHOCH(CH_3)_2}$$

Alkoxy hydroperoxides obtained from the ozonolysis of cyclic molecules appear not to exist in the simple hydroperoxide form if the other end of the chain contains an aldehyde group (40). Where intramolecular reactions are sterically possible, cyclic hydroxy peroxides are produced, or, where only intermolecular reactions can occur readily, polymeric hydroxy peroxides are formed. These interactions are to be expected, since hydroperoxides tend to add to the carbonyl group of aldehydes and ketones to give hemiperacetals and peracetals (198).

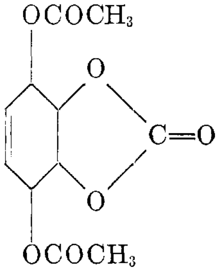
The intramolecular reaction occurs during the ozonolysis of phenanthrene (38, 577), naphthalene (48), or indene (561) in methanol or ethanol (Section IV). Cholesteryl acetate (367, 368) and the cyclohexene derivative XLI (203) also appear to yield cyclic hydroxy peroxides (XXXIX or XL from cholesteryl acetate, and XLII from XLI). The tendency for cyclization to occur exists even if the other end of the chain is a ketone. The product of the ozonolysis of the cyclic sulfone (XXa) of 2,3-dimethyl-1,3-butadiene in methanol appears to be an equilibrium mixture of XLIII and XLIV, at least in solution (211). In contrast to these results the ozonolysis product of 5-acetamido-1,4-dihydronaphthalene was assigned an open-chain structure (No. 6 in table 1) (456). The evidence, however, was not conclusive.



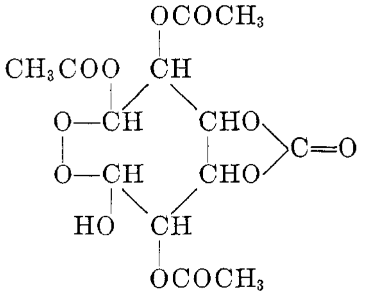
XXXIX



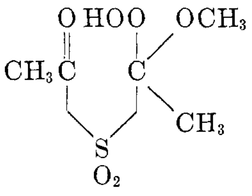
XL



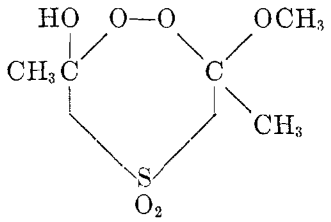
XLI



XLII

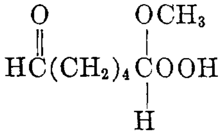


XLIII



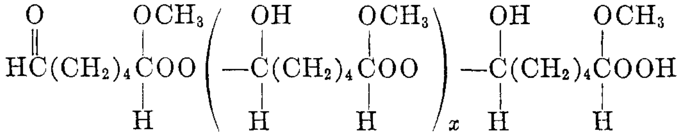
XLIV

The intermolecular reaction occurs during the ozonolysis of cyclohexene in methanol. The product appears to be a mixture with a methoxyl content between the extremes XLVI and XLVII (40). It most likely is formed by hemiperacetalization of XLV to XLVI, followed by partial acetalization.



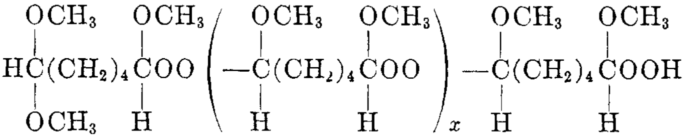
$$H\overset{O}{\overset{\|}{C}}(CH_2)_4\underset{H}{\overset{OCH_3}{C}}OOH$$

XLV



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

XLVI



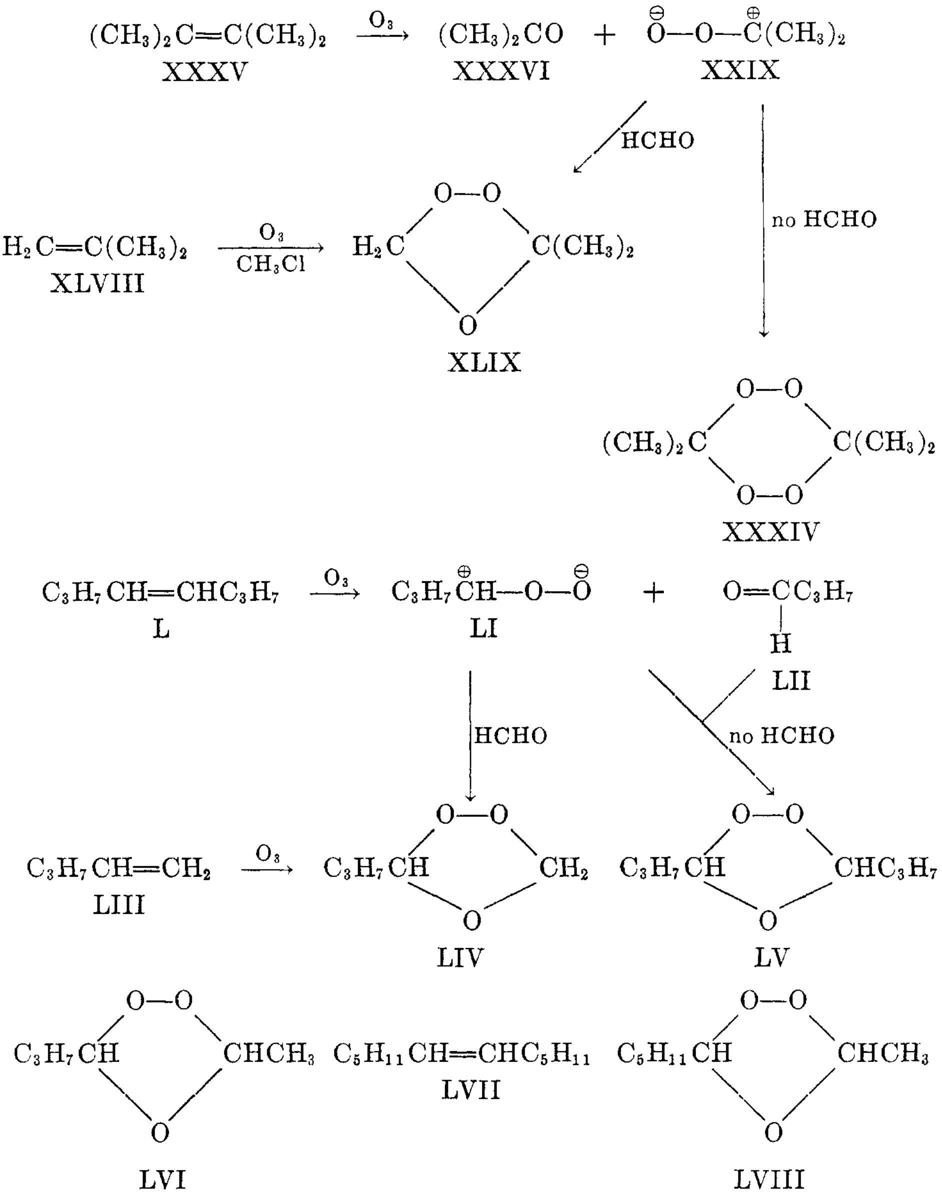
$$H\underset{OCH_3}{\overset{OCH_3}{C}}(CH_2)_4\underset{H}{\overset{OCH_3}{C}}OO\left(-\underset{H}{\overset{OCH_3}{C}}(CH_2)_4\underset{H}{\overset{OCH_3}{C}}OO\right)_x-\underset{H}{\overset{OCH_3}{C}}(CH_2)_4\underset{H}{\overset{OCH_3}{C}}OOH$$

XLVII

3. Confirmatory evidence for Criegee mechanism

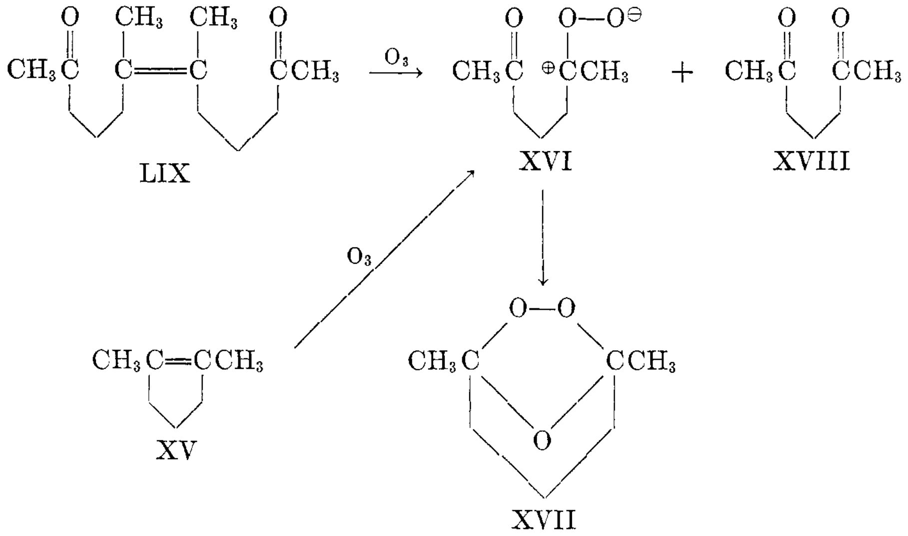
The existence of the zwitterion intermediate VI in ozonolysis has been demonstrated in three different ways. The first deals with the ozonolysis of several alkenes in inert solvents containing an excess of a reactive aldehyde. From tetramethylethylene (XXXV) in the presence of formaldehyde was obtained isobutene ozonide (XLIX) instead of dimeric (XXXIV) and polymeric peroxides (205, 210). 4-Octene (L), in the presence of formaldehyde and of acetaldehyde, gave 1-pentene ozonide (LIV) and 2-hexene ozonide (LVI), respectively, instead of 4-octene ozonide (LV) (84, 205). 6-Dodecene (LVII), in the presence of acetaldehyde, produced 2-octene ozonide (LVIII) instead of 6-dodecene ozonide (84). In these instances the zwitterions (e.g., XXIX and LI) reacted with the most reactive substance (formaldehyde) and/or that substance (formaldehyde or acetaldehyde) present in highest concentration, rather than with themselves or with the aldehyde (e.g., LII) moieties produced simultaneously with them. The fact that 4-octene ozonide (LV) did not react with formaldehyde under the conditions of these transformations is evidence that the reactants were the zwitterions (201).

The second demonstration of the existence of the zwitterion intermediate involved the ozonolysis of 6,7-dimethyl-6-dodecene-2,11-dione (LIX) in an inert solvent. The products were 2,6-heptanedione (XVIII) and the ozonide

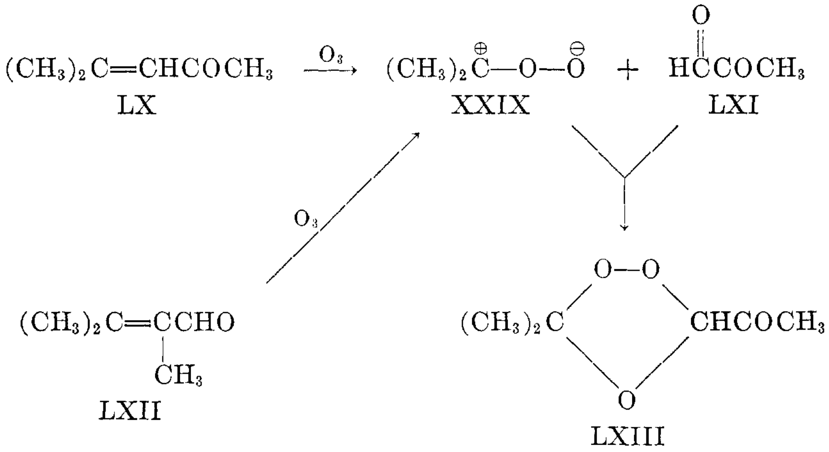


(XVII) of 1,2-dimethylcyclopentene (XV), showing that the same zwitterion (XVI) was formed in the ozonolyses of both LIX and XV (379).

The isolation of the same ozonide (LXIII) from ozonolyses of mesityl oxide (LX) and 2,3-dimethylcrotonaldehyde (LXII) in inert solvents is the third confirmation of the existence of the zwitterion intermediate (200, 201). For this to happen, intermediates XXIX and LXI would have to be common to both reactions. It is assumed that methylglyoxal (LXI) reacted through its aldehyde group to form LXIII (201).



The Criegee mechanism explains the fact that cis and trans isomers give the same ozonide. This has been reported in the cases of stilbene and isostilbene (207), the di-*t*-butylethylenes (201), and the dimethyl, diethyl, and diphenyl esters of fumaric and maleic acids (273, 378). The complete breakdown into the zwitterion and aldehyde followed by recombination of these fragments would lead to the more stable ozonide in each case. The finding that the trans isomer of a given pair reacts faster than the cis isomer (53, 121, 380, 433), however, is not yet understood. Thermochemical calculations indicate that the heat of formation of an ozonide is greater from cis than from trans isomers (116).

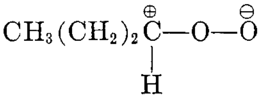


The fact that 3-heptene (LXIV) gave a different ozonide (or mixture of ozonides), as shown by infrared spectra, than did an equimolar mixture of 3-hexene (LXV) and 4-octene (L) (201, 202) initially seems contradictory to the Criegee mechanism. Since either 3-heptene or the mixture of 3-hexene and 4-octene should yield both zwitterions LI and LXVII and both aldehydes LXVI and LII, it might be expected that, through recombinations of these, identical mixtures of the ozonides of 3-heptene, 3-hexene, and 4-octene would be produced. Criegee (201) has explained the fact that this does not happen on the basis that the olefins react in a "solvent cage." In more detail this would mean that the lifetime of the zwitterion is very short and that it stabilizes itself immediately by interaction with the nearest available reactive molecule. This is the aldehyde molecule produced along with it. The zwitterion can react appreciably with another aldehyde only if an excess of the foreign aldehyde is added previously to the reaction mixture. It is likely that some exchange did occur in the cases of 3-heptene and the mixture of 3-hexene and 4-octene, but the major products were the ozonides of each individual olefin.

$CH_3(CH_2)_2CH{=}CHCH_2CH_3$ LXIV

$CH_3(CH_2)_2CH{=}CH(CH_2)_2CH_3$ L

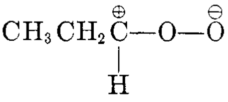
$CH_3CH_2CH{=}CHCH_2CH_3$ LXV



$CH_3(CH_2)_2\underset{\displaystyle H}{\overset{\oplus}{C}}-O-\overset{\ominus}{O}$

LI

CH_3CH_2CHO LXVI



$CH_3CH_2\underset{\displaystyle H}{\overset{\oplus}{C}}-O-\overset{\ominus}{O}$

LXVII

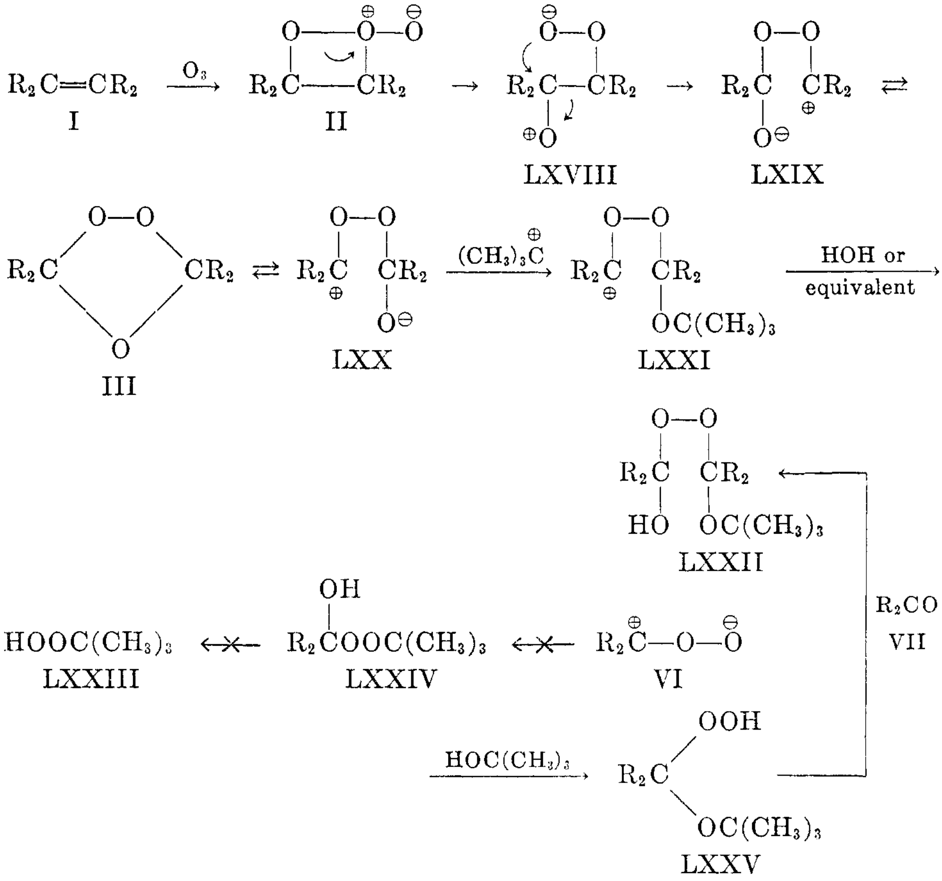
$CH_3(CH_2)_2CHO$ LII

4. Milas mechanism

Milas (406, 407, 409) has proposed a different mechanism (I → II → LXVIII → LXIX, etc.) for the ozonolysis reaction in order to account for the isolation of products of type LXXII from ozonolyses of several olefins in mixtures of *tert*-butyl alcohol and concentrated sulfuric acid and for the reported isolation of the ozonide of tetramethylethylene. According to this mechanism, an ozonide (LXIX $\rightleftarrows$ III $\rightleftarrows$ LXX) is an intermediate in all ozonolyses, dimeric and polymeric peroxides are produced by decompositions of LXIX or LXX, followed by polymerization of the resulting zwitterion (type VI), and compounds of type LXXII are produced by interaction of LXIX or LXX with *tert*-butyl carbonium ions. The mechanism was supported by the fact that no product from the reaction of zwitterions of type VI with *tert*-butyl carbonium ions (e.g., LXXIII or LXXIV) was isolated from ozonolyses in mixtures of *tert*-butyl alcohol and sulfuric acid (407).

Although it is possible that the mechanism of ozonolysis is different under the drastic conditions of Milas and coworkers (407), the formation of LXXII is readily understandable on the basis of the Criegee mechanism (i.e., I → VI → LXXV → LXXII). Since the concentration of *tert*-butyl alcohol itself was much greater than that of *tert*-butyl carbonium ions (407), zwitterion VI should be converted to LXXV rather than to LXXIV. Interaction of LXXV with VII to produce LXXII is to be expected under the strongly acidic conditions of the reaction mixture (198). The material assumed to be the ozonide of tetramethylethylene

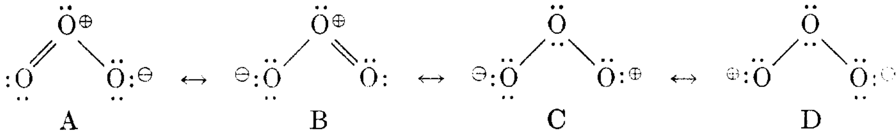
(407) has been shown to have a much higher active oxygen content and, thus, more likely to be a polymer of zwitterion XXIX (210).



B. INITIAL ATTACK OF OZONE: ROUTE TO THE ZWITTERION INTERMEDIATE

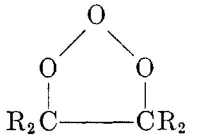
The major contribution of Criegee (preceding section) has been to characterize the active oxygen-containing ozonolysis products and the zwitterion (VI) intermediate leading to their formation. The Criegee mechanism, however, does not elucidate the nature of the initial attack by ozone, nor does it satisfactorily define the course of the reaction from the initial attack by ozone to the zwitterion (VI) intermediate.

Essential to the study of the initial attack by ozone is an understanding of the structure of the ozone molecule itself. It seems finally to be settled that the ozone molecule has an obtuse angle (116°45′ ± 30′) and a bond length of 1.278 ± 0.002 A. (259, 260, 317, 548; *cf.* 2, 35, 226, 231, 283, 315, 316, 418, 502, 510). It is not paramagnetic (259, 260, 315, 316, 543, 548) and probably is diamagnetic in the gaseous state (9). On this basis it can be described as a hybrid of the principal structures LXXVIA, B, C, and D (548). The molecular orbital theory description (548) is that the four valence orbitals of the apex oxygen atom consist of three sp^2 hybrids which lie in a plane and a pure p orbital which is normal to the plane. Two of the sp^2 orbitals form localized σ-molecular orbitals with a bonding orbital of each end oxygen atom, while the p orbital forms π molecular orbitals with orbitals of the terminal atoms. The electrons of the π orbitals are not localized, but are moving throughout the molecule. The third sp^2 hybrid of the apex oxygen is directed upward along the symmetry axis and has an unshared electron pair. The surprisingly low dipole moment of the ozone molecule (0.56 ± 0.05 Debye unit) (317, 548) has been explained on the basis that the large dipole of the third sp^2 hybrid opposes the large primary moment expected from canonical forms such as LXXVIA and B (265, 548).

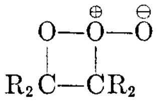


LXXVI

Prior to 1957, two major types of initial attack by ozone had been proposed. Both lead to an initial ozone adduct of either type LXXVII or type II.



LXXVII



II

One mechanism classifies ozone, osmium tetroxide, and diazoacetic ester as "double-bond reagents" and presumes that they make a one-step, four-center attack on a double bond, or on the bond of an aromatic system with the lowest "bond (or ortho) localization energy" (most double-bond character) (26, 27, 28, 29, 30, 31, 33, 34, 159, 161, 162, 163, 165, 232, 338, 355). With such a mechanism it is meaningless to distinguish between an ionic and a radical type of attack.

The other mechanism proposes a two-step attack, the first step being electrophilic in regard to the ozone molecule (88, 234, 329, 511, 512, 514, 577, 584, 587, 589). Such an attack should occur at the position of lowest "atom-localization energy" of an aromatic system (163, 165, 166, 167, 232). Meinwald (399) has pointed out that the electrophilic center of the ozone molecule must be a terminal atom rather than the previously assumed (329, 406, 407, 512, 584, 588, 589) central atom. Only with a terminal atom is an open sextet of electrons readily available (structures C and D of hybrid molecule LXXVI). Analogy is found in the diazonium ion ($R-\overset{\oplus}{N}\equiv N: \leftrightarrow R-\overset{\cdot\cdot}{\ }=\overset{\oplus}{N}:$).

The principal argument for the one-step attack is that the ozonolysis of pyrene occurs at the bond of lowest bond-localization energy, whereas electrophilic substitution occurs at the carbon atoms of lowest atom-localization energies (Section IV,C).

Wibaut and coworkers (88, 234, 329, 511, 512, 514, 577, 584, 587, 589) have been the principal proponents for an initial electrophilic attack. They showed that catalysts for electrophilic reactions, such as boron trifluoride and aluminum and ferric chlorides, accelerate the rates of ozonolysis of benzene and its derivatives. These rates also increased as the polarity of the solvent increased. A comparison of the rates of ozonolysis of various aromatic compounds showed a parallelism between ozonolysis and electrophilic substitution reactions (Section IV).

Olefinic compounds behave similarly. Substances with halogen atoms directly attached to a doubly bonded carbon atom react very slowly with ozone (53, 433, 540). Phenyl and carbonyl groups likewise lower the rate of ozone absorption at a double bond (433).

Further evidence for the two-step attack comes from the ozonolysis of anthracene and of certain unsymmetrical olefins. Ozonolysis of anthracene occurred at the atoms of lowest atom-localization energy to give anthraquinone in good yield; the bond of lowest bond-localization energy is the 1,2-bond (Section IV,C).

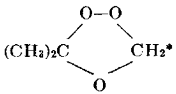
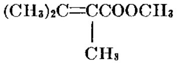
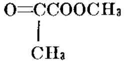
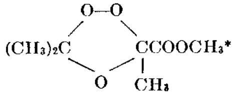
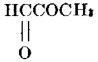
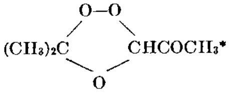
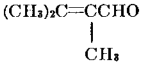
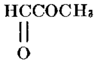
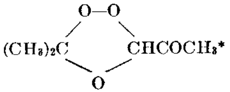
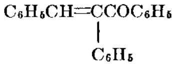
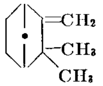
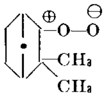
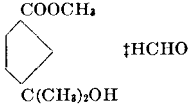
Upon ozonolysis of unsymmetrical olefins the double bone is ruptured in such a way as to produce zwitterion VI predominantly from one particular side and the aldehyde or ketone moiety from the other (37, 44, 45, 53, 54, 399). Some examples are shown in table 2. In examples 1 to 4 the predominantly formed fragments must have been as shown, because the other possible ketone in each case (acetone) does not react with zwitterions to form ozonides (210). The specificity of reaction was proven in the cases of *cis*- and *trans*-1,2-dibenzoylpropene (LXXVIIIa) by ozonizing in methanol and trapping the zwitterion moiety in the form of its methoxy hydroperoxide (44, 45, 53). The yields of phenylglyoxal (LXXXIV) and hydroperoxide LXXXVI from the trans isomer were 61 per cent and 74 per cent, respectively. Preferential cleavage of *cis*-1,2-dibenzoyl-1-phenylethylene (LXXVIIIb) also resulted in phenylglyoxal (LXXXIV) and zwitterion LXXXVb (53). These results can be explained by the changes LXXVIII → LXXIX → LXXX → LXXXIII → LXXXIV + LXXXV, and LXXXV → LXXXVI (44, 45). In the case of LXXVIIIb, the resonance effect of the phenyl group must have been the controlling factor. The results with examples 1 to 6 of table 2 can be explained similarly.

Such a mechanism would predict the products phenylglyoxal (LXXXIV) and zwitterion XCV from 1,2-dibenzoyl-1-methoxyethylene (LXXXVII → LXXXVIII → LXXXIX → XCII → LXXXIV + XCV), a result which, however, is contrary to experiment (53, 54). The products were hydroperoxide XCVI (from zwitterion XCVII) and XCVIII in 85 per cent and 75 per cent yields, respectively. Apparently the inductive effect rather than the resonance effect of the methoxyl group governed the course of the reaction. This also appears to be true with examples 7 and 8 of table 2.

In an effort to find a mechanism consistent with the conflicting data presented, the initial formation of a complex (e.g., LXXXI or XC) between the electrophilic terminal oxygen atom of the ozone molecule and the π electrons of the unsaturated molecule was suggested (39, 54). Such a complex should form at the

TABLE 2

Products from ozonolyses of unsymmetrical olefins

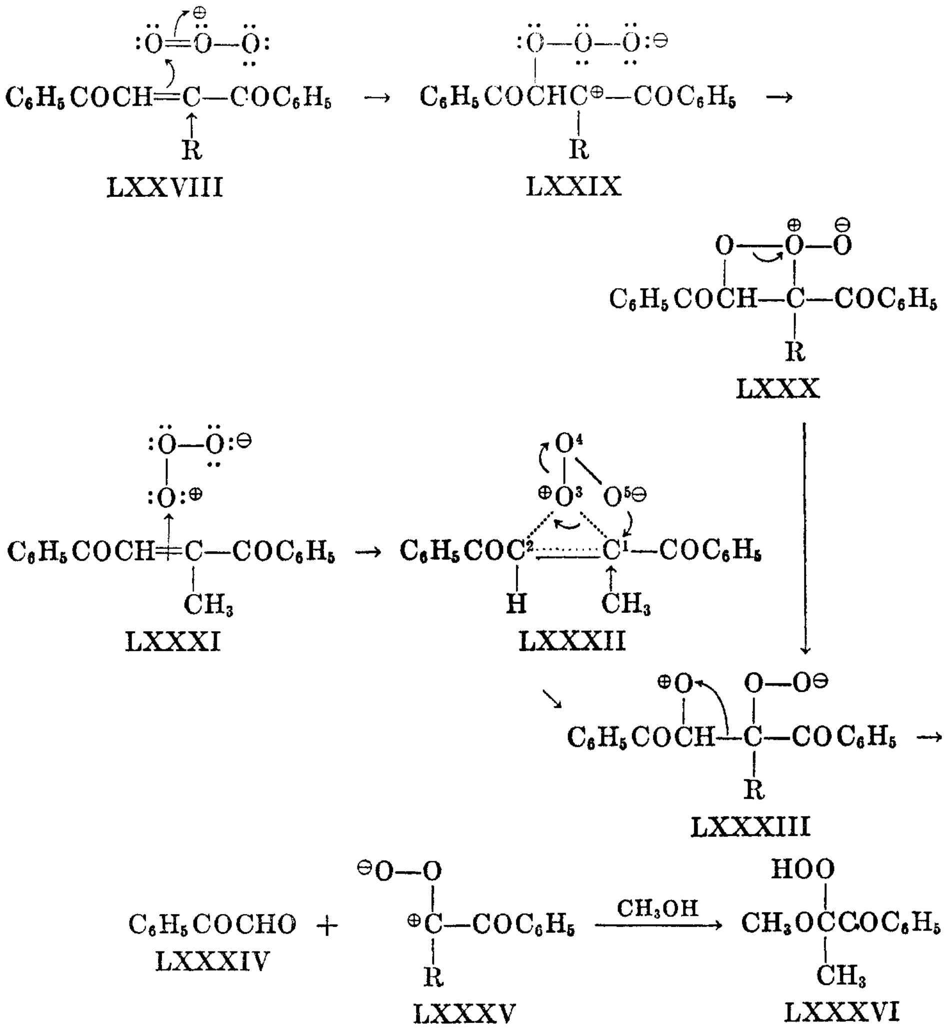
No.	Reference	Compound	Zwitterion	Carbonyl Compound	Final Product(s)
1............	(205)	$(CH_3)_2C{=}CH_2$	$(CH_3)_2\overset{\oplus}{C}\text{—}O\text{—}\overset{\ominus}{O}$	HCHO	
2............	(200, 201)	 $(CH_3)_2C{=}\underset{CH_3}{\underset{\vert}{C}}COOCH_3$	$(CH_3)_2\overset{\oplus}{C}\text{—}O\text{—}\overset{\ominus}{O}$	 $O{=}\underset{CH_3}{\underset{\vert}{C}}COOCH_3$	
3............	(200, 201)	$(CH_3)_2C{=}CHCOCH_3$	$(CH_3)_2\overset{\oplus}{C}\text{—}O\text{—}\overset{\ominus}{O}$	 $H\underset{O}{\underset{\Vert}{C}}COCH_3$	
4............	(200, 201)	 $(CH_3)_2C{=}\underset{CH_3}{\underset{\vert}{C}}CHO$	$(CH_3)_2\overset{\oplus}{C}\text{—}O\text{—}\overset{\ominus}{O}$	 $H\underset{O}{\underset{\Vert}{C}}COCH_3$	
5............	(206)	 $C_6H_5CH{=}\underset{C_6H_5}{\underset{\vert}{C}}COC_6H_5$	$C_6H_5\overset{\oplus}{C}H\text{—}O\text{—}\overset{\ominus}{O}$	$C_6H_5COCOC_6H_5$	$C_6H_5COCOC_6H_5$, C_6H_5COOH*†
6............	(37)			HCHO	
7............	(103, 221)	$p\text{-}CH_3OC_6H_4CH{=}CHCH_3$	$CH_3\overset{\oplus}{C}H\text{—}O\text{—}\overset{\ominus}{O}$	$p\text{-}CH_3OC_6H_4CHO$	Infrared spectra showed large amounts of free aromatic aldehydes
8............	(103, 221)	$3,4\text{-}(CH_3O)_2C_6H_3CH{=}CHCH_3$	$CH_3\overset{\oplus}{C}H\text{—}O\text{—}\overset{\ominus}{O}$	$3,4\text{-}(CH_3O)_2C_6H_3CHO$	

* Inert solvent.

† Benzoic acid presumably formed by rearrangement of zwitterion $C_6H_5\overset{\oplus}{C}HO\text{—}\overset{\ominus}{O}$ (Section II, C, 2).

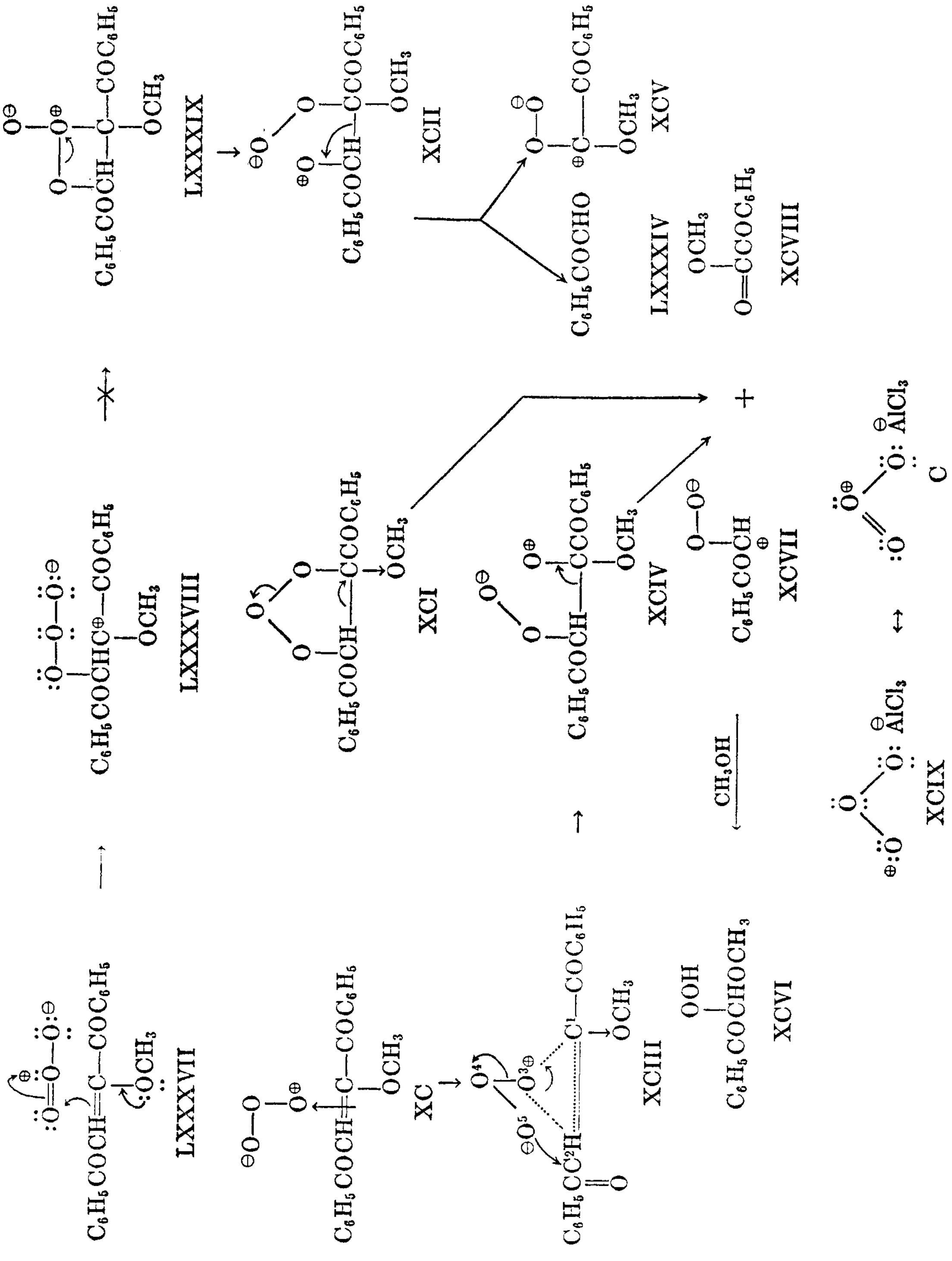
‡ Methanol as solvent; cyclopentane derivative by a rearrangement of the methoxy hydroperoxide formed from the zwitterion (Section II, C, 2).

bond of lowest bond-localization energy rather than at the carbon atom of lowest atom-localization energy. In the presence of aluminum chloride and similar catalysts, the attacking reagent could be a complex such as XCIX (or XCIX ↔ C), in which the electrophilic character of the ozone molecule is enhanced.

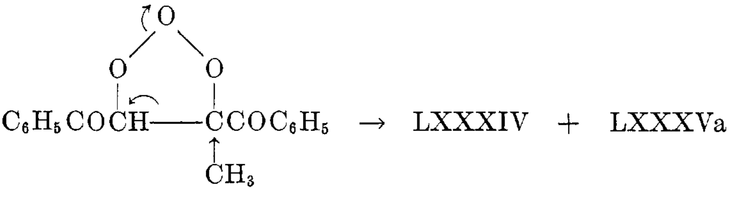


a: R = CH_3. b: R = C_6H_5.

The π complex (e.g., LXXXI or XC) should collapse quickly to a structure such as LXXXIII. Assuming that the collapse is by a concerted process, it is not unreasonable that the permanent inductive effects rather than the time-variable resonance effects of the groups around the original double bond should determine (with unsymmetrical molecules) at which carbon atom a carbon–oxygen bond is first formed. In example LXXXI the methyl group repels the electrons (and the attracted ozone molecule), so that the first carbon–oxygen bond begins to


LXXXVII
LXXXVIII
LXXXIX
XC
XCI
XCII
XCIII
XCIV
XCV
LXXXIV
XCVI
XCVII
XCVIII
XCIX
CH3OH
C

form between atoms 2 and 3 (structure LXXXII). The inductive effect of the methoxyl group in example XC is in the opposite direction, and the first carbon–oxygen bond begins to form between atoms 1 and 3 (structure XCIII). Simultaneous with these partial bond formations, the negative end of the ozone molecule (atom 5 in LXXXII and XCIII) begins to attack the other, now partially positive, carbon atom of the double bond (atom 1 in LXXXII and atom 2 in XCIII). Since there is still some attraction between the π electron-attracted terminal oxygen atom of the ozone molecule and both carbon atoms of the original double bond (atoms 1, 2, and 3 in LXXXII and XCIII), the bond between oxygen atoms 3 and 4 (in LXXXII and XCIII) becomes strained and is cleaved, producing LXXXIII and XCIV.



CI

Alternatively, it seems possible for a competition to exist between a two-step attack leading to a four-membered ring and a one-step attack leading to a five-membered ring, the decomposition of which would be controlled by the inductive effects of the surrounding groups (e.g., XCI → XCVII + XCVIII and CI → LXXXIV + LXXXVa) (386, 534). The former mechanism would be favored by polar solvents or ionic catalysts (e.g., XCIX) and the latter by nonpolar solvents. The conflicting results with pyrene and anthracene were decisive only with a nonpolar solvent in the first case and a polar solvent in the second case (Section IV,C).

The intermediates (e.g., LXXX, LXXXIII, XC, and XCI) of the various mechanisms would be expected to be unstable; this is consistent with the facile cleavage of a double bond at low temperatures. The heat of reaction of ozone with an olefinic bond is roughly 100 kcal. per mole (115).

The π complex theory explains all results except those with LXXVIIIb. The dual mechanism theory is consistent with the results of table 2, most of which were obtained in nonpolar solvents. It would predict, however, that compound LXXXVII should behave like compounds LXXVIII, since the same polar solvent was used for the ozonolysis of each.

At the present time it does not seem possible to choose among the alternatives presented or to suggest better ones. For the sake of simplicity, however, the π complex mechanism will be employed in the following sections.

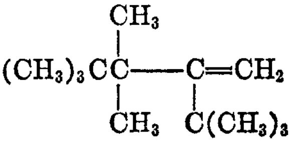
C. ABNORMAL OZONOLYSES: REARRANGEMENTS DURING DECOMPOSITIONS OF PEROXIDIC OZONOLYSIS PRODUCTS

The techniques, and that which can be said concerning the mechanisms, of the conversion of peroxidic ozonolysis products to nonperoxidic materials are discussed in Section VIII,C. The present section discusses the decomposition of peroxidic ozonolysis products to so-called "abnormal" products. Most of these "abnormal ozonolyses" can be classified either as (*1*) those in which the double bond is only partially cleaved and the final products contain the same number of carbon atoms as the original olefin, or (*2*) those in which rearrangements occur and the major product contains fewer than the expected number of carbon atoms.

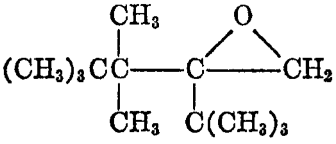
1. Ozonolyses in which the double bond is partially cleaved

Ozonolyses of olefins which are sterically hindered on one side of the double bond often result in the direct formation of epoxides, or rearrangement products thereof, containing the same number of carbon atoms as the starting material (22, 61, 62, 67, 271, 336, 398, 478). Examples are compounds CII (61) and CIV (271), which yielded CIII and CVII, respectively. Highly acid-sensitive epoxides (CVI) have been isolated as precursors to enols CVII (200, 201).

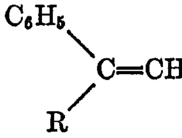
The formation of CXI as a minor ozonolysis product of α-fenchene (CVIII) (352, 353) probably involves an epoxide (CVIII → CIX → CX → CXI). This


$(CH_3)_3CC(CH_3)_2C(=CH_2)C(CH_3)_3$

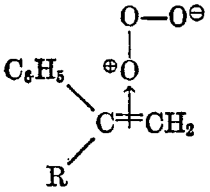
CII



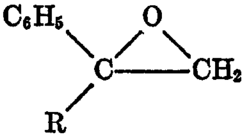
CIII



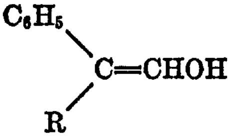
CIV



CV

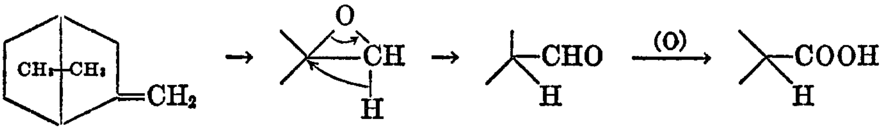


CVI

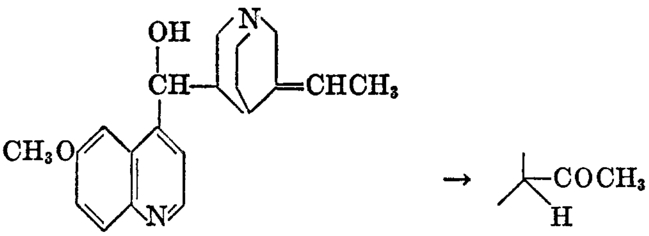


CVII

R = mesityl or isoduryl.



CVIII CIX CX CXI

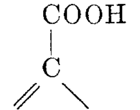


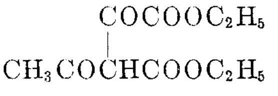
CXII CXIII

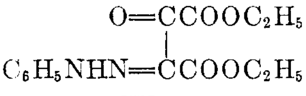
also would explain the formation of CXIII by ozonation of β-isoquinine (CXII) (601). In fact, it was never definitely established that the product was CXIII instead of an epoxide. Similar cases also are known (252, 420).

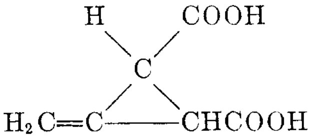
These reactions can be explained by the initial formation of a π complex (CV) (Section II,B). Because of steric hindrance, the complex can stabilize itself more easily by losing a molecule of oxygen and forming an epoxide (CVI) than by collapsing to a zwitterion such as V (Section II,B). The loss of oxygen during an attempt to complete a two-step attack (Section II,B) would also explain these results. Ozonolyses of compounds sterically hindered on both sides of the double bond occur very slowly or not at all (12, 415). For example, the bimolecular rate constants for ozonolyses of mesitylene and hexamethylbenzene are 250 and 15,000, respectively, whereas those for 1,3,5-tri-*tert*-butylbenzene and hexaethylbenzene are only 40 and 202, respectively (12).

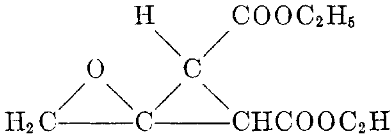
Feist's acid (254, 255), which originally was assigned structure CXIV because ozonolysis of its diethyl ester yielded CXV but no formaldehyde (275), has been shown to have structure CXVII (96, 249, 250, 337, 375, 376, 452). Bottini and Roberts (96) have suggested that the ozonolysis occurred as follows: CXX → CXXI → CXXII → CXXIII → CXXIV → CXXV → CXV. The reactions involved are reasonable, but are quite different from any so far encountered during ozonolysis. The mechanism also appears inapplicable to the analogous failure of methylenecyclopropane to give more than a trace of formaldehyde upon ozonolysis (276).

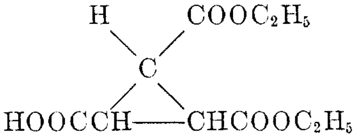

CXIV


$$CH_3CO\overset{COCOOC_2H_5}{\overset{|}{C}}HCOOC_2H_5$$
CXV

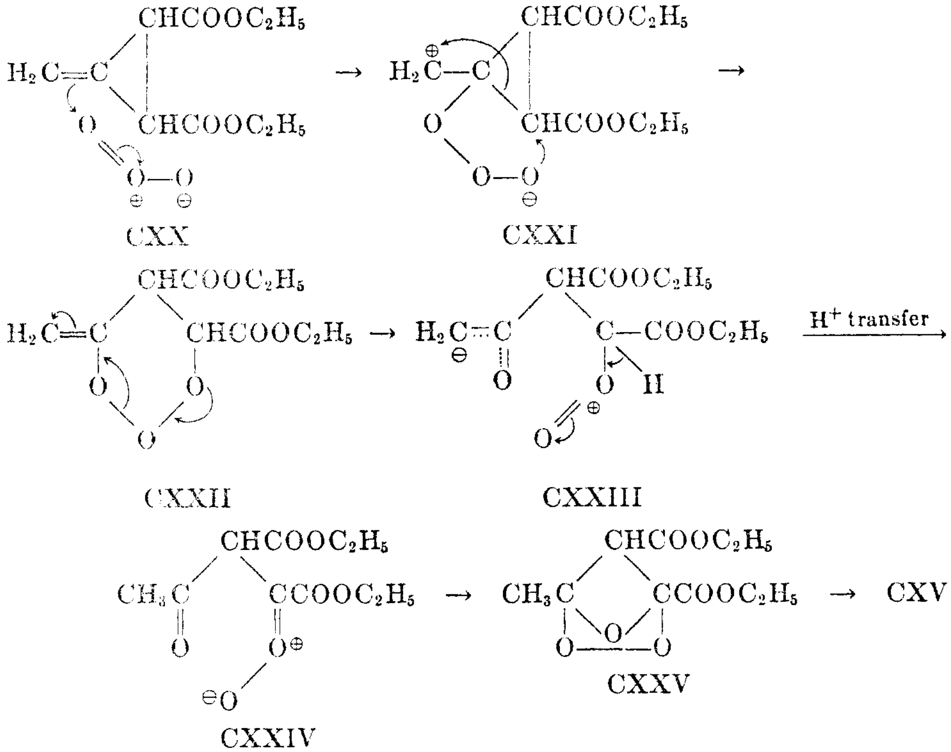

$$C_6H_5NHN{=}\overset{O{=}CCOOC_2H_5}{\overset{|}{C}}COOC_2H_5$$
CXVI


CXVII

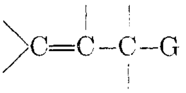
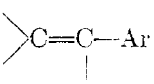

CXVIII


CXIX

The identification of CXV was based on its analysis, solubility in base, and conversion to an unreported amount of CXVI (275). It seems possible that the material actually was the isomeric acid CXIX, produced by rearrangement of the epoxide (CXVIII) and oxidation of the corresponding aldehyde.



2. *Rearrangements*

Many of the "abnormal ozonolyses" involving rearrangements have been listed and reviewed by Leffler (364) and Depoorter (230). The most thorough studies have been made by Young (605), Späth (524, 525), Criegee (206), and Witkop (597, 598, 599) and their coworkers. In general it can be said that varying amounts of "abnormal" products will result if the olefin being ozonized possesses either the system  $>C{=}C{-}C{-}G$ (G is N, O, or S) or the system  $>C{=}C{-}Ar$ (Ar is an aryl group bearing N, O, or S) (206, 364).

Young and coworkers (230, 364, 605) have ozonized a number of allylic compounds of the types $RCH{=}CHCHR'G$ and $RCHGCH{=}CHR'$ (R is H or alkyl and G is halogen, OH, NR_2, OR, or OCOR) in inert solvents and have quantitatively identified the carboxylic acids obtained by a mild oxidative work-up procedure (Section VIII,C,1). They showed that no "abnormal" products were obtained when G was Cl, Br, or $OCOCH_3$ and that, including these groups, the extent to which G promoted abnormal results varied roughly as follows: Cl, Br, or $OCOCH_3$ < $OC_6H_4NO_2$-*p* < OC_6H_5 < OH < OCH_2CH_3 < $N(CH_2CH_3)_2$. Examples of the "abnormal" behavior are CXXVI, which gave, besides formic acid (75 per cent), acetic acid (25 per cent) instead of lactic acid, and CXXVII, which yielded, besides acetic acid (46 per cent), formic acid (54 per cent) instead of diethylaminoacetic acid. The percentages shown are of the particular acid in the total acid mixture. The "abnormal" products were shown to result neither from allylic rearrangements of the starting materials nor from the oxidative work-up procedure (605). In each case where abnormal products were obtained in considerable amounts, spontaneous decomposition of the peroxidic ozonolysis products occurred with evolution of carbon monoxide.

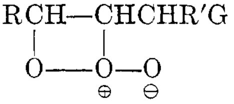
$$\underset{\text{CXXVI}}{CH_3CHOHCH{=}CH_2} \qquad \underset{\text{CXXVII}}{CH_3CH{=}CHCH_2N(CH_2CH_3)_2}$$

Similar "abnormal" ozonolyses of allylic compounds have been reported by other workers (239, 349, 427, 441, 443). One group (441, 442) stated that ethyl allylic ethers, in contrast to methyl allylic ethers, do not give "abnormal" results. They failed, however, to give experimental evidence.

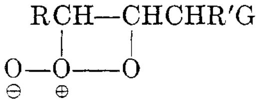
Young and coworkers (605) and Leffler (364) have proposed mechanisms for these "abnormal" reactions based on rearrangement of a "molozonide" (II). Young's mechanism requires molozonide CXXIX and Leffler's requires CXXX, both obtained by ozonation of CXXVIII.

$RCH{=}CHCHR'G$

CXXVIII



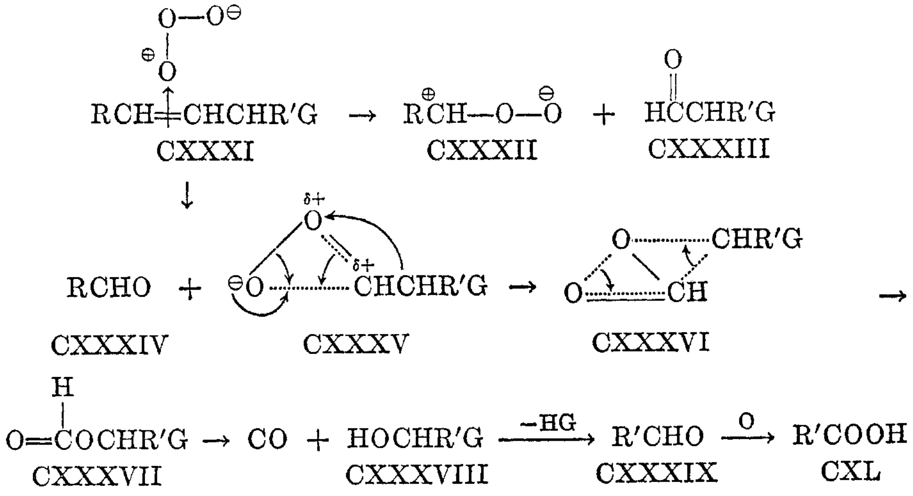
CXXIX



CXXX

R or R′ = H, alkyl, or aryl; G = OH, OR, NR₂, etc.

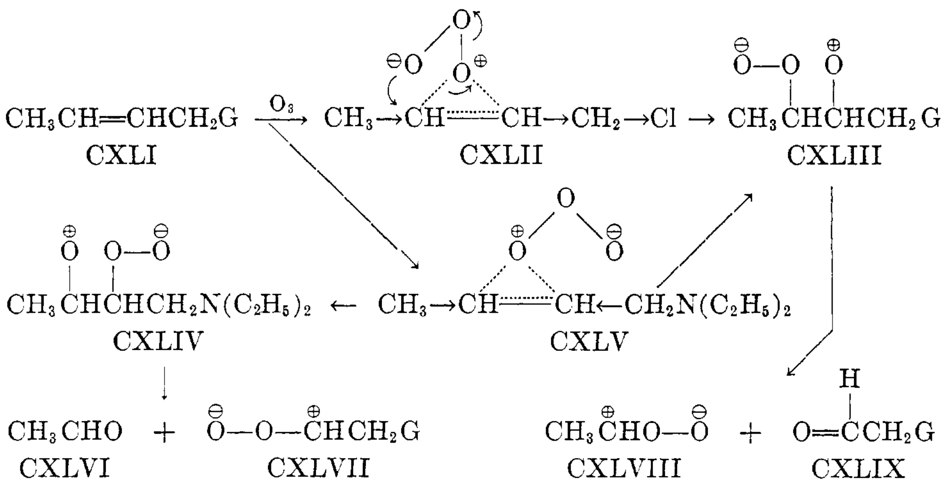
In view of the discussion in Sections II,A and II,B, it appears more likely that (*1*) rearrangement occurs at the zwitterion (CXXXV) stage, (*2*) the extent to which rearrangement occurs depends on the extent to which zwitterion CXXXV



R or R′ = alkyl or aryl; G = OH, OR, NR₂, etc.

is formed in preference to zwitterion CXXXII, and (*3*) the extent to which zwitterion CXXXV is formed depends on the inductive effects of groups G, R, and R′ of the initial π complex (CXXXI). The rearrangement step (CXXXV → CXXXVII) belongs to the general type involving a 1,2-shift to a positively charged oxygen atom (364). A possible transition state is CXXXVI, which is similar to that proposed recently for other peroxide rearrangements (228, 229). The path to the final products involves CXXXVII → CXXXIX or CXL.

The degree to which group G in CXXVIII promotes rearrangement (605) increases as its $-I$ (electron-attracting) effect decreases. This is understandable on the basis of the mechanism (Section II,B) for collapse of an initial π complex. Crotyl chloride (CXLIa) should give little or no rearrangement, because the strong $-I$ effect of the chloro group makes the entire chloromethyl group (CXLII) slightly electron attracting. This, coupled with the $+I$ effect of the methyl group on the other side of the original double bond (CXLII), causes the π complex to collapse predominantly in the direction (CXLII → CXLIII) which yields zwitterion CXLVIII rather than CXLVIIa (the one required for rearrangement). In contrast, the $-I$ effect of the diethylamino group (in CXLV) is not so great as that of the chloro group (in CXLII) and the diethylaminomethyl group is able to compete favorably with the methyl group for control over the collapse of the π complex (CXLV). Thus, zwitterion CXLVIIb (the one required for rearrangement) and CXLVIII are produced in nearly equal amounts. Similarly, the competition of inductive effects in controlling the decomposition of a five-membered ring or the formation of a four-membered ring would explain these results (Section II,B).

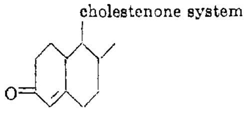
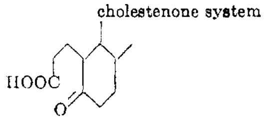
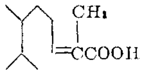
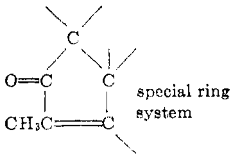
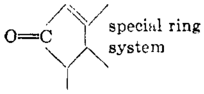
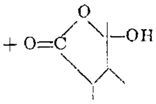
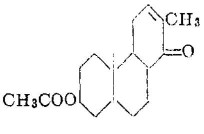
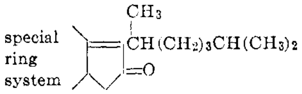
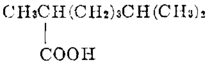


a: G = Cl. b: G = $N(C_2H_5)_2$.

Another factor of importance in determining the extent to which rearrangement occurs should be the migratory aptitude of the migrating group (CH_2G in CXLVII). This appears to increase as the electron-release ability of group G

TABLE 3

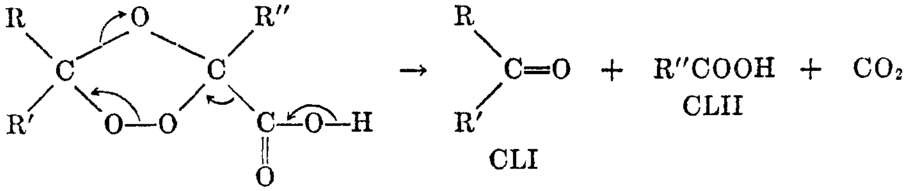
"Abnormal" ozonolysis products from α,β-unsaturated carbonyl compounds

No.	Compound	"Abnormal" Product	Yield	References
			per cent	
1.	$CH_3CH{=}CHCOOH$	$HCOOH$ CO_2	5 Undetermined	(605) (122)
2.	$CH_3CH{=}CHCHO$	$HCOOH$	10	(605)
3.	$CH_3CH{=}CHCOCH_2CH_3$	$HCOOH$ CH_3CH_2COOH	13 72	(605) (605)
4.	$C_6H_5CH{=}CHCOONa$	CO_2	Undetermined	(126)
5.			40-60	(93, 227, 552, 553)
6.	steroid ring system	CH_3COOH	82	(67)
7.		CH_3COOH	20	(65)
8.		HCOOH + 	—	(63)
9.		CH_3COOH	50-60	(193)
10.		 $CH_3\underset{\displaystyle COOH}{\underset{\vert}{C}H}(CH_2)_3CH(CH_3)_2$	—	(14, 15)

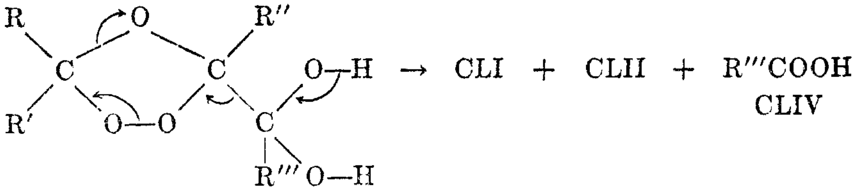
increases, as might be expected. Rearrangement occurs with CXLIb, but not with CXLIa.

In table 3 are listed some "abnormal" ozonolyses of α,β-unsaturated acids, aldehydes, and ketones. It is possible that some of these results were due to overozonation or oxidation. In a number of cases, however, the experimental details indicate that this was not a major factor.

Barton and Seoane (67) have proposed that these reactions occur by the mechanism illustrated in CL for an α,β-unsaturated acid. For an unsaturated aldehyde or ketone, the suggested decomposition involves the hydrate of the carbonyl group, as shown in CLIII. Similar mechanisms were suggested for the "abnormal" ozonolyses of allylic compounds. Although these mechanisms are reasonable in the cases of most α,β-unsaturated acids, aldehydes, and ketones and allylic alcohols, they do not appear to be applicable to allylic ethers or allylic tertiary amines. They also do not account for the carbon monoxide which often is evolved, and they require the formation of an ozonide.

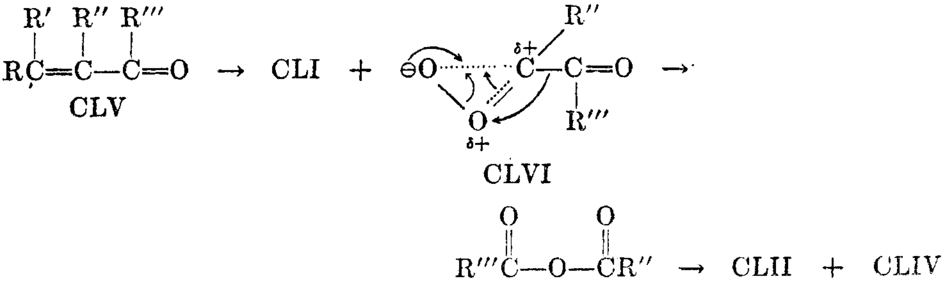


CL CLI CLII



CLIII CLIV

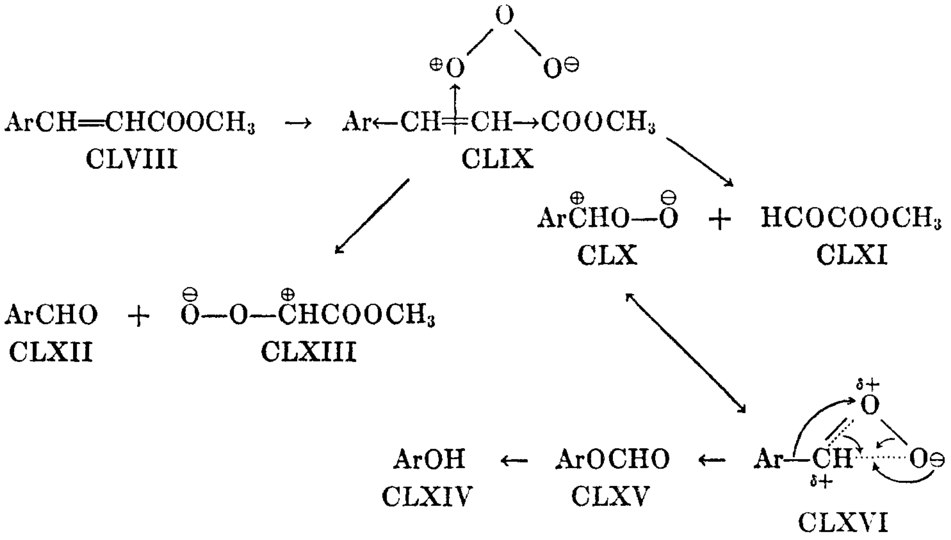
The results shown in table 3 can be explained by the zwitterion rearrangement mechanism (CLV → CLVI → CLVII), although certain difficulties are involved. The required zwitterion (CLVI) should not be formed predominantly, according to the π complex collapse theory (Section II,B). The yields of "abnormal" products in most cases, however, are not high. In those cases where they are high, perhaps overoxidation occurred or else the required zwitterion was produced through equilibrium with the ozonide. It is difficult to understand why these rearrangements should occur so readily, since the migratory aptitudes of carboxyl, formyl, and acyl groups should be low. The facile decompositions of certain acyl alkoxy hydroperoxides, however, appear to involve similar acyl migrations (44) (e.g., CXCVI at end of section; *cf.* also Section III). A similar rearrangement mechanism has been suggested by Karrer and Haab (331).



CLV CLVI CLVII

$$\mathrm{R'''\overset{\displaystyle O}{\overset{\|}{C}}-O-\overset{\displaystyle O}{\overset{\|}{C}}R''} \rightarrow \mathrm{CLII + CLIV}$$

The formation of phenols as "abnormal" ozonolysis products of methoxylated methyl cinnamates (524, 525) is easily explained by the zwitterion rearrangement mechanism. Zwitterions CLX and CLXIII should be produced from CLVIII, for example, in nearly equal amounts. Migratory aptitudes of alkoxylated aryl groups are great and rearrangement (CLXVI) should occur readily to give CLXV, which should decompose to CLXIV. The aldehydes (CLXII) obtained as "normal" ozonolysis products also react with ozone to give phenols (525, 559). This was shown not to be the principal source of the phenols, however, by the fact that in most cases the yield of a given phenol was less by ozonation of the corresponding aldehyde than by ozonolysis of the cinnamate (525, 559). Compound CLXIV, for example, was obtained in 48 per cent yield from CLVIII and in 4 per cent yield from CLXII.

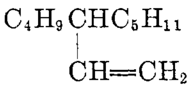


Ar is $C_6H_2(OCH_3)_3$-2,4,5.

Certain benzofurans (560), indoles (197, 378, 598), and indenones (206) also undergo rearrangement during ozonolysis (Sections IV and V).

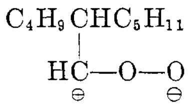
Zwitterion rearrangement seems to occur as a minor competing reaction even though the starting material is not of the types mentioned at the beginning of this section. Ziegler and coworkers (607) have found that the percentage of "abnormal" products varies with the oxidative method used in the work-up procedure. In general, oxidations with silver oxide and peracetic acid give the least and the greatest amounts, respectively, of these products. "Abnormal" products reported by these and other authors were 2–8 per cent valeric acid and 0.8–1.2 per cent butyric acid from 6-dodecene (607), 4.7 per cent glutaric and 1.8 per cent succinic acid by the liquid-phase ozonolysis (607) and 10 per cent formic acid by the vapor-phase ozonolysis (244) of cyclohexene, 13–30 per cent of a mixture of 5-decanol (CLXIX) and 5-decanone and 1–7 per cent of acids with four to six carbon atoms from 3-butyl-1-octene (CLXVII) (607), small amounts of levulinic acid (CLXXIII, apparently by decarboxylation of CLXXII)

(607), succinic acid (607), and β-carboxyglutaric acid (CLXXIV) (395) from vinylcyclohexene (CLXXI), and pinononic acid (CLXXVI) (528) and pinic acid (CLXXVII) (262, 311) from α-pinene (CLXXV).



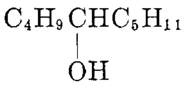
$$\begin{matrix} C_4H_9CHC_5H_{11} \\ | \\ CH{=}CH_2 \end{matrix}$$

CLXVII



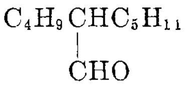
$$\begin{matrix} C_4H_9CHC_5H_{11} \\ | \\ \underset{\oplus}{HC}{-}O{-}\underset{\ominus}{O} \end{matrix}$$

CLXVIII



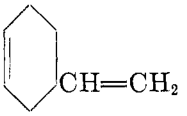
$$\begin{matrix} C_4H_9CHC_5H_{11} \\ | \\ OH \end{matrix}$$

CLXIX

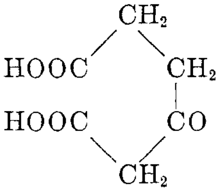


$$\begin{matrix} C_4H_9CHC_5H_{11} \\ | \\ CHO \end{matrix}$$

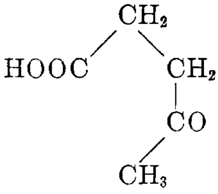
CLXX



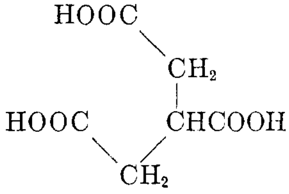
CLXXI



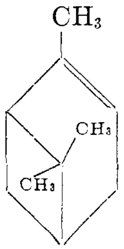
CLXXII



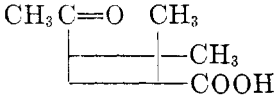
CLXXIII



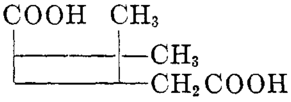
CLXXIV



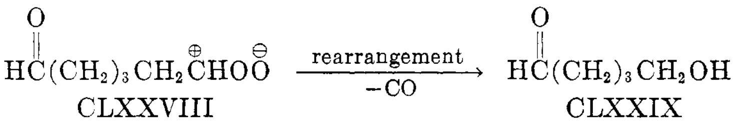
CLXXV



CLXXVI

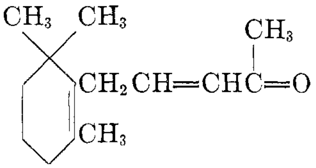


CLXXVII

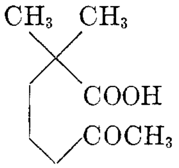


$$\overset{O}{\overset{\|}{HC}}(CH_2)_3CH_2\overset{\oplus}{C}HO\overset{\ominus}{O} \xrightarrow[-CO]{\text{rearrangement}} \overset{O}{\overset{\|}{HC}}(CH_2)_3CH_2OH$$

CLXXVIII CLXXIX



CLXXX



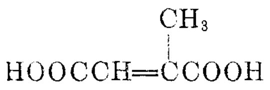
CLXXXI

It is apparent that these substances have resulted not only from rearrangement but also from oxidation of either "normal" or rearrangement products. Oxidation of aldehydes is known to give by-products of lower carbon content (364, 526, 527, 558, 559, 560, 607). Thus, during the ozonolysis of CLXVII, CLXIX and 5-decanone could have arisen both from rearrangement of zwitterion CLXVIII and by oxidation of CLXX, the normal ozonolysis product. Succinic acid could have arisen from cyclohexene by rearrangement of zwitterion CLXXVIII and further oxidation of the product (CLXXIX). The C_4-C_6 acids from the ozonolysis of CLXVII probably were produced by the ozone-initiated oxygen oxidation (Section VII,C) of 5-decanone. By one or more of these paths all of the products mentioned above, as well as the reported isolation in 10–40 per cent yield of geronic acid (CLXXXI) from the ozonolysis of CLXXX (320, 321, 408), can be accounted for.

Certain other "abnormal" ozonolysis results are more difficult to explain. Examples are the formation of small amounts of carbon dioxide, methane, and hydrogen from oleic acid (470), methane and hydrogen from 2-butene and 1-butene, respectively (98, 131), lauryl acetate (CLXXXIII) from the geometrical isomers brassidyl and erucyl acetates (CLXXXII) (530), formaldehyde from the geometrical isomers citraconic and mesaconic acids (CLXXXIV) (121), acetaldehyde from humulone (CLXXXVb) and cohumolone (CLXXXVa) (314), and 1,2-cyclohexanediol from cyclohexene (vapor phase) (244).

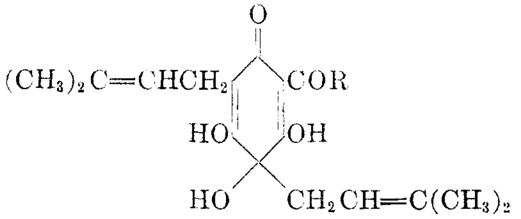
$CH_3(CH_2)_7CH{=}CH(CH_2)_{11}CH_2OCOCH_3$ CLXXXII

$CH_3(CH_2)_{10}CH_2OCOCH_3$ CLXXXIII



$HOOCCH{=}C(CH_3)COOH$

CLXXXIV



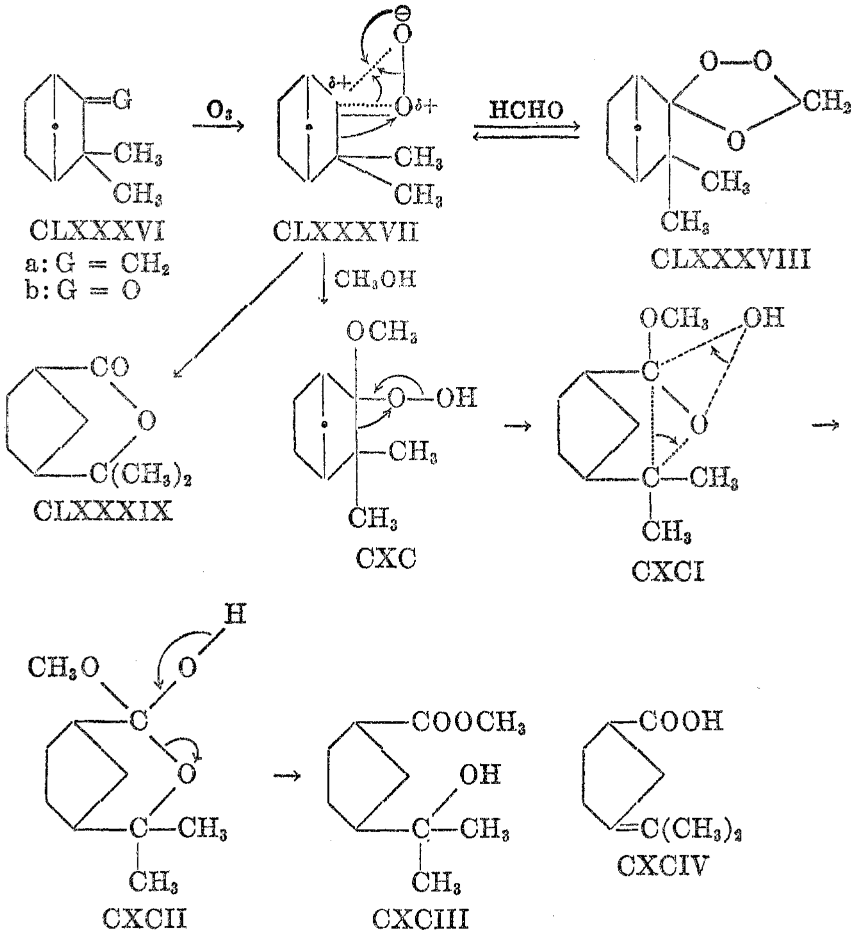
CLXXXV

a: R = isopropyl
b: R = isobutyl

Most of the "abnormal" results so far described were obtained in inert solvents. Milas and Nolan (409) have shown that rearrangements can often be avoided by ozonizing in methanol and using a reductive work-up procedure. The probable explanation is that the zwitterion reacts with the solvent to give an alkoxy hydroperoxide before it has a chance to undergo rearrangement.

Alkoxy hydroperoxides sometimes rearrange readily. Camphene (CLXXXVIa) gives very little of the expected camphenilone (CLXXXVIb) under usual ozonolysis conditions (37). The major products are a lactone (CLXXXIX) and an unsaturated acid (probably CXCIV) (*cf.* 291, 501) in inert solvents and ester CXCIII in methanol (37). In inert solvents, rearrangement of zwitterion CLXXXVII probably occurs. The methanol reaction must involve rearrangement of the methoxy hydroperoxide (CXC), since the lactone (CLXXXIX) is not converted to the ester (CXCIII) under the conditions of the reaction (37). The rearrangement steps (CXC → CXCI → CXCII → CXCIII) have ample analogy (198, 546). The transition state (CXCI) is similar to one proposed for other peroxide rearrangements (228, 229). These rearrangements perhaps occur so readily because of strain in the camphene ring system or because of steric hindrance in CLXXXVII and CXC.

Methoxy hydroperoxides (CXCVI) from ozonolyses of compounds CXCV in methanol decompose upon gentle heating in polar solvents (e.g., methanol) or in the cold in the presence of a base (44). The products are benzoic acid (CXCVIII) and, presumably, methyl formate (CXCIXa) from CXCVIa and methyl acetate



CLXXXVI

a: G = CH_2
b: G = O

CLXXXVII

CLXXXVIII

CLXXXIX

CXC

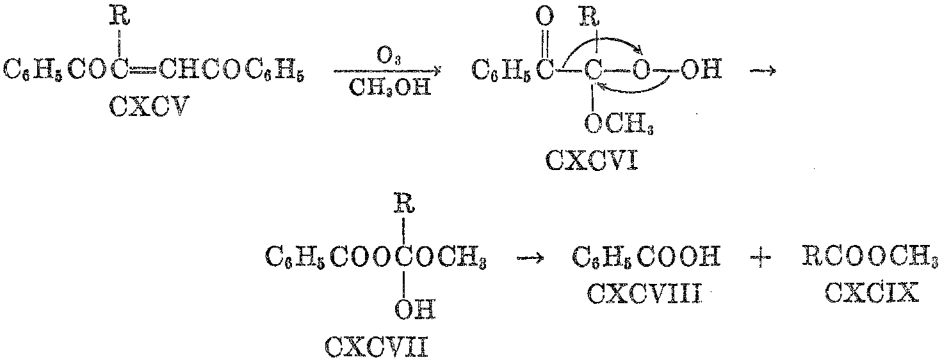
CXCI

CXCII

CXCIII

CXCIV

(CXCIXb) from CXCVIb. The decomposition in methanol, if not the others, must involve rearrangement (CXCVI → CXCVII) rather than solvolysis of CXCVI, since the latter should give methyl benzoate instead of benzoic acid (44).



$$C_6H_5CO\overset{R}{C}{=}CHCOC_6H_5 \xrightarrow[CH_3OH]{O_3} C_6H_5\overset{O}{\overset{\|}{C}}-\underset{OCH_3}{\overset{R}{C}}-O-OH \rightarrow$$

CXCV

CXCVI

$$C_6H_5COO\underset{OH}{\overset{R}{C}}OCH_3 \rightarrow C_6H_5COOH + RCOOCH_3$$

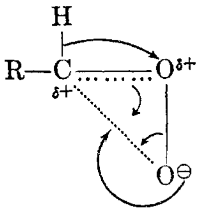
CXCVII

CXCVIII

CXCIX

a: R = H. b: R = CH_3.

The decomposition of peroxidic ozonolysis products of certain olefins (type $RCH{=}CHR$) to carboxylic acids also can be rationalized by the zwitterion rearrangement mechanism (CC → CCI). In essence, Rieche (470) suggested this earlier but did not represent the rearranging fragment (CC) as a zwitterion.



CC

$\rightarrow$ RCOOH

CCI

III. Ozonolysis of the Triple Bond

Ozonolysis of acetylenic compounds is much less common than ozonolysis of olefinic compounds (208, 380). Two types of nonperoxidic products have been obtained, carboxylic acids (from complete cleavage of the triple bond) and α-dicarbonyl compounds (by partial cleavage of the triple bond). The α-dicarbonyl compounds usually have been minor products and have been assumed to be intermediates in the formation of carboxylic acids (380). A typical example is stearolic acid (CCII), which gave 69–80 per cent yields of azelaic acid (CCIII) and a 4 per cent yield of 9,10-diketostearic acid (CCIV) (339). An exception is an 81 per cent yield of glyoxal from acetylene (154). Paillard and Wieland (450) proposed an anhydride intermediate in the formation of carboxylic acids.

$$CH_3(CH_2)_7C{\equiv}C(CH_2)_7COOH \qquad HOOC(CH_2)_7COOH$$

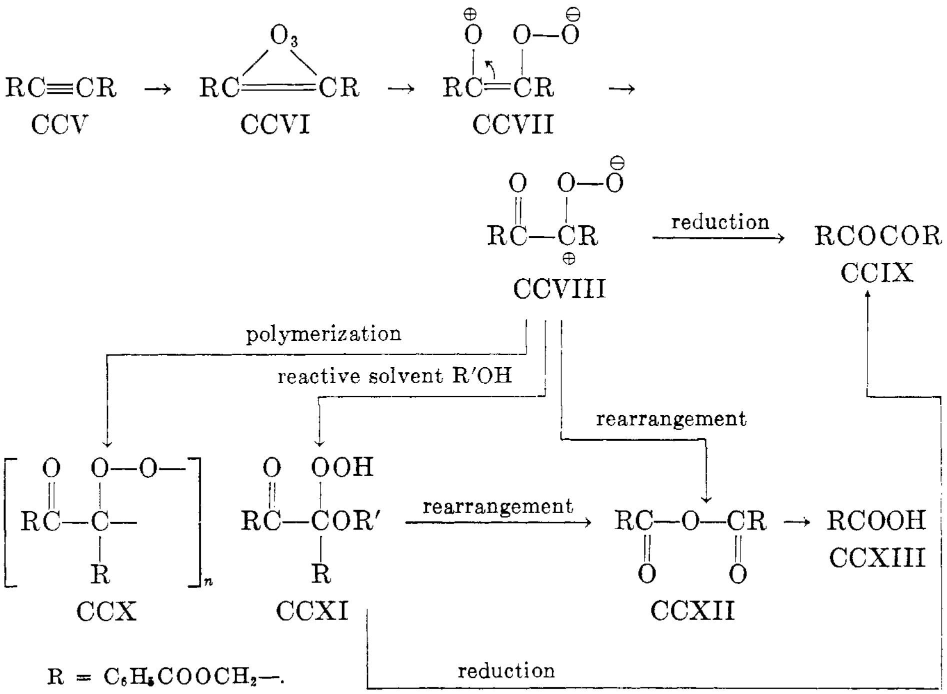
CCII CCIII

$$CH_3(CH_2)_7COCO(CH_2)_7COOH$$

CCIV

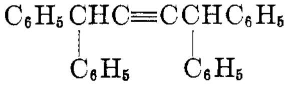
A thorough study of the ozonolysis of 1,4-dibenzoxy-2-butyne (CCV) has led to a mechanism (CCV → CCXIII) for the ozonolysis of acetylenic compounds similar to that for olefins (208). The product from an inert solvent was the polymeric ketoperoxide CCX, while that from a carbon tetrachloride–acetic acid mixture was an acetoxy hydroperoxide (CCXI). Reduction and alkaline rearrangement of CCXI gave diketone CCIX and carboxylic acid CCXIII, respectively, in high yields. Thermal decomposition of CCXI gave anhydride CCXII. The reduction to the diketone (CCIX) and rearrangement to the acid (CCXIII) also were carried out without isolating the acetoxy hydroperoxide (CCXI). Similar results were obtained with 1,4-diacetoxy-2-butyne (CCV: R is CH_3COOCH_2—). The diketone conversion was carried out with CCXIV, CCXV, and CCXVI (208). Through proper choice of "work-up" procedure good yields of either carboxylic acids or α-dicarbonyl compounds appear possible.

The exact structure of intermediate CCVI was left in doubt (208). It could be either a π complex (Section II,B) or an actual addition compound. The zwitterion intermediate (CCVIII) can react in any of four ways, as shown. The rearrange-



ment (to CCXII) is completely analogous to those discussed in Section II,C,2, involving either zwitterion CCVIII, itself, or hydroperoxide CCXI.

$C_6H_5C{\equiv}CC_6H_5$
CCXIV



$C_6H_5\underset{C_6H_5}{CH}C{\equiv}C\underset{C_6H_5}{CH}C_6H_5$
CCXV

$CH_3(CH_2)_3C{\equiv}C(CH_2)_3CH_3$
CCXVI

$CH_3CH{=}CHC{\equiv}CC{\equiv}CCH{=}CHCH_3$
CCXVII

$HOOCC{\equiv}CC{\equiv}CCOOH$
CCXVIII

Hydrocarbons with multiple triple and double bonds, such as CCXVII, react preferentially at the double bonds (e.g., CCXVII → CCXVIII (90, 91)).

IV. Ozonolysis of Aromatic Compounds[1]

The ozonolysis of aromatic compounds has been studied extensively since 1940. In general, these reactions occur less readily than do ozonolyses of olefinic compounds. The various aromatic systems also have different reactivities. The order of decreasing ease of ozonolysis for simple, unsubstituted systems qualitatively appears to be: simple alkenes > anthracene > phenanthrene > naphthalene > benzene.

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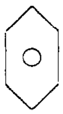
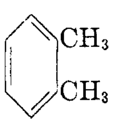
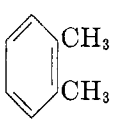
[1] Symbols such as  designate an aromatic ring system.

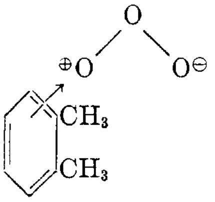
A. BENZENE AND DERIVATIVES

Wibaut and coworkers (88, 234, 286, 329, 354, 355, 512, 514, 567, 570, 578, 580, 581, 584, 587, 589) have studied the rates of ozonolysis of benzene and naphthalene and certain of their derivatives and have identified the nonperoxidic products from these reactions. In the benzene series the following qualitative rate relationships were observed: hexamethylbenzene > mesitylene > xylenes > toluene > benzene > halobenzenes; anisole >> benzene > ethyl benzoate; toluene > benzyl chloride > benzal chloride > benzotrichloride. Andrews (12) has confirmed some of these relationships under homogeneous rather than the usual heterogeneous conditions used by Wibaut and coworkers. By using dilute carbon tetrachloride solutions of ozone (10^{-3} to 10^{-5} M) and following the changes in ozone concentration spectrophotometrically, he was able to obtain the following bimolecular rate constants: benzene, 1.9; toluene, 10; *o*-xylene, 40; mesitylene, 250; hexamethylbenzene, 15,000.

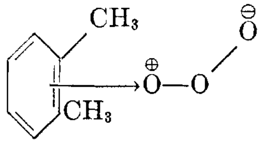
Ozonolysis of *o*-xylene gave 20–26 per cent yields of a mixture containing approximately the molar ratio of 3:2:1 of glyoxal (CCXXXII), methylglyoxal (LXI), and biacetyl (CCCXXXIII), respectively (286, 580, 581). This


CCXIX

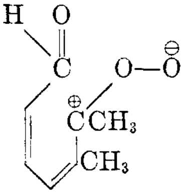

CCXX



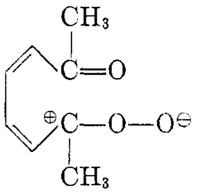
CCXXI



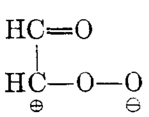
CCXXII

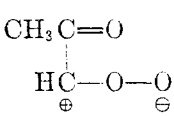


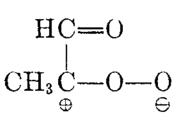
CCXXIII

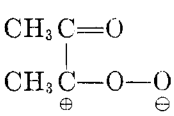


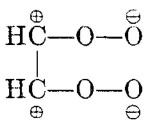
CCXXIV

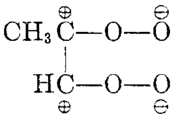

$$\begin{array}{l}\mathrm{HC{=}O}\\ \;|\\ \underset{\oplus}{\mathrm{HC}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXV

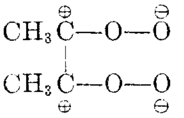

$$\begin{array}{r}\mathrm{CH_3C{=}O}\\ |\;\;\;\;\;\\ \underset{\oplus}{\mathrm{HC}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXVI

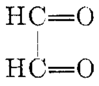

$$\begin{array}{r}\mathrm{HC{=}O}\\ |\;\;\;\;\;\\ \underset{\oplus}{\mathrm{CH_3C}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXVII

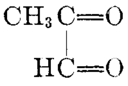

$$\begin{array}{l}\mathrm{CH_3C{=}O}\\ \;\;\;\;\;|\\ \underset{\oplus}{\mathrm{CH_3C}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXVIII

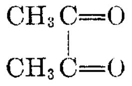

$$\begin{array}{l}\overset{\oplus}{\mathrm{HC}}\mathrm{{-}O{-}}\overset{\ominus}{\mathrm{O}}\\ \;|\\ \underset{\oplus}{\mathrm{HC}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXIX


$$\begin{array}{r}\overset{\oplus}{\mathrm{CH_3C}}\mathrm{{-}O{-}}\overset{\ominus}{\mathrm{O}}\\ |\;\;\;\;\;\;\;\;\\ \underset{\oplus}{\mathrm{HC}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXX


$$\begin{array}{l}\overset{\oplus}{\mathrm{CH_3C}}\mathrm{{-}O{-}}\overset{\ominus}{\mathrm{O}}\\ \;\;\;\;\;|\\ \underset{\oplus}{\mathrm{CH_3C}}\mathrm{{-}O{-}}\underset{\ominus}{\mathrm{O}}\end{array}$$
CCXXXI


$$\begin{array}{l}\mathrm{HC{=}O}\\ \;|\\ \mathrm{HC{=}O}\end{array}$$
CCXXXII


$$\begin{array}{r}\mathrm{CH_3C{=}O}\\ |\;\;\;\;\;\\ \mathrm{HC{=}O}\end{array}$$
LXI


$$\begin{array}{l}\mathrm{CH_3C{=}O}\\ \;\;\;\;\;|\\ \mathrm{CH_3C{=}O}\end{array}$$
CCXXXIII

is the expected ratio on the assumption that the Kekulé structures (CCXIX and CCXX) react equally, and is quantitative confirmation of the earlier work of Levine and Cole (373, 380). Similar results were obtained with 1,2,4-trimethylbenzene (286).

Although the early interpretations of these data were somewhat naive (286, 373), the ideas later were modernized into an argument for an electrophilic attack by ozone upon a hybrid molecule to give two different monoaddition compounds in equal amounts (512, 589). Both the rate (11) and the product studies are consistent with the idea (Section II,B) that these initial products are localized π complexes (e.g., CCXXI and CCXXII), although the results can also be explained by four- or five-membered ring intermediates (Section II,B).

Wibaut and coworkers (512, 589) have assumed that the final peroxidic ozonolysis product is a triozonide. According to the Criegee mechanism (Section II,A), CCXXI and CCXXII should collapse into zwitterions such as CCXXIII and CCXXIV. Since these arise from a six-membered ring, cyclization to an ozonide should not occur (207, 209). Further ozonolysis of CCXXIII and CCXXIV should result in polymers of zwitterions CCXXV, CCXXVI, CCXXVII, CCXXVIII and/or, perhaps, CCXXIX, CCXXX, and CCXXXI. Reduction of these materials should yield CCXXXII, LXI, and CCXXXIII in the proportions found by experiment (286).

The zwitterions also undergo decomposition to substances such as formic, acetic, and oxalic acids. These decompositions probably include rearrangement (Section II,C,2).

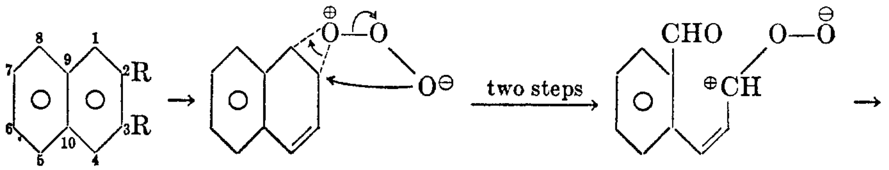
B. NAPHTHALENE AND DERIVATIVES

Naphthalene (CCXXXIVa) reacts readily with two mole-equivalents of ozone (48, 290, 329, 498, 584), after which absorption continues slowly, presumably until five mole-equivalents of ozone have reacted (329, 584). Ozonolysis of methylated naphthalenes occurs preferentially in the methylated ring at the 1,2- and 3,4-bonds (329, 578, 584). The products from 2,3-dimethylnaphthalene (CCXXXIVb) were biacetyl (CCXXXIII), glyoxal (CCXXXII), methylglyoxal (LXI), and 4,5-dimethylphthalic acid in low yield and phthalic acid (CCXLb) and derivatives of phthalaldehyde (CCXLa) in good yield.

Various interpretations of these results have been given (329, 354, 578, 584). A clearer insight into the reactions has come from the characterization of the peroxidic ozonolysis products of naphthalene (48). In methanol solution the cyclic peroxide CCXLII was produced in 90–95 per cent yield. This undoubtedly arose from interaction of zwitterion CCXXXVIII with methanol, followed by cyclization of the addition product (CCXLI). The formation of zwitterion CCXXXVIII is consistent with the attack of ozone on the 1,2- and 3,4-bonds of naphthalene [the bonds with the lowest bond-localization energies (161, 232)] to produce π complexes (CCXXXV) (Section II,B) which react further via CCXXXV, CCXXXVI, and CCXXXVII. Ozone attack on the remaining benzene system of CCXXXVIII, CCXLI, or CCXLII) would be slow.

Wibaut and Kampschmidt (329, 584) have assumed that in inert solvents a diozonide is produced. It seems more likely that the product is either a mono-ozonide (CCXXXIXa from the cyclization of CCXXXVIII) or a polymer of CCXXXVIII. The isolated material was very unstable (48), as might be expected of a structure such as CCXXXIX (*cf.* compound XXVI, Section II,A,2) (207, 241).

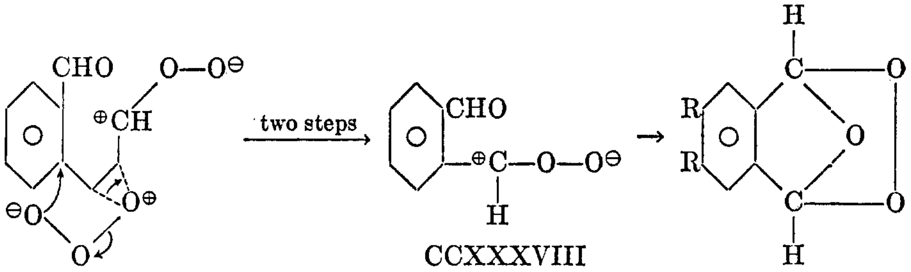
By analogy, the major reaction with 2,3-dimethylnaphthalene (CCXXXIVb) should lead to ozonide CCXXXIXa and the minor reaction to ozonide CCXXXIXb. Biacetyl (CCXXXIII) and glyoxal (CCXXXII) probably arose from reduction of zwitterions CCXXVIII and CCXXV, which would be produced along with CCXXXIXa and b. Methylglyoxal (LXI) probably was produced by further ozonolysis of ozonide CCXXXIXb (*cf.* *o*-xylene, Section IVa), rather than by ozone attack at the 1,9-, 2,3-, and 4,10-bonds of CCXXXIVb, since no *o*-benzoquinone was found (329, 584).



CCXXXIV CCXXXV CCXXXVI

a: R = H

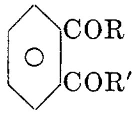
b: R = CH_3



CCXXXVII CCXXXVIII CCXXXIX

a: R = H

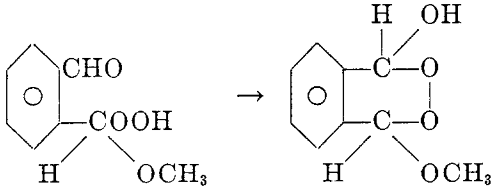
b: R = CH_3



CCXL

a: R = R′ = H

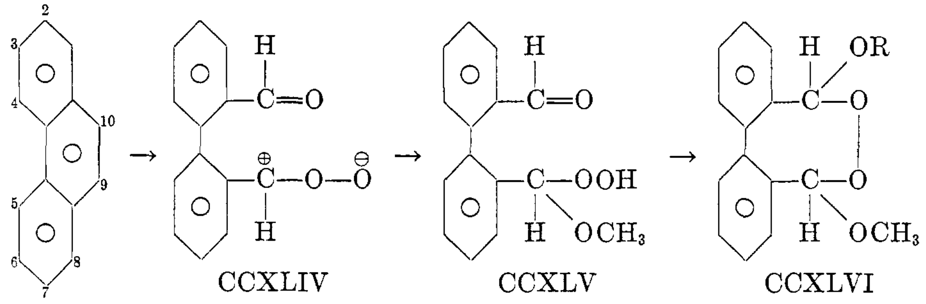
b: R = R′ = OH



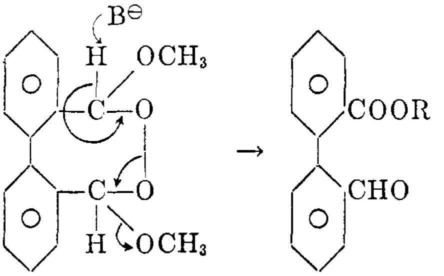
CCXLI CCXLII

C. POLYCYCLIC AROMATIC SYSTEMS

Contrary to the report of Harries (290, 380), ozonolysis of phenanthrene (CCXLIII) occurs exclusively at the 9,10-bond [the bond of lowest bond-localization energy (161, 232)] and only one mole-equivalent of ozone is readily absorbed (38, 51, 436, 488, 577). The initial product in methanol solution is methoxy hydroperoxide CCXLV, formed through reaction of the solvent with zwitterion CCXLIV (38). This cyclizes to CCXLVIa, which can be precipitated from the cold reaction mixture (38, 52, 577). Further reaction occurs with the solvent at room temperature to give CCXLVIb (38, 577). Base-catalyzed decomposition of CCXLVIb occurs readily to give CCXLVIIIa or b in high yield. The changes shown in CCXLVII are probably involved (38).

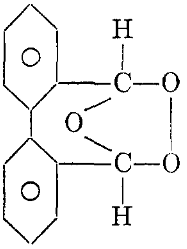


CCXLIII CCXLIV CCXLV CCXLVI

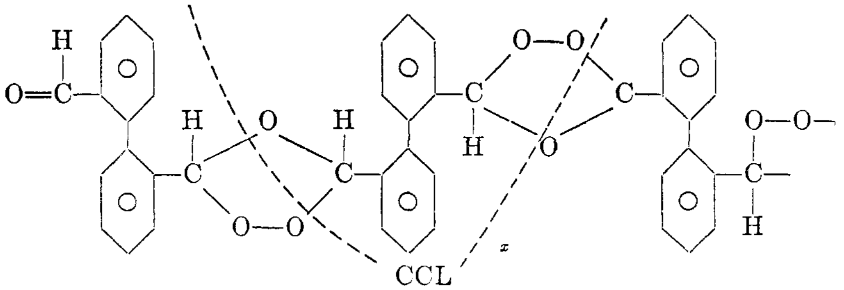


CCXLVII CCXLVIII

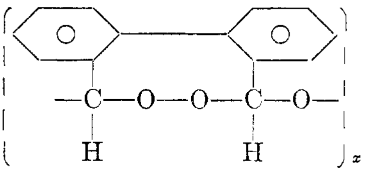
a: R = H
b: R = CH_3



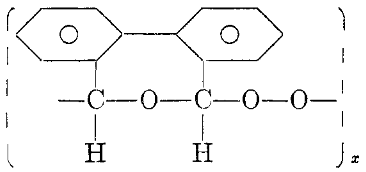
CCXLIX



CCL



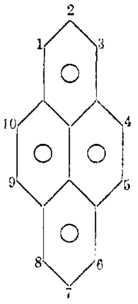
CCLI



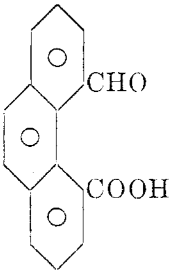
CCLII

The ozonolysis of phenanthrene in inert solvents was reported to yield a monomeric monoözonide (CCXLIX) (488). Later work showed the material to be a polymer of CCXLIV (51, 52, 577). Its structure is probably CCL rather than CCLI or CCLII, since its infrared spectrum showed a weak carbonyl band (52).

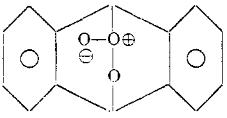
Ozone should attack naphthalene and phenanthrene where it does whether it seeks the bond of lowest bond-localization energy or the position of lowest atom-localization energy (232). These positions are different, however, in the cases of pyrene and anthracene (232). Ozone, like the "double-bond" reagent osmium tetroxide (187), attacked the 4,5-bond of pyrene (CCLIII), the bond of lowest bond-localization energy (29, 31, 161, 232, 256, 430, 556, 557), in an inert solvent to give CCLIV in high yield (32, 50). Electrophilic substitution occurs at position 1, 3, 6, or 8, the positions of lowest atom-localization energy (29, 31, 232, 557).



CCLIII



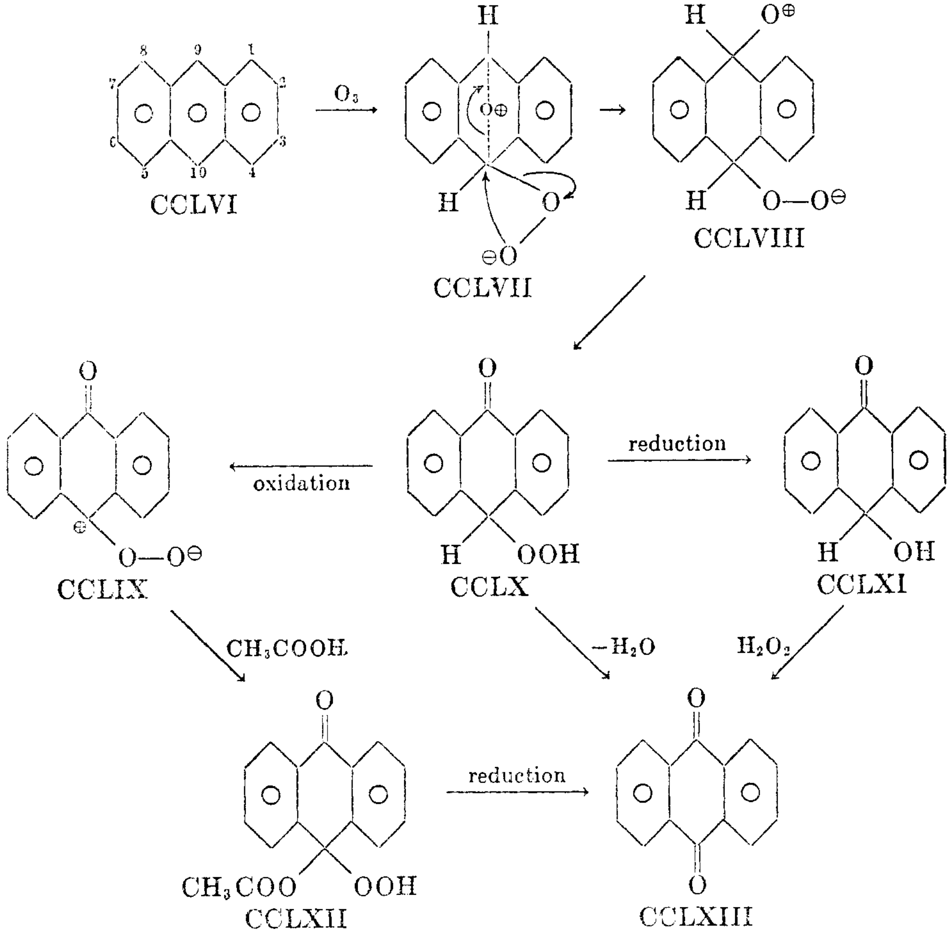
CCLIV



CCLV

In the case of anthracene (CCLVI) the bond of lowest bond-localization energy is the 1,2-bond (161, 232); this is where attack by osmium tetroxide occurred (188). Ozone, like other electrophilic reagents, attacked carbon atoms 9 and 10 (42, 45, 293, 476), which are the positions not only of lowest atom-localization energy but also of lowest para-localization energy (160, 164, 165, 232). The product from acetic acid solvent was anthraquinone (CCLXIII) in 70–75 per cent yield (42, 43, 45). Three moles of ozone per mole of anthracene were required. Some anthraquinone precipitated during the ozonolysis. The rest was obtained, along with anthrahydroquinone (or its tautomer CCLXI), by reduction of a peroxidic ozonolysis product.

These results can be explained by an initial attack by ozone at the positions of lowest atom- or para-localization energy to give either CCLV (analogous to oxygen addition) or π complex CCLVII. Collapse of CCLVII or decomposition of CCLV would give CCLVIII, which could rearrange to CCLX. Reactions of CCLX involving CCLXI, CCLIX, and CCLXII will account for all of the

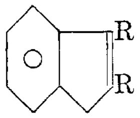


described phenomena except the requirement of three moles of ozone per mole of anthracene. Perhaps 25–30 per cent of the anthracene reacts at the bond of lowest bond-localization energy. This should lead to destruction of both outer rings of anthracene and should account for a considerable amount of the required three mole-equivalents of ozone.

1,4-Addition of ozone also appears to occur with furans and pyrroles (Section V,C) (47, 54) but not with 1,3-butadiene (528). Probably such an attack is possible only with cyclic systems where the ends of the conjugated system are close together.

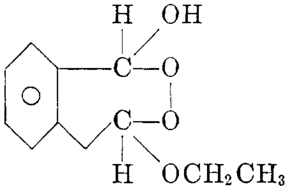
D. AROMATIC-ALIPHATIC CONDENSED-RING SYSTEMS

Ozonolysis of aromatic-unsaturated aliphatic condensed-ring systems occurs exclusively in the aliphatic ring. Examples are 1,4-dihydronaphthalene and derivatives (456), indene (561), 1,2-diphenylindene (36), and 2,3-disubstituted indenones (206). Ozonolysis of indene (CCLXIVa) in ethanol results in a good yield of a cyclic peroxide (CCLXV or CCLXVI) (561). The reaction course is analogous to that outlined earlier for naphthalene and phenanthrene (Sections

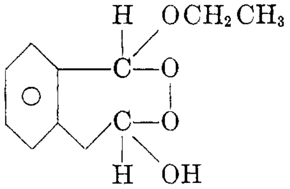


CCLXIV

a: R = H
b: R = C_6H_5

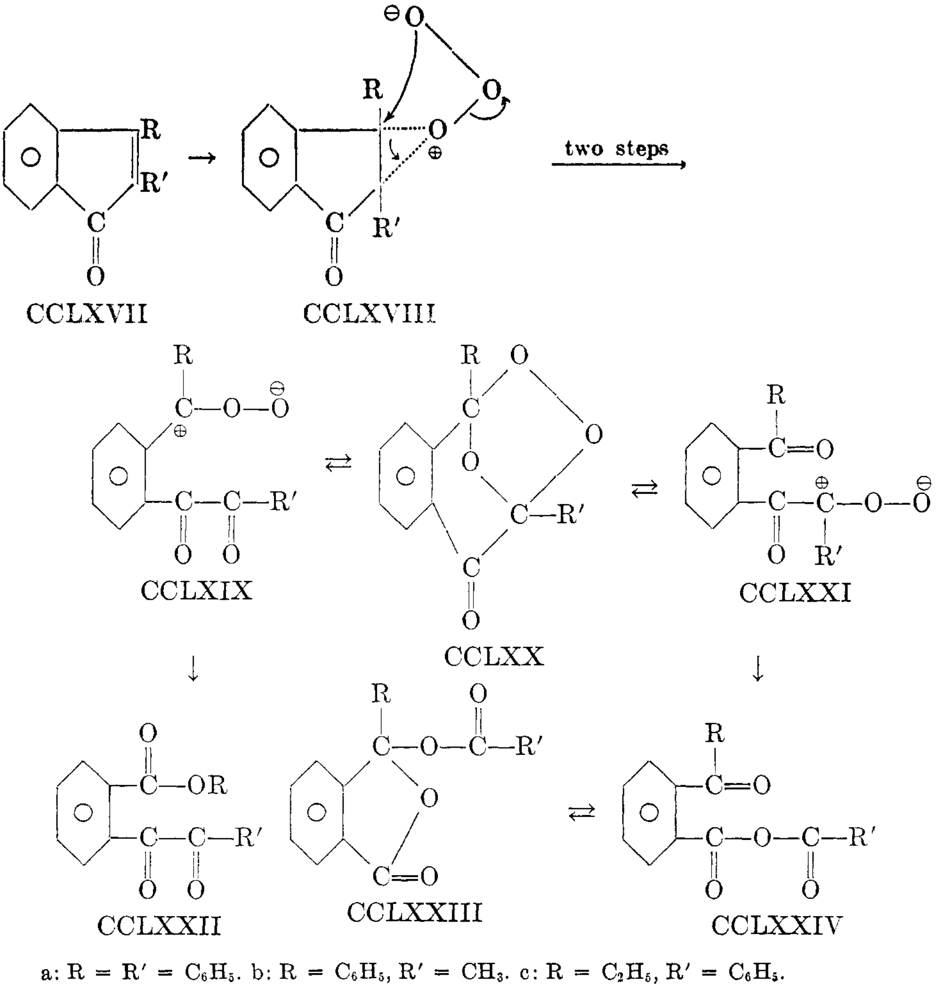


CCLXV



CCLXVI

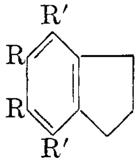
IV,B and C). 1,2-Diphenylindene (CCLXIVb) (*cf.* 57) and certain 2,3-disubstituted indenones (CCLXVII) form ozonides (e.g., CCLXX) in high yield, regardless of whether the solvent is reactive or inert (Section II,B) (36, 206). The driving force for cyclization of the corresponding zwitterion (e.g., CCLXIX) is so great that it occurs in preference to reaction with the solvent.

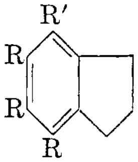


a: R = R′ = C_6H_5. b: R = C_6H_5, R′ = CH_3. c: R = C_2H_5, R′ = C_6H_5.

Rearrangements (Section II,C,2) occur during ozonolyses of 2,3-disubstituted indenones (CCLXVII) (206), whereby anhydrides (CCLXXIII $\rightleftarrows$ CCLXXIV) are produced either directly or by decomposition of the pure ozonides (CCLXX). Thus, Frank and coworkers (266) erroneously reported the product (CCLXXIIIc) from the ozonolysis of CCLXVIIc to be an unusually stable ozonide. Ozonide CCLXXa rearranged along two paths. Spontaneous decomposition apparently involved zwitterion CCLXXIa to produce anhydride CCLXXIIIa. In the presence of acetic anhydride and sulfuric acid, both CCLXXIIIb and CCLXXIIa (from CCLXIXa) were produced (206).

A study of the ozonolysis of indane (CCLXXVa or CCLXXVIa) led Long and Fieser (381) to believe, in agreement with the hypothesis of Mills and Nixon (411), that structure CCLXXVIa reacted in preference to CCLXXVa. The results were indecisive however (29), and Wibaut and de Jong (583) reached the opposite conclusion by studying the ozonolyses of 5,6-dimethylindane (CCLXXVb or CCLXXVIb) and 4,7-dimethylindane (CCLXXVc or CCLXXVIc) from the viewpoint used in studies on *o*-xylene (Section IV,A) (286). This is in agreement with the molecular orbital calculations of Longuet-Higgins and Coulson (382), which showed that the bond between the rings has considerable double-bond character.

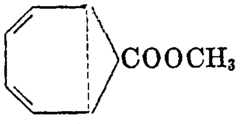

CCLXXV

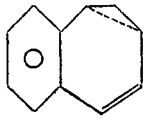

CCLXXVI

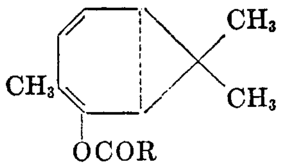
a: R = R′ = H
b: R = CH_3, R′ = H
c: R′ = CH_3, R = H

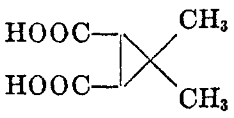
E. PSEUDO-AROMATIC SYSTEMS

Compounds CCLXXVII and CCLXXIX, as well as tropilidene itself, have been shown to have either the indicated or a cycloheptatriene-type structure,


CCLXXVII

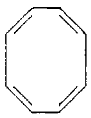

CCLXXVIII

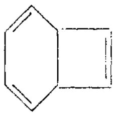

CCLXXIX

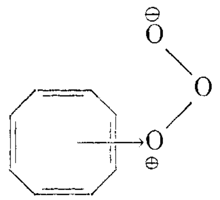

CCLXXX

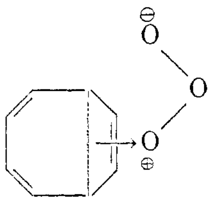
but not a norcaradiene-type structure (191, 236). The same should hold true for CCLXXVIII. Ozonolysis results favor the indicated structures. Compound CCLXXVII reacted readily with two mole-equivalents of ozone and compound CCLXXVIII with one (513). From compounds CCLXXIX good yields of *cis*-caronic acid (CCLXXX) were obtained (190, 192). The ease with which ozonolysis occurred indicated that the substances are not highly aromatic.

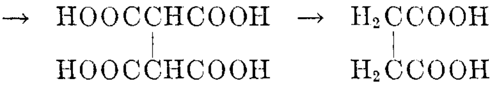
The ease of ozonolysis of cycloöctatetraene (CCLXXXI) is consistent with its nonaromatic character (588). Three and one-half mole-equivalents of ozone were readily absorbed, and glyoxal, ethanetetracarboxylic acid (CCLXXXV), and succinic acid (CCLXXXVI) were isolated in low yield (568, 588). Wibaut and Sixma (588) explained these results by a mechanism similar to that of Friess and Boekelheide (269) for the conversion of CCLXXXI to derivatives of CCLXXXII. In view of previous discussions, it seems better to assume that an initial π complex is formed, which is a hybrid of CCLXXXIII and CCLXXXIV. Further reaction of CCLXXXIV would lead to CCLXXXV and CCLXXXVI. Glyoxal could arise from either CCLXXXIII or CCLXXXIV.


CCLXXXI


CCLXXXII


CCLXXXIII


CCLXXXIV



$$\rightarrow \begin{array}{c} \text{HOOCCHCOOH} \\ | \\ \text{HOOCCHCOOH} \end{array} \rightarrow \begin{array}{c} \text{H}_2\text{CCOOH} \\ | \\ \text{H}_2\text{CCOOH} \end{array}$$

CCLXXXV CCLXXXVI

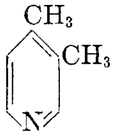
V. Ozonolysis of Heterocyclic Compounds

Very few heterocyclic compounds had been ozonized at the time the review by Long (380) was written. Since then, the action of ozone on pyridines, quinolines, pyrroles, furans, indoles, and 4-pyrones has been studied.

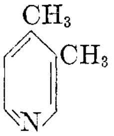
A. PYRIDINES AND 4-PYRONES

The pyridine ring is much less reactive toward ozone than is the benzene ring (356, 505, 511, 585). It is difficult to find a solvent which neither reacts with the pyridine derivative nor reacts with ozone more readily than does the pyridine derivative.

Ozonolysis of unsymmetrically substituted homologs of pyridine gave products to be expected from either Kekulé-type structure (e.g., methylglyoxal from CCLXXXVII and glyoxal and biacetyl from CCLXXXVIII (356, 585) (*cf.* Section IV,A)). Formic acid, acetic acid, pyruvic acid, oxalic acid, glyoxalic acid, and ammonia also were isolated or identified (356, 505, 585). Although the yields invariably were low, it was concluded that ozonolysis could be useful in proofs of structure of pyridine compounds (505).

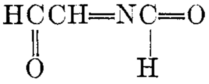


CCLXXXVII



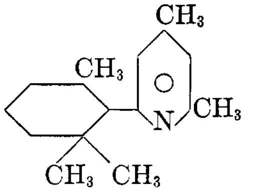
CCLXXXVIII

It has been assumed that ozone attacks the pyridine nucleus only at carbon–carbon bonds to produce substances such as CCLXXXIX (from CCLXXXVIII), which later are hydrolyzed to amides and finally to ammonia (356, 505, 585). In support of this, Sixma (511) has found that the ratio of ozone absorbed to ammonia produced is always equal to 2. Amides have been isolated in two instances: CCXCI from CCXC (506) and CCXCIII from CCXCII (377).

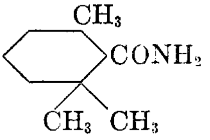


$H\underset{\underset{O}{\|}}{C}CH{=}N\underset{\underset{H}{|}}{C}{=}O$

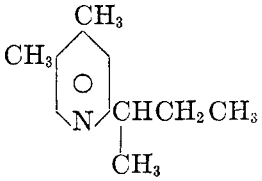
CCLXXXIX



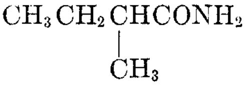
CCXC



CCXCI



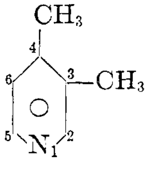
CCXCII



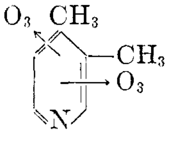
$CH_3CH_2\underset{\underset{CH_3}{|}}{CH}CONH_2$

CCXCIII

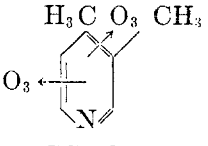
These results are consistent with an initial attack by ozone at the 2,3- and/or 5,6-bonds (CCXCIV), the bonds of pyridine with the most double-bond character (383). Further attack by another mole of ozone should occur immediately to give CCXCV and CCXCVI (represented as π complexes for reasons given in Section II,B) or decomposition products thereof. Decomposition of CCXCV and CCXCVI in the manner described in Section IV should lead to the described products.



CCXCIV



CCXCV

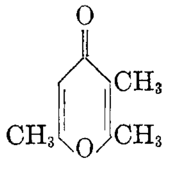


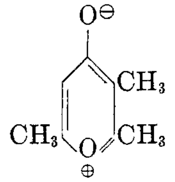
CCXCVI

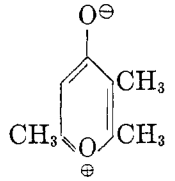
In view of data described in Section VI, it is surprising that the carbon–nitrogen double bond in structures such as CCXCV or CCLXXXIX should be more resistant to ozone attack than is the pyridine nucleus itself. Also, there is evidence that ozone can complex with pyridine at the nitrogen atom with the eventual formation of pyridine oxide (515, 516, 517).

4-Pyrones react with ozone in a manner similar to pyridines. Two moles of ozone per mole of pyrone react (571, 572, 574, 582). Table 4 lists the products isolated from 4-pyrone and two of its homologs.

Such products as glyoxal from 4-pyrone, methylglyoxal from 2,6-dimethyl-4-pyrone, and methylglyoxal and biacetyl from 2,3,6-trimethyl-4-pyrone (CCXCVII) cannot arise from the classical structures of these substances (e.g., CCXCVII) (582). The 4-pyrones can be represented as resonance hybrids of several structures: for example, CCXCVII, CCXCVIII, CCXCIX, and CCC (268). It appears that ozone can attack the hybrid molecule (CCCI) at bonds 2-3 and 5-6, 3-4 and 5-6, or 2-3 and 4-5. Thus, from attack at the positions shown in the simplified π complex CCCII (from 2,6-dimethyl-4-pyrone) could arise mesoxalic dialdehyde (OCHCOCHO); from CCCIII and CCCIV (in the case of 2,3,6-trimethyl-4-pyrone) could arise methylglyoxal and biacetyl, respectively. The other products could be produced from any one of the π complex types.


CCXCVII


CCXCVIII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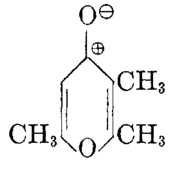
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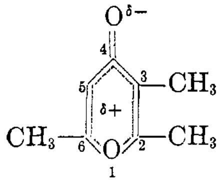
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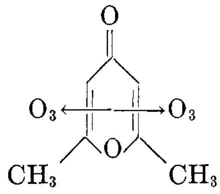
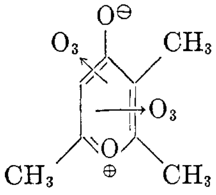
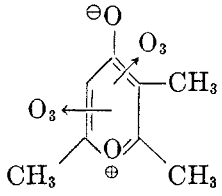

CCCII


CCCIII


CCCIV

Similar results have been found with 4-thiapyrones (see table 4) (572).

B. QUINOLINES, ISOQUINOLINES, AND BENZOPYRYLIUM SALTS

The ozonolysis of quinoline ring systems appears not to have been studied until 1940, when the method was found to be useful in the identification of alkyl side chains on the carbocyclic ring (485, 486).

Wibaut and coworkers (89, 575, 576) have found quinoline (CCCV) and its homologs to combine the properties of pyridine and naphthalene in their behavior toward ozone. The major attack by ozone occurs initially on the carbocyclic ring at the 5,6- and 7,8-bonds (e.g., CCCVI), after which the remaining

TABLE 4*

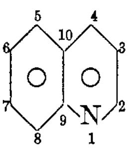
Ozonolyses of pyrones

Pyrone Compound	HCOCOOH	CHOCHO	CH_3COCHO	$CH_3COCOCH_3$	CHOCOCHO	CH_3COOH	HCOOH
4-Pyrone	0.12	0.12			0.03		3.1
2,6-Dimethyl-4-pyrone	0.2		0.16		0.03	1.5	1.1
2,3,6-Trimethyl-4-pyrone	0.11†		0.08	0.07		1.85	
2,6-Dimethyl-4-thiapyrone	0.04		0.02		0.12	0.53	0.82

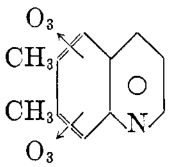
* The values shown are moles of product per mole of pyrone.

† Also 0.11 mole of pyruvic acid was obtained.

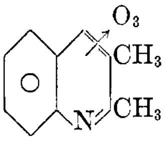
pyridine ring is attacked slowly. A minor reaction involves initial attack on the heterocyclic ring, apparently only at the 3,4-bond (e.g., CCCVII), followed by further attack on the carbocyclic ring.



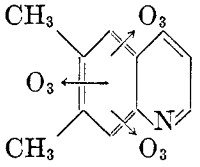
CCCV



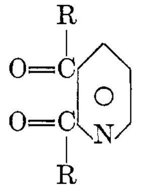
CCCVI



CCCVII



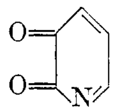
CCCVIII



CCCIX

a: R = H

b: R = OH

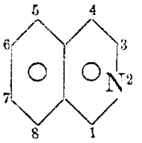


CCCX

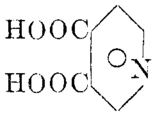
Evidence for the described course of reaction came from data on the absorption of ozone (89), on determinations of ammonia (after hydrolysis) at various intervals (89), and from identification of the reaction products (575, 576). The products from quinoline were either glyoxal and 2,3-diformylpyridine (CCCIXa) or oxalic acid and quinolinic acid (CCCIXb), depending on the work-up procedure. 6,7-Dimethylquinoline (via CCCVI) gave biacetyl and 2,3-diformylpyridine (CCCIXa). No trace of methylglyoxal or pyridine-2,3-quinone (CCCX) was obtained from 6,7-dimethylquinoline, indicating that no attack occurred at the 6,7-, 5,10-, or 8,9-bonds (CCCVIII). Similar results were obtained with 5,8-dimethylquinoline. Evidence for the minor reaction was isolation of biacetyl (via CCCVII) after reaction of 1.5 mole-equivalents of ozone with 2,3-dimethylquinoline (576). These results are consistent with the fact that the 5,6- and

7,8-bonds of quinoline have the most double-bond character (383) and should be the most susceptible to π complex formation.

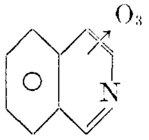
The ozonolysis of isoquinoline (CCCXI) took a different course. Data on the absorption of ozone and the determination of ammonia indicate that initial attack by ozone occurs to the extent of about 60 per cent on the heterocyclic ring and 40 per cent on the carbocyclic ring (89). The attack on the heterocyclic ring apparently involves only one mole-equivalent of ozone, whereas the carbocyclic ring attack involves two (89). Products isolated were phthalic acid (CCXLb) in 50 per cent yield and cinchomeronic acid (CCCXII) in 45 per cent yield (374). These results are to be expected on the basis that the 3,4-bond of isoquinoline (CCCXI), followed closely by the 7,8- and 5,6-bonds, has the most double-bond character (383). Initial attack therefore, should occur in near equal amounts in the two rings.



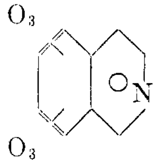
CCCXI



CCCXII

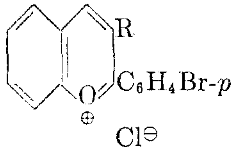


CCCXIII

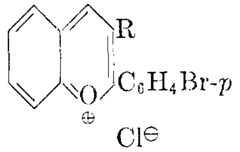


CCCXIV

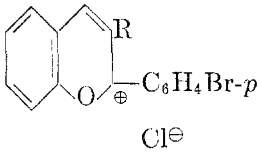
Benzopyrylium salts appear to be resonance hybrids of structures like CCCXV, CCCXVI, CCCXVII, and CCCXVIII (563). Ozonolysis results are consistent



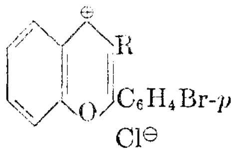
CCCXV



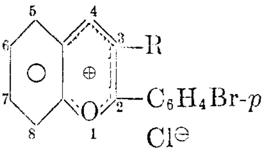
CCCXVI



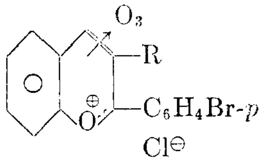
CCCXVII



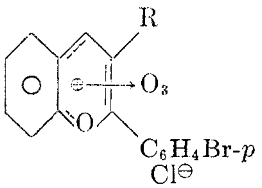
CCCXVIII



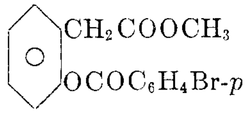
CCCXIX



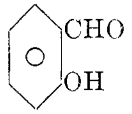
CCCXX



CCCXXI



CCCXXII



CCCXXIII

$C_6H_5COCOC_6H_4Br$-*p*
CCCXXIV

BrC_6H_4COOH-*p*
CCCXXV

a: R = C_6H_5. b: R = OCH_3.

TABLE 5

Products from ozonolyses of pyrroles and furans

Compound	Glyoxal	Methylglyoxal	Biacetyl
	per cent	*per cent*	*per cent*
Pyrrole	15		
1-Phenylpyrrole	38		
2,4-Dimethylpyrrole		41	
2,5-Dimethylpyrrole	3.2	20.6	
1,2,5-Trimethylpyrrole*	1	2	
1-Ethyl-2,5-dimethylpyrrole*	1.6	4.4	
2-Methylpyrrole*	7	1.2	
1,2-Dimethylpyrrole	5.1	8.3	
2,3-Dimethylpyrrole	+	4.3	11.5
1-Ethyl-2,3-dimethylpyrrole		2.9	8.6
Furan	46		
2,5-Dimethylfuran	20	28	
2,3,5-Trimethylfuran		+	+
2,3-Dimethylfuran	10.5	13	7
2-Methylfuran†	+	+	

* Pronounced resinification lowered the yields.

† Total yield of 30 per cent of a mixture of 5 parts of glyoxal and 2 parts of methylglyoxal.

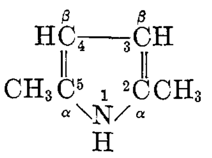
with this theory. Products isolated were salicylaldehyde (CCCXXIII) and *p*-bromobenzil (CCCXXIV), from attack on the 3,4-bond, and *p*-bromobenzoic acid (CCCXXV) from attack on the 2,3-bond of CCCXIXa (509). Compounds CCCXXIII and CCCXXII were obtained from attack on the 3,4-bond and 2,3-bond, respectively, of CCCXIXb; *p*-bromobenzoic acid (CCCXXV) also was a product (509).

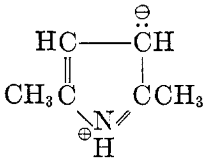
Shriner and Moffett (509) looked upon these reactions as involving structures CCCXVII and CCCXVIII rather than CCCXV and CCCXVI. A better explanation would seem to be an attack by ozone on the hybrid molecule (CCCXIX) at either the 3,4-bond (e.g., CCCXX) or the 2,3-bond (e.g., CCCXXI).

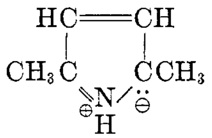
C. PYRROLES AND FURANS

Wibaut and coworkers have ozonized pyrrole (569, 571, 572, 574, 579) and furan (326, 569, 571, 572, 574) and certain of their homologs in inert solvents at low temperatures. The reactions were fast, resinification often occurred, and the yields of final products generally were low. Approximately two moles of ozone per mole of compound was absorbed. Good yields of ammonia or primary amines were obtained from the pyrroles. In all cases formic acid (from α-unsubstituted pyrroles and furans) and acetic acid (from α-methylpyrroles and furans) were isolated. The other products are shown in table 5.

Particularly to be noted are the yields of methylglyoxal (LXI) from 2,5-dimethylpyrrole, 1,2,5-trimethylpyrrole, 1-ethyl-2,5-dimethylpyrrole, 2-methylpyrrole, 1,2-dimethylpyrrole, 2,5-dimethylfuran, and 2-methylfuran, and the yields of biacetyl (CCXXXIII) from 2,3-dimethylpyrrole, 1-ethyl-2,3-dimethylpyrrole, 2,3-dimethylfuran, and 2,3,5-trimethylfuran. These substances cannot arise from cleavage of the double bonds of the classical valence structures of pyrroles and furans (e.g., CCCXXVI).


CCCXXVI

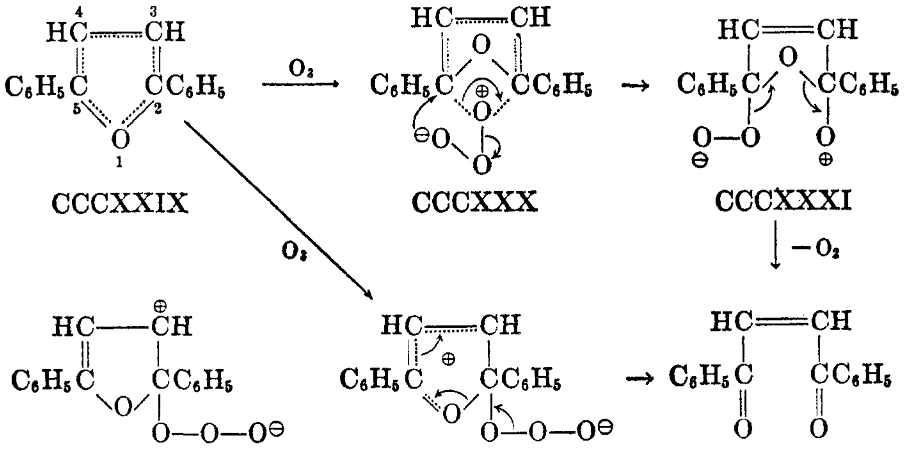

CCCXXVII


CCCXXVIII

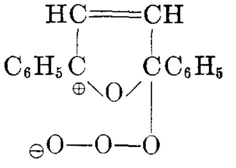
Wibaut and coworkers (326, 569, 571, 572, 574, 579) have suggested that the "abnormal" products result from an attack by ozone on ionic structures (e.g., CCCXXVIII) which contribute to the hybrid molecules of furans and pyrroles (e.g., CCCXXVI ↔ CCCXXVII ↔ CCCXXVIII) (194, 246).

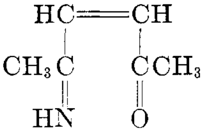
The ozonolysis of 2,5-diphenylfuran (CCCXXIX) in methanol has furnished a clearer insight into the reactions (47). During the absorption of one mole-equivalent of ozone, all of the furan reacted and a 12 per cent yield of *cis*-1,2-dibenzoylethylene (CCCXXXIV) precipitated. Absorption of two mole-equivalents of ozone produced phenylglyoxal (LXXXIV) (14 per cent yield) (via CCCXXXIV) and benzoic acid (81 per cent yield).

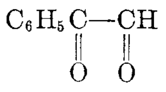
These products could result from competing initial attacks by ozone at the 2,3-bond (major reaction) and the 2- and 5-positions (minor reaction) of the hybrid molecule (CCCXXIX). Benzoic anhydride probably was an intermediate in the formation of benzoic acid. The cis isomer is the labile isomer of 1,2-dibenzoylethylene (358). In order for it to be produced in preference to the


CCCXXIX CCCXXX CCCXXXI

CCCXXXII CCCXXXIII CCCXXXIV


CCCXXXV


CCCXXXVI

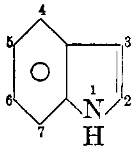

LXXXIV

trans isomer, the double bond between atoms 3 and 4 of the original furan system (CCCXXIX) would have to form either before or at the same time ring cleavage occurs. This is best accounted for by a 1,4-addition mechanism (CCCXXIX → CCCXXX → CCCXXXI → CCCXXXIV). The 1,4-addition product is represented as a π complex (CCCXXX) (Section II,B). It could just as well involve two atoms of the ozone molecule. An alternative mechanism for formation of CCCXXXIV involves an electrophilic attack of ozone at a reactive α-position (246, 414), followed by the concerted shift of electrons and loss of oxygen shown in the hybrid molecule, CCCXXXIII. A more likely fate for CCCXXXIII, however, would appear to be completion of 1,2-addition at atom 3 (CCCXXXII) or 1,4-addition at atom 5 (CCCXXXV).

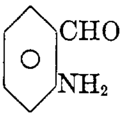
In the case of pyrroles the 1,4-addition would lead to an intermediate such as CCCXXXVI. Hydrolysis of this or of ozonolysis products thereof would yield ammonia.

D. INDOLES AND BENZOFURANS

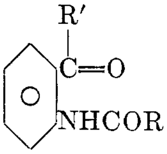
The ozonolysis of indole and its derivatives has been studied extensively (76, 184, 197, 330, 378, 401, 402, 437, 438, 451, 489, 592, 593, 595, 596, 597, 598, 599). In each instance attack by ozone occurred in the heterocyclic ring, with cleavage of the 2,3-bond (CCCXXXVII). The product from indole (CCCXXXVII) was a condensation trimer of *o*-aminobenzaldehyde (CCCXXXVIII) (592). Acylamino aldehydes, acids, or ketones (CCCXXXIX) were obtained from 2- and/or 3-substituted indoles (76, 437, 592).



CCCXXXVII



CCCXXXVIII



CCCXXXIX

R = alkyl, aryl, or H

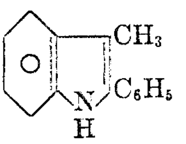
R′ = alkyl, aryl, H, or OH

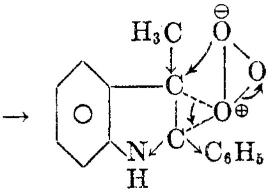
Only 2,3-disubstituted indoles form stable ozonides (or other peroxidic ozonolysis products) (184, 197, 330, 378, 401, 402, 437, 451, 597, 598, 599). Ozonolysis of 3-methyl-2-phenylindole (CCCXL) in either inert or reactive solvents gave a peroxidic material to which Criegee and Lohaus (197, 378) assigned a hydroperoxide (CCCXLIII) rather than an ozonide structure, on the bases that it gave a weak lead tetraacetate test for a hydroperoxide (213) and that the corresponding *N*-methyl compound did not give a crystalline peroxidic ozonolysis product. They considered CCCXLIII to be produced by an intramolecular addition of the benzoylamino and zwitterion groups of CCCXLII.

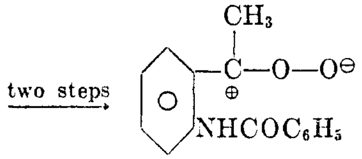
Witkop and coworkers (451, 597, 598, 599) concluded that this and analogous peroxidic ozonolysis products from the 6-methoxy derivative of CCCXL and from 2-*p*-anisyl-3-methylindole functioned as ozonides (CCCXLIV) in basic or acidic medium and as the tautomeric hydroperoxides in neutral medium.

Evidence came principally from infrared and ultraviolet spectra, which showed hydroxyl, hydroperoxy, and —C=N— groups under neutral but not under acidic or basic conditions.

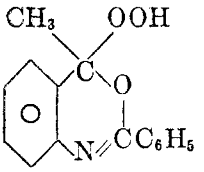
Rearrangement of ozonide CCCXLIV occurred under both acidic and basic conditions (197, 378, 598). From the acid-catalyzed decomposition CCCXLV was obtained in 93 per cent yield (598). Base-catalyzed rearrangement gave low yields of CCCL (from the acetylation of CCCXLV or of intermediates leading to its formation) and CCCLI (from acyl migration in CCCXLV; *cf.* 365) (598). It was suggested that the acid-catalyzed rearrangement proceeds through intermediates CCCXLVII and CCCXLVIII (598).

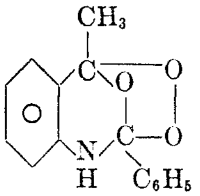

CCCXL

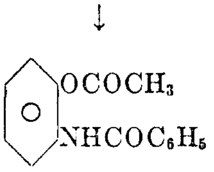

CCCXLI

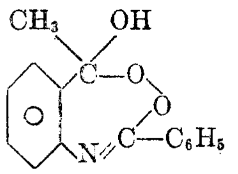


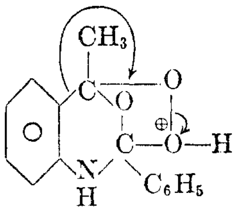
CCCXLII


CCCXLIII


CCCXLIV


CCCXLV


CCCXLVI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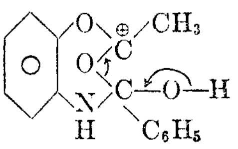
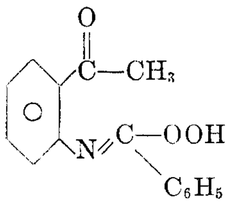
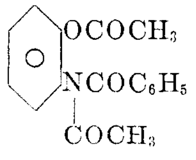
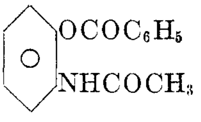

CCCXLVIII


CCCXLIX

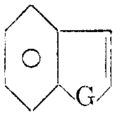

CCCL


CCCLI

The attack of ozone on the 2,3-bond of the indole ring system is consistent with previously described theory (Section II,B), since this bond has the most double-bond character (383). Zwitterion CCCXLII should result preferentially from the collapse of π complex CCCXLI (Section II,B). Cyclization of CCCXLII could yield either hydroperoxide CCCXLIII or ozonide CCCXLIV. The rearrangements are of the type discussed in Section II,C,2 and probably involve zwitterion CCCXLII (from decomposition of CCCXLIV) rather than the ozonide itself.

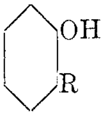
The proposed tautomerism between CCCXLIV and CCCXLIII (598, 599) requires attack of a hydrogen ion on a peroxidic oxygen atom of CCCXLIV rather than on the ether-type oxygen atom. It seems more likely, as suggested by studies concerning the hydrolysis of ozonides (470) (Section VIII,C,3), that the tautomerism involves CCCXLIV and CCCXLVI. Structure CCCXLVI is analogous to certain cyclic structures obtained from ozonolyses of naphthalene and phenanthrene in methanol (Section IV). The evidence presented for the hydroperoxide structure (CCCXLIII) (378, 599) can also be rationalized by structure CCCXLVI. The lead tetraacetate test, which was weak (378), could reflect a further equilibrium with CCCXLIX. The band in the infrared spectrum assigned to the hydroperoxy group (599) could, instead, result from the peroxy group in CCCXLVI (71).

Like indoles, benzofurans (CCCLIIa), benzothiophenes (CCCLIIb), and benzodifurans (CCCLV) were attacked by ozone in the heterocyclic ring or rings. Ozonolysis of benzofuran (CCCLIIa) gave salicyclic acid (CCCLIIIa) (25 per cent), salicylaldehyde (CCCLIIIb) (40 per cent), and catechol (CCCLIIIc) (10 per cent) (560). Similar results were obtained with 2-methyl- and 3-methylbenzofurans and 3,7-dimethylbenzofuran (560). Likewise, benzothiophene (CCCLIIb) was converted to CCCLIVa (30 per cent), CCCLIVb (20 per cent), and CCCLIVc (50 per cent) (560). In these cases oxidation of the initially formed compounds of type CCCLIII (SH in place of OH) undoubtedly occurred. The conversions to CCCLIIIc and CCCLIVc involve rearrangements of the type discussed in Section II,C,2.

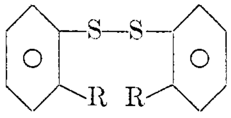


CCCLII

a: G = O
b: G = S

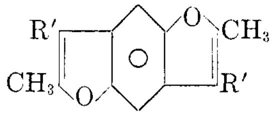


CCCLIII



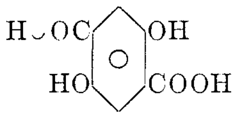
CCCLIV

a: R = COOH
b: R = CHO
c: R = OH

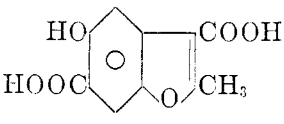


CCCLV

a: R′ = H
b: R′ = $COOC_2H_5$
c: R′ = $COCH_3$



CCCLVI



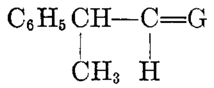
CCCLVII

A stable diozonide (m.p. 132–134°C.) in 24 per cent yield and a stable monoozonide (m.p. 115° (d.)) in 22 per cent yield were obtained from CCCLVb (78). The diozonide was hydrolyzed to CCCLVI and the monoözonide to CCCLVII (78). Compounds CCCLVa and CCCLVc gave similar results.

VI. Ozonolysis of the Carbon–Nitrogen Double Bond

The work of Wibaut and coworkers with pyridine, quinoline, and isoquinoline and their homologs has indicated that ozone does not attack carbon–nitrogen double bonds (Sections V,A and V,B). Ozonolyses of isoxazoles also have been reported to occur only at the carbon–carbon double bond (350, 351, 380, 400).

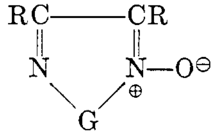
In contrast to these results are the reported conversions by ozone of the imine CCCLVIIIa to the aldehyde CCCLVIIIb (357; *cf.* 594), of certain osotriazole oxides (CCCLIXa) (412) and furazan oxides (CCCLIXb) (341, 343), but not the parent osotriazoles and furazans, to α-diketones (or keto aldehydes) and carboxylic acids, respectively, and of the dinitrophenylhydrazones CCCLX to the corresponding ketones (263). In none of these cases, however, was it shown definitely that the cleavage was caused by ozone rather than by oxygen, or what role hydrolysis played in the conversions.



$$C_6H_5\underset{CH_3}{\underset{|}{CH}}-\underset{H}{\underset{|}{C}}=G$$

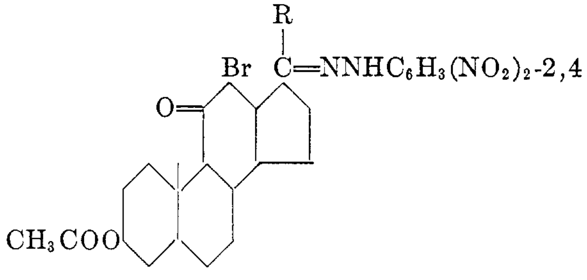
CCCLVIII

a: G = NH
b: G = O



CCCLIX

a: G = NHC_6H_5
b: G = O



CCCLX

a: R = CH_2OCOCH_3
b: R = $COOCH_3$
c: R = $CH(OCOCH_3)_2$

$ArCH{=}NAr'$

CCCLXI

a: Ar = Ar′ = C_6H_5.
b: Ar = C_6H_5, Ar′ = $C_6H_4NO_2$-*m*.

$(CH_3)_2C{=}NNHC_6H_3(NO_2)_2$-2,4

CCCLXII

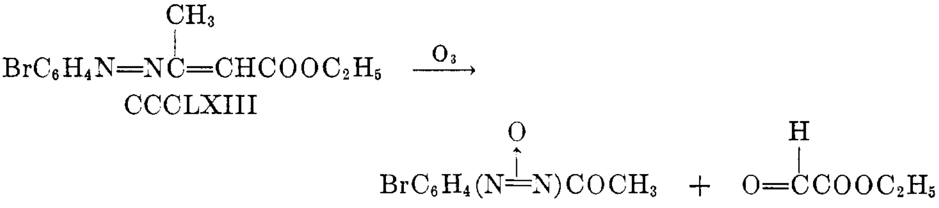
Studies with acetone 2,4-dinitrophenylhydrazone (CCCLXII) and certain Schiff bases (CCCLXI) have shown that the attacking reagent in these reactions actually is ozone (467). Upon ozonolysis of CCCLXII in acetic acid, two moles of ozone were absorbed and a peroxidic solution was obtained which gave acetone upon reduction. Ozonolyses of the Schiff bases CCCLXI, using either ozone–nitrogen or ozone–oxygen mixtures, gave 40–60 per cent yields of benzaldehyde or benzoic acid.

VII. Ozone as an Oxidant

Considerable progress has been made in the elucidation of the reactions of ozone with such substances as saturated hydrocarbons, alcohols, aldehydes, ethers, amines, phosphines, arsines, and organic sulfides. These reactions appear to be of at least two distinct types. One involves an electrophilic attack by ozone and the other an ozone-initiated oxidation in which oxygen is the principal reactant. In the latter case ozone behaves as a radical reagent. It appears possible for ozone also to react as a nucleophilic reagent (364), although this has not yet been established.

A. AMINES, PHOSPHINES, ARSINES, AND SULFIDES

The reactions of ozone with tertiary amines, phosphines, arsines, sulfides, and sulfoxides belong to the category of electrophilic attack by ozone. Long (380) stated that amines, in general, are not attacked by ozone. Primary and secondary aliphatic amines, however, are decomposed by ozone (533) and tertiary amines are converted to the corresponding amine oxides (313, 389, 521, 532). Oxide formation has been reported for certain unsaturated diazo compounds (CCCLXIII → CCCLXIV) (7).

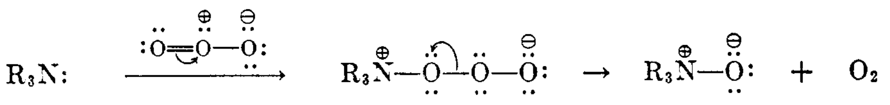


$$\mathrm{BrC_6H_4N{=}N\overset{CH_3}{\overset{|}{C}}{=}CHCOOC_2H_5} \xrightarrow{O_3} \mathrm{BrC_6H_4(N\overset{O}{\overset{\uparrow}{=}}N)COCH_3} + \mathrm{O{=}\overset{H}{\overset{|}{C}}COOC_2H_5}$$

CCCLXIII

CCCLXIV CCCLXV

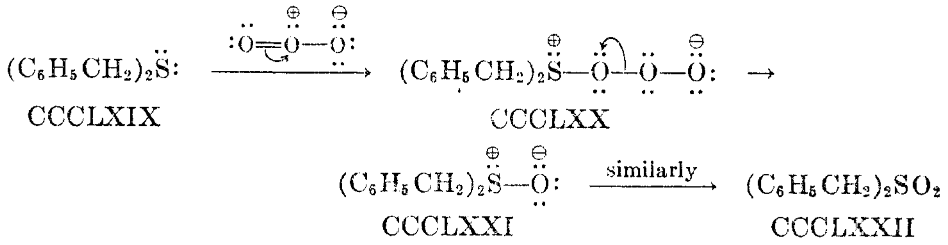
The absorption of ozone by tertiary amines was rapid; approximately one mole-equivalent of ozone reacted and yields of amine oxides were generally high (313, 389). Similar results were obtained with triphenylphosphine and triphenylarsine (313). Maggiolo (389) and Horner (313) and coworkers logically assume the reactions to occur by the electrophilic attack of a terminal atom of ozone, followed by loss of oxygen (CCCLXVI → CCCLXVIII). It would be difficult to explain these reactions in terms of an attack by ozone involving the central atom.



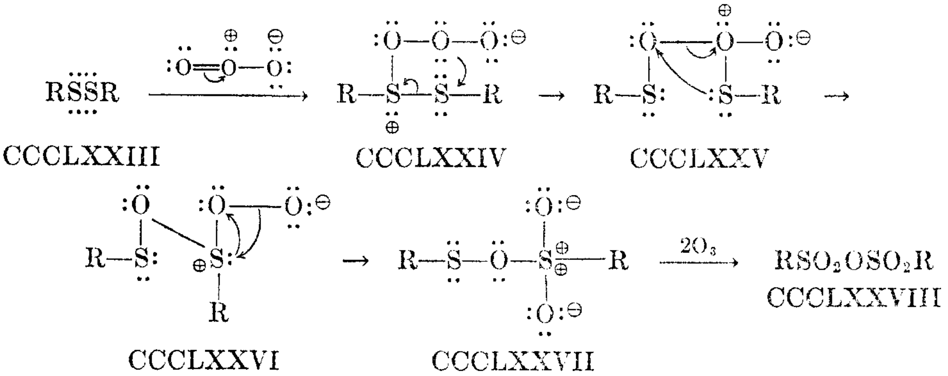
$$\mathrm{R_3N{:}} \xrightarrow{\mathrm{:\ddot{O}{=}\overset{\oplus}{\ddot{O}}{-}\overset{\ominus}{\ddot{O}}:}} \mathrm{R_3\overset{\oplus}{N}{-}\ddot{O}{-}\ddot{O}{-}\overset{\ominus}{\ddot{O}}:} \rightarrow \mathrm{R_3\overset{\oplus}{N}{-}\overset{\ominus}{\ddot{O}}:} + \mathrm{O_2}$$

CCCLXVI CCCLXVII CCCLXVIII

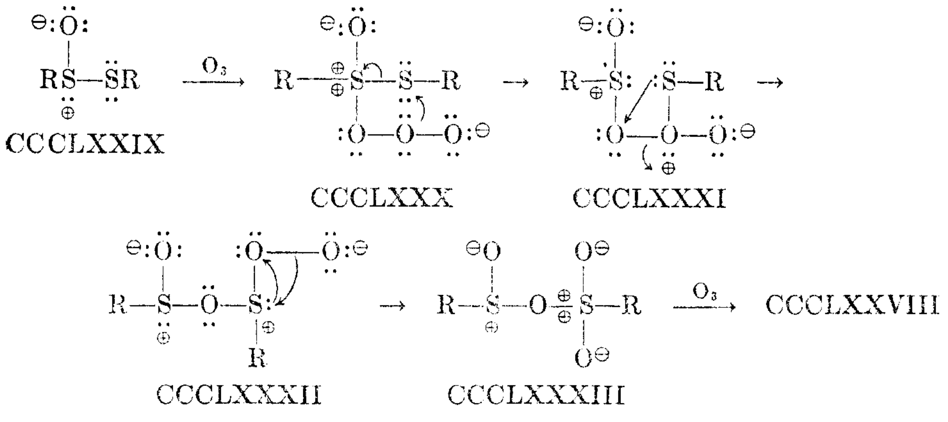
Organic sulfides react similarly. The products usually are sulfones, but sulfoxides often can be isolated as intermediates (58, 59, 92, 313, 387, 457). Dibenzyl sulfide (CCCLXIX), for example, was converted quantitatively to either the sulfoxide (CCCLXXI) or the sulfone (CCCLXXII) (387). Maggiolo and Blair (387) and Horner and coworkers (313) found the reactions to be stoichiometric for one mole of ozone per mole of sulfide to the sulfoxide and two moles of ozone to the sulfone. Barnard (59), however, reported the absorption of ozone to be somewhat less than this and concluded that oxygen enters into the reaction to a degree dependent on the oxidizability of the sulfide. In either case, the major course of the reaction appears to be analogous to that of tertiary amines (e.g., CCCLXIX → CCCLXX → CCCLXXI → CCCLXXII).



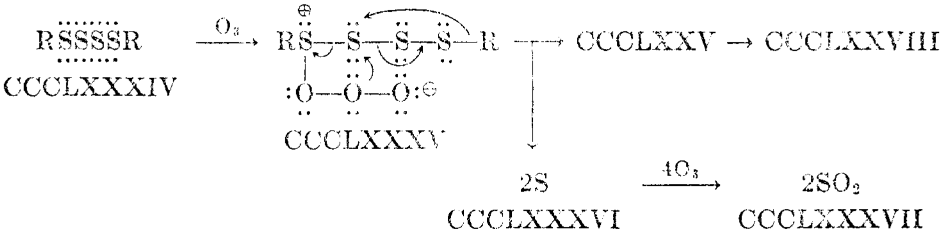
CCCLXIX CCCLXX CCCLXXI CCCLXXII



CCCLXXIII CCCLXXIV CCCLXXV CCCLXXVI CCCLXXVII CCCLXXVIII



CCCLXXIX CCCLXXX CCCLXXXI CCCLXXXII CCCLXXXIII



CCCLXXXIV CCCLXXXV CCCLXXXVI CCCLXXXVII

$$C_6H_5CH_2SSCH_2C_6H_5 \rightarrow C_6H_5CH_2SO_2SCH_2C_6H_5$$

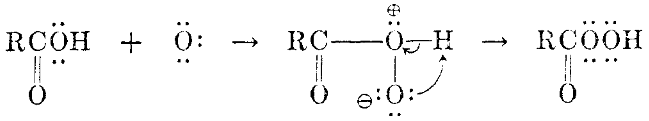
CCCLXXXVIII CCCLXXXIX

Disulfides (CCCLXXIII), thiosulfinates (CCCLXXIX), and polysulfides (CCCLXXXIV) have been converted to sulfonic anhydrides (CCCLXXVIII) in high yield by ozone (58, 59). The disulfides required 2.5 to 3 mole-equivalents of ozone, thiosulfinates about 2 mole-equivalents, and tetrasulfides 5.5 to 6 mole-equivalents. Sulfur dioxide was shown to be formed in the tetrasulfide reaction, and thiosulfinates were shown not to be intermediates in the disulfide oxidations. Mechanisms were proposed involving the changes CCCLXXIII → CCCLXXV → CCCLXXVI → CCCLXXVII → CCCLXXVIII for the disulfide reaction, the changes CCCLXXIX → CCCLXXXI → CCCLXXXII → CCCLXXXIII → CCCLXXVIII for the thiosulfinate reaction, and CCCLXXXIV → CCCXXV + CCCLXXXVI, followed by CCCXXV → CCCXXVI → CCCXXVII → CCCXXVIII and CCCXXXVI → CCCXXXVII, for the tetrasulfide reaction (58, 59). In view of results with monosulfides, it is logical to assume that the attack by ozone was electrophilic in all of these reactions, giving CCCLXXIV, CCCLXXX, and CCCLXXXV as the primary intermediates.

Dibenzyl disulfide (CCCLXXXVIII) appears to be unusual. Barnard (59) reports that it was oxidized to sulfur dioxide, sulfuric acid, benzaldehyde, and benzoic acid, whereas Horner and coworkers (313) found that after the absorption of two mole-equivalents of ozone, the benzyl ester of benzylthiosulfonic acid (CCCLXXXIX) was obtained.

B. CARBOXYLIC ACIDS

Carboxylic acids react only slightly with ozone under normal conditions. Paillard and Briner (449) found a very low conversion of glacial acetic acid to peracetic acid. Taube (538, 539) has reported that under the influence of ultraviolet light the oxidation of acetic acid to peracetic acid by ozone becomes significant. He interprets the reaction as involving the electrophilic attack of electronically excited oxygen atoms rather than of ozone itself (XCD → XCDII).



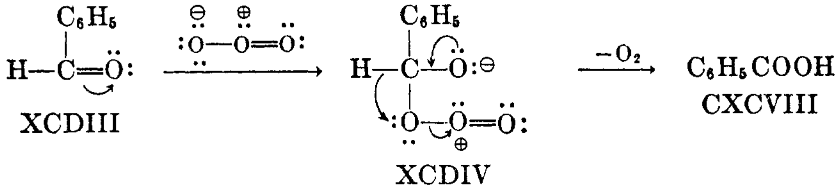
$$\underset{\mathrm{O}}{\overset{\|}{\mathrm{RC}}}\mathrm{OH} + \mathrm{O} \rightarrow \underset{\mathrm{O}}{\overset{\|}{\mathrm{RC}}}\text{——}\underset{\ominus\mathrm{O}}{\overset{\oplus}{\mathrm{O}}}\text{—}\mathrm{H} \rightarrow \underset{\mathrm{O}}{\overset{\|}{\mathrm{RC}}}\mathrm{OOH}$$

XCD XCDI XCDII

C. ALDEHYDES, KETONES, ALCOHOLS, ETHERS, AND SATURATED HYDROCARBON GROUPINGS

The remaining reactions of ozone as an oxidant appear to be of the type in which oxygen enters into the reaction and ozone serves primarily as the initiator of the reaction. Briner and coworkers (99, 101, 105, 106, 107, 109, 110, 112, 113, 117, 118, 119, 125, 129, 130, 137, 138, 139, 140, 141, 142, 143, 153, 217, 218, 221) have studied extensively the action of ozone on aldehydes. Ozone–oxygen mixtures were found to oxidize benzaldehyde and other aldehydes to a mixture of the corresponding acid and per acid (*cf.* 242, 258, 380), probably by an ozone-initiation mechanism (101) (equations 10–13, end of section). The absorption of ozone was slow and the extent of oxidation was greater than could be accounted for by the amount of ozone absorbed. Infrared data showed, however, that the oxidation rate was greatly increased by the presence of ozone. After treatment of benzaldehyde with 0.76 per cent ozone for 10 min., characteristic bands of perbenzoic acid had developed more strongly than they had after 3 hr. treatment with oxygen alone. Increase of the ozone concentration to 3.4 per cent afforded no further acceleration in the development of the perbenzoic acid bands, and the ratio of the amount of oxygen in the final products to the amount of ozone used up was much less than when 0.76 per cent ozone was used. The accelerating action of ozone was found to be in effect at very low concentrations of ozone, certainly as low as 0.01 per cent. As further evidence that the principal oxidizing agent was oxygen and not ozone, it was found that if the ozone concentration was held constant while the oxygen concentration was decreased (through replacement by nitrogen), the amount of oxidation decreased.

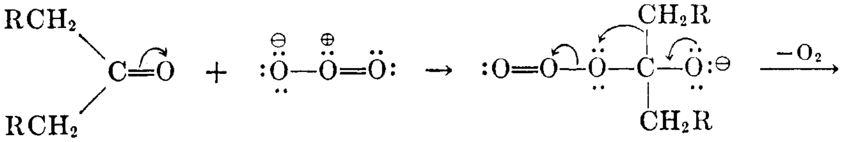
In experiments using ozone–nitrogen mixtures containing no more than 1 per cent oxygen, benzoic acid, but no perbenzoic acid, was obtained (105). This possibly was due to a nucleophilic attack by ozone, itself, to give XCDIV, followed by loss of oxygen.



XCDIII XCDIV CXCVIII

Olefins prevent ozone-initiated autoxidation because they react more readily with ozone than do the other substances to be oxidized (112, 113, 221). Infrared spectra taken during the ozonolysis of *trans*-stilbene showed the immediate development of the characteristic carbonyl band of benzaldehyde (1706 cm.$^{-1}$). This became stronger as the ozonolysis proceeded. It was not until the ozonolysis was complete that the band began to decrease in intensity and characteristic bands of perbenzoic acid began to appear. Apparently earlier work which led to the conclusion that, during ozonolyses of cinnamaldehyde (217) and crotonaldehyde (218), ozonides of the starting materials and cinnamic and crotonic acids were produced simultaneously has some other explanation.

The oxidation of ketones to carboxylic acids in good yield by ozone–oxygen mixtures has been reported (242, 295, 531). The reactions were slower than the aldehyde reactions and no intermediate or by-products were isolated. Examples are adipic acid from cyclohexanone (295, 531), pentadecanedioic acid from cyclopentadecanone (531), and acetic and propionic acids from diethyl ketone (242). It was supposed originally (242, 531) that these reactions involved the ozonides of the enol forms of the ketones. A more logical suggestion was a nucleophilic attack by ozone (XCDV → XCDVI) (364) to produce an ester (XCDVII), followed by further oxidation of the ester. If this were the main course of the reaction, however, it would appear that some of the ester should have been isolated. Although the nucleophilic attack by ozone might become important in the absence of oxygen, it appears that with ozone–oxygen mixtures the major reaction is an ozone-initiated oxidation by oxygen analogous to those shown at the end of this section for aldehydes and ethers.



XCDV XCDVI

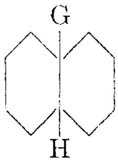
$$\underset{\text{XCDVII}}{RCH_2COOCH_2R} \xrightarrow[\text{oxidation}]{\text{further}} \underset{\text{XCDVIII}}{RCH_2COOH} + \underset{\text{CCI}}{RCOOH}$$

The review by Long (380) discusses the reactions of alcohols and ethers with ozone, in which aldehydes, carboxylic acids, esters, and peroxides are obtained. Most noteworthy is the 70–80 per cent yield of isoamyl isovalerate (CD) from isoamyl ether (XCDIX) (257). The oxidation of alcohols by ozone has been utilized in the carbohydrate field (403, 404). The ozonation of sugar alcohols in aqueous solution led to aldoses which were identified as phenylhydrazones, osazones, and formazans. The oxidation by ozone of a secondary alcohol to a ketone in high yield has been reported (440). A patent has been issued for the oxidation of cyclohexanol to adipic acid in the presence of ozone (295). The probable mechanisms of these reactions are illustrated at the end of the section.

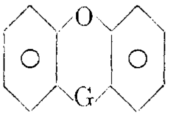
$$\underset{\text{XCDIX}}{(CH_3)_2CHCH_2CH_2OCH_2CH_2CH(CH_3)_2} \xrightarrow{O_3} \underset{\text{CD}}{(CH_3)_2CHCH_2COOCH_2CH_2CH(CH_3)_2}$$

The attack of ozone on activated methyl, methylene, and methylidyne groups is well known (243, 380). Some recent examples are the conversion of decalin (CDIa) to 9-decalol (CDIb) (454), of xanthenes (CDIIa) to xanthones (CDIIb) (176), of fluorene (CDIVa) to fluorenone (CDIVb) (176), of anthrone (CDIII) to anthraquinone (176), of diphenylmethane to benzophenone (176), of *O*-dimethylcitromycin (CDVa) to *O*-dimethylcitromycinone (CDVb) (176, 475), of cumene (CDVIa) to cumene hydroperoxide (CDVIb) (472), of *tert*-butylcyclohexane to a mixture of adipic acid and *tert*-butyladipic acids (185), of xylenes to phthalic acids (294) and certain oxidations in the steroid field (66, 67). Similar oxidations involving aromatic rings include the oxidation of phenol to hydroquinone and of aniline to *o*-aminophenol and analogous reactions in the naphthalene field (492). These were carried out under alkaline conditions.

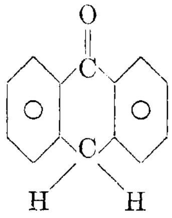
The oxidation of methane to methanol and formaldehyde by means of ozone-oxygen mixtures has been reported from time to time (240, 292, 413, 447, 522, 566). It has been suggested that the high-temperature reaction is initiated by oxygen atoms from the decomposition of ozone (347). A commercial process for



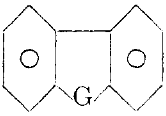
CDI
a: G = H
b: G = OH



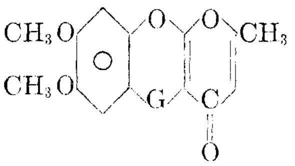
CDII
a: G = CH_2
b: G = CO



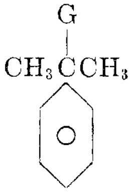
CDIII



CDIV
a: G = CH_2
b: G = CO



CDV
a: G = CH_2
b: G = CO



CDVI
a: G = H
b: G = OOH

the production of formaldehyde from the oxidation of methane, using ozone and barium peroxide catalysts, reportedly was in the developmental stage in Germany during World War II (312, 504). Luetić and Brihta (384), however, tried the method without successs. In view of the ease with which aldehydes are oxidized by ozone-oxygen mixtures, it would appear difficult to obtain practical yields of formaldehyde by this method.

Briner and coworkers (108, 120, 171) have found that the results of oxidation of propane, butane, hexane, heptane, octane, and other alkanes by ozone–oxygen mixtures parallel the results of the similar oxidations of aldehydes, with the exception that higher temperatures are required (150–400°C.).

Schubert and Pease (493, 494, 495) have investigated the action of ozone–oxygen mixtures on various alkanes at 25–50°C. and at 110°C. and higher temperatures. No noticeable oxidation of isobutane occurred until 260–270°C. in the absence of ozone, but it occurred readily even at 25°C. in the presence of ozone. Oxygen entered more and more into the reaction as the temperature was increased, and at about 275°C. the reaction merged into normal slow combustion. Similar results were noted for propane and *n*-butane. Ozone completely eliminated the induction period required for the oxidation of saturated hydrocarbons by oxygen.

The products from oxidations of methane, propane, *n*-butane, and isobutane at 25–50°C. are shown in table 6 (493, 494, 495). In the case of isobutane, the molar quantity of *tert*-butyl alcohol obtained was approximately twice that of acetone, the sum of the two was roughly equivalent to the ozone consumed, and the sum of the molar quantities of the minor products (methanol, carbon dioxide, and formic acid) approached that of acetone. These minor products

TABLE 6

Moles of product per mole of ozone consumed from ozonation of alkanes

Hydrocarbon	Temperature	HCOOH	CO_2	CH_3OH	Acetone	*tert*-Butyl Alcohol	Gram-atoms of Oxygen in Product
	°C.						
CH_4	50	0.12	0.2	0.02			0.86
C_3H_8	50	0.13	0.77	0.02	0.42		2.24
n-C_4H_{10}	50	0.20	0.82	0.05			2.09*
i-C_4H_{10}	25	0.02	0.16	0.01	0.26	0.68	1.31
	50	0.03	0.16	0.03	0.44	0.75	1.60

* A substance thought to be a per acid was also produced.

and acetone were shown not to originate from *tert*-butyl alcohol. At higher temperatures (110°C. and above) the products were the same, with the exception that considerable quantities of *tert*-butyl hydroxymethyl peroxide (CDX) were obtained.

On the basis of these results Schubert and Pease (493, 494, 495) proposed the following mechanism:

$$RH + O_3 \rightarrow RO\cdot + HOO\cdot \qquad (1)$$

$$RO\cdot + RH \rightarrow ROH + R\cdot \qquad (2)$$

$$RO\cdot \rightarrow R'{=}O + R\cdot'' \qquad (3)$$

$$R\cdot + O_2 \rightarrow ROO\cdot \qquad (4)$$

$$ROO\cdot + RH \rightarrow ROOH + R\cdot \qquad (5)$$

The principal difference between the low-temperature reactions of straight-chain and branched-chain hydrocarbons is that only with the branched-chain hydrocarbons does reaction 3 occur (CDVII → XXXVI + CDVIII). The methyl radical (CDVIII) apparently is converted to methanol, formic acid, and carbon dioxide. The principal difference between the low-temperature reaction, the rate of which depends on the concentrations of both ozone and hydrocarbon, and the high-temperature reaction, in which oxygen is the principal oxidizing agent, is that reaction 5 does not occur at the low temperatures. Chain-termination reactions of the radicals $HO_2\cdot$ and $RO_2\cdot$ apparently occur

$$\underset{\text{CDVII}}{(CH_3)_3CO\cdot} \quad \rightarrow \quad \underset{\text{XXXVI}}{CH_3COCH_3} \quad + \quad \underset{\text{CDVIII}}{CH_3\cdot}$$

instead. At higher temperatures, however, hydroperoxides (e.g., CDIX) are produced and the chain continues. The conversion of CDIX to *tert*-butyl hydroxymethyl peroxide (CDX) apparently involves reactions 6 to 8 (495).

$$CH_3\cdot + O_3 \rightarrow CH_3O_2\cdot \qquad (6)$$

$$CH_3O_2\cdot \rightarrow HCHO + \cdot OH \qquad (7)$$

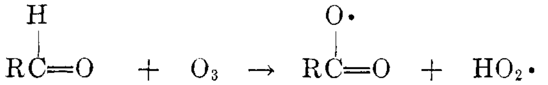
$$\underset{\text{CDIX}}{(CH_3)_3COOH} + HCHO \rightarrow \underset{\text{CDX}}{(CH_3)_3COOCH_2OH} \qquad (8)$$

Schubert and Pease (495) suggest that all oxidations by oxygen are initiated by small quantities of ozone always present and that they become self-sustaining at temperatures around 300°C. through regeneration of ozone by means of reactions such as 9. Recent work concerning the origin of "smog" indicates

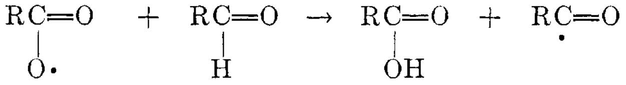
$$RO_2\cdot + O_2 \rightarrow RO\cdot + O_3 \tag{9}$$

that ozone is produced during the oxidation of hydrocarbons in the atmosphere (284, 285).

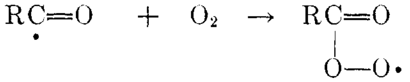
The ozone-initiated oxidation mechanism can be carried over to the ozone-initiated oxidations of aldehydes, as illustrated in equations 10 to 13.



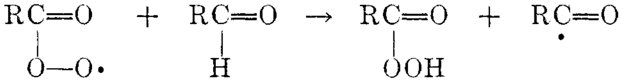
$$R\overset{\overset{H}{|}}{C}{=}O + O_3 \rightarrow R\overset{\overset{O\cdot}{|}}{C}{=}O + HO_2\cdot \tag{10}$$



$$R\underset{\underset{O\cdot}{|}}{C}{=}O + R\underset{\underset{H}{|}}{C}{=}O \rightarrow R\underset{\underset{OH}{|}}{C}{=}O + R\underset{\bullet}{C}{=}O \tag{11}$$

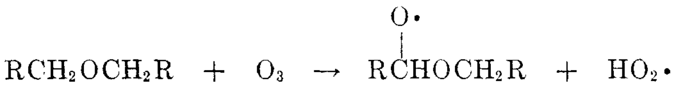


$$R\underset{\bullet}{C}{=}O + O_2 \rightarrow R\underset{\underset{O{-}O\cdot}{|}}{C}{=}O \tag{12}$$

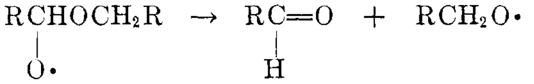


$$R\underset{\underset{O{-}O\cdot}{|}}{C}{=}O + R\underset{\underset{H}{|}}{C}{=}O \rightarrow R\underset{\underset{OOH}{|}}{C}{=}O + R\underset{\bullet}{C}{=}O \tag{13}$$

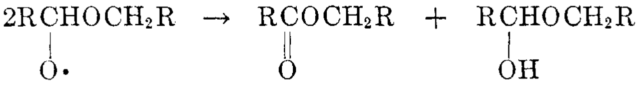
By similar mechanisms the oxidations of ketones, alcohols, and ethers can be rationalized. This is illustrated for ethers by equations 14 to 25.



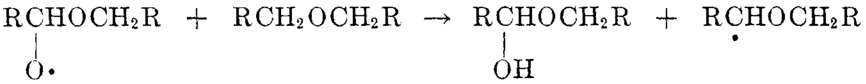
$$RCH_2OCH_2R + O_3 \rightarrow R\overset{\overset{O\cdot}{|}}{C}HOCH_2R + HO_2\cdot \tag{14}$$



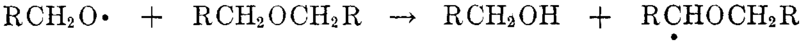
$$R\underset{\underset{O\cdot}{|}}{C}HOCH_2R \rightarrow R\underset{\underset{H}{|}}{C}{=}O + RCH_2O\cdot \tag{15}$$



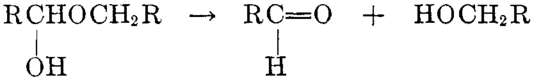
$$2R\underset{\underset{O\cdot}{|}}{C}HOCH_2R \rightarrow R\underset{\underset{O}{\|}}{C}OCH_2R + R\underset{\underset{OH}{|}}{C}HOCH_2R \tag{16}$$



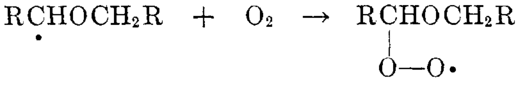
$$R\underset{\underset{O\cdot}{|}}{C}HOCH_2R + RCH_2OCH_2R \rightarrow R\underset{\underset{OH}{|}}{C}HOCH_2R + R\underset{\bullet}{C}HOCH_2R \tag{17}$$



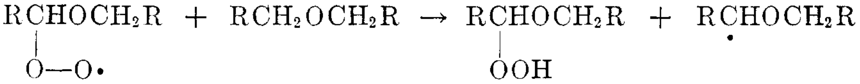
$$RCH_2O\cdot + RCH_2OCH_2R \rightarrow RCH_2OH + R\underset{\bullet}{C}HOCH_2R \tag{18}$$



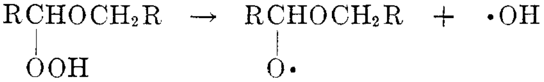
$$R\underset{\underset{OH}{|}}{C}HOCH_2R \rightarrow R\underset{\underset{H}{|}}{C}{=}O + HOCH_2R \tag{19}$$



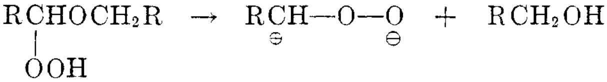
$$R\underset{\bullet}{C}HOCH_2R + O_2 \rightarrow R\underset{\underset{O{-}O\cdot}{|}}{C}HOCH_2R \tag{20}$$



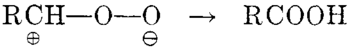
$$\mathrm{R\underset{\underset{O{-}O\bullet}{|}}{C}HOCH_2R + RCH_2OCH_2R \rightarrow R\underset{\underset{OOH}{|}}{C}HOCH_2R + R\underset{\bullet}{C}HOCH_2R} \tag{21}$$



$$\mathrm{R\underset{\underset{OOH}{|}}{C}HOCH_2R \rightarrow R\underset{\underset{O\bullet}{|}}{C}HOCH_2R + \bullet OH} \tag{22}$$



$$\mathrm{R\underset{\underset{OOH}{|}}{C}HOCH_2R \rightarrow R\underset{\oplus}{C}H{-}O{-}\underset{\ominus}{O} + RCH_2OH} \tag{23}$$



$$\mathrm{R\underset{\oplus}{C}H{-}O{-}\underset{\ominus}{O} \rightarrow RCOOH} \tag{24}$$

$$\mathrm{RCH_2OH \rightarrow RCHO \rightarrow RCOOH} \tag{25}$$

The review by Long (380) states that amino acids are not attacked by ozone. Bergel and Bolz (74) have shown, however, that reaction does occur and that aldehydes, ammonia, and hydrogen peroxide are the major products (490). The mechanism is unknown; it may be similar to those just described.

The oxidation of coal, carbon black, lamp black, and humic acids by ozone has been reported (3, 235, 342). The products were largely water-soluble acids and carbon dioxide.

VIII. Utilization of Ozonation

A. EXPERIMENTAL TECHNIQUES

1. Sources of ozone

For many years the principal source of ozone has been from oxygen or air by an electrical discharge. A number of laboratory ozonators of this type have been described, several of which are small and simple to make (10, 94, 277, 297, 519, 565). Some can be put together from common laboratory equipment without glass blowing (247, 461, 555). A laboratory ozonator is commercially available from the Welsbach Corporation for work requiring reproducible ozone concentrations which can be varied over a range of several per cent.

Ozone can be made by the electrolysis of sulfuric acid or perchloric acid solutions (85, 86, 100, 128, 155, 361, 459, 497) in concentrations as high as 58 per cent (361). A practical laboratory ozonator of this type has been described (85, 86). The photochemical production of ozone from oxygen also is being investigated (102, 132, 133, 134, 419).

2. Apparatus

For most ozonolyses the usual reaction vessels of the gas-absorption type are satisfactory. One type has an inserted inlet tube with a porous disc or finger at the end (178); another has a sealed-in inlet at the bottom with a sealed-in porous disc just above it (41). For special purposes more elaborate equipment has been described (59, 88, 280, 386, 407).

3. Solvents

Many different solvents have been used in ozonolysis. Among the solvents which do not react with the zwitterion intermediate (Section II,A) are alkanes (pentane, hexane, petroleum ether) (48, 207, 209, 214), cyclohexane (36), benzene (392), carbon tetrachloride (206, 392), chloroform (512, 576), methylene chloride (65, 67), methyl chloride (205), ethyl chloride (210, 473), ethyl bromide (520), ethyl acetate (597), acetone (214), formamide (592), ether (334, 335), tetrahydrofuran (491), nitromethane (262), and acetic anhydride (476). Examples of solvents which do react with the zwitterion intermediate are methanol (38, 40), ethanol (561, 562), isopropyl alcohol (245, 471), *tert*-butyl alcohol (407), formic acid (238, 360, 591), acetic acid (36, 37), propionic acid (37), water (421, 422), and water–acetone mixtures (211).

Greenwood (278) has studied the effect of ozone on various solvents at temperatures in the range of −25°C. to 25°C. Water, acetic acid, ethyl chloride, carbon tetrachloride, and trichlorofluoromethane were rated as the best solvents from the viewpoint of unreactivity toward ozone. The poorest were methanol and ethanol; in between were methylene chloride, chloroform, ethyl bromide, propyl chloride, 1,2,2-trichloro-1,1,2-trifluoroethane, pentane, and ethyl acetate.

Such comparisons are somewhat misleading. Although methanol, for example, is strongly attacked by ozone when pure, it does not react appreciably when a reactive olefin is dissolved in it and the temperature is kept below −20°C. (38, 40). Methanol and similar solvents which react with the zwitterion intermediate (Section II,A) often allow better yields of normal nonperoxidic products than do the more commonly used inert solvents (38, 40; *cf.* 488).

Formic acid has been described as a good solvent for the preparation of aldehydes by ozonolysis, in that less oxidation to carboxylic acids occurred in the cases tried (238). In contrast, it has been shown that formic acid is a superior solvent for decompositions of alkoxy hydroperoxides to carboxylic acids (41).

4. Following the course of ozonations

There are a number of simple methods for determining when an ozonation is finished. If the reactant readily absorbs ozone the completion of the reaction becomes apparent when iodine is released in a potassium iodide trap following the ozonation vessel (591). The deterioration of natural rubber tubing attached to the ozonolysis vessel likewise indicates that ozone is in the effluent gas (262). A blue color of the cold (−50°C. or below) reaction mixture characterizes a saturated solution of ozone (392).

For ozonations of less reactive materials, qualitative tests for unsaturation can be made on the reaction mixture with tetranitromethane (67, 310, 549) or bromine solutions (233, 448). The bromine test has been used quantitatively (280). Another method is to determine the percentage of ozone in the incoming gas, the total volume of gases passing through the reaction mixture, and the amount of ozone which passes into the potassium iodide trap following the reaction vessel. The reaction can then be stopped when the theoretical amount of ozone has reacted (545). More elaborate methods involve the use of infrared (516, 517) and/or ultraviolet spectra (8, 63, 65, 515, 516).

5. Special techniques

In most reactions of ozone with organic substances an oxygen stream containing 2–10 per cent ozone is passed into a solution or suspension of the organic material in a liquid medium. Occasionally, the organic material is added to a solution of ozone (564). Vapor-phase ozonolyses also have been reported (131, 149, 150, 168, 169, 244, 528). The peroxidic ozonolysis products from vapor-phase ozonolyses have not been characterized, but the nonperoxidic products are essentially the same as obtained from liquid-phase ozonolyses (169, 244). Kinetic studies indicate that the reactions initially are second order, but that additional more complicated reactions also occur (168). Although no explosions were mentioned in the vapor-phase work, mixtures of ethylene and ozone have been reported to explode instantly, even at low temperatures (434, 435).

Methods also have been developed for carrying out ozonolyses and other ozone reactions essentially in the absence of oxygen. Such techniques are important in cases where oxygen as well as ozone can react (Section VII,C). One method involves the use of pure liquid ozone. Both liquid and solid ozone are known and procedures have been developed for their safe handling (156, 157, 158, 325, 455, 496, 543, 544). Each is blue-black in color. In ozonolyses, either pure liquid ozone is allowed to evaporate and come into contact with a solution of the organic compound, or else the pure vapor is premixed with an inert gas such as nitrogen (311). Another method involves the adsorption of ozone from the usual ozone–oxygen stream on silica gel at low temperatures (186, 542). The ozone is then desorbed by an inert gas such as nitrogen, helium, or argon and led into the ozonolysis reaction mixtures. Cold liquid dichlorodifluoromethane or chlorotrifluoromethane will dissolve ozone from ozone–oxygen mixtures at low temperatures, after which the ozone can be recovered by means of an inert gas (186).

B. IDENTIFICATION OF PEROXIDIC OZONOLYSIS PRODUCTS

The various peroxidic ozonolysis products (Section II,A) can be distinguished from one another in a number of ways. The elemental, hydroxyl, alkoxyl, and acyloxyl analyses and/or molecular weights of the different types usually are definitive. Molecular weight determinations are best carried out cryoscopically in solvents such as benzene, bromoform, 1,2-dichloroethane, etc. (51, 52, 577). The Rast method is not reliable, because decomposition often occurs at the operating temperature (51, 52, 577). Molecular refractivities have been used in the characterization of liquid ozonides; they are reliable if the value of 2.11 is used for the peroxidic oxygen atom (207).

Certain qualitative and quantitative tests are useful. Almost all peroxidic compounds oxidize iodide ion to iodine (196, 198, 546, 586). In general, the ease of the reaction with peroxidic ozonolysis products is in the order: hydroperoxides > ozonides > dimeric peroxides (196). Quantitatively, the reaction is reliable only with ozonides or hydroperoxides which yield ketones upon reduction (196, 207). With ozonides or peroxides which should give aldehydes upon reduction, rearrangement to carboxylic acids (Section II,C,2) often occurs, resulting in low values. Dimeric peroxides often react too slowly to give good results. Hydroperoxides can be distinguished from other peroxidic ozonolysis products by means of lead tetraacetate, which decomposes most hydroperoxides with the release of molecular oxygen (196, 213). Only hydroperoxides with a carbonyl group adjacent to the hydroperoxide group or to the carbon atom bearing the hydroperoxide group fail to give the reaction (208). Sometimes even these react if methanol or benzene is used as the solvent (44). Hydroperoxides often can be characterized by acylation with benzoyl, *p*-nitrobenzoyl, or 3,5-dinitrobenzoyl chlorides to give crystalline per esters (198, 214).

Infrared spectra can be of importance in the identification of peroxidic ozonolysis products; for example, in showing the presence or absence of hydroxyl and carbonyl groups. There has been considerable confusion in the literature concerning the infrared spectra of ozonides (71, 488), owing to the fact that Briner and coworkers (111, 151, 152, 181, 182, 219, 220, 222, 223, 224, 225, 535) attributed bands in the carbonyl region (5.6–6.2 μ) to these substances. The spectra were of ozonolysis mixtures rather than of pure ozonides, and the bands in question were due to aldehydes and ketones (112, 113). Pure ozonides of compounds which have no carbonyl group in their structure do not absorb in the 5.6–6.2 μ region (207, 272).

At the present time there appears to be no infrared band characteristic of all ozonides. Criegee, Kerckow, and Zinke (207) reported that thirteen out of eighteen ozonides studied by them absorbed at 9.4–9.6 μ, but that the others absorbed at 8.8–9.4 μ or 9.6–10 μ (202). Other workers have obtained similar results (70, 112, 113, 114, 272, 273). These bands are thought to be characteristic of an ether linkage (60, 507).

There is evidence that peroxides of all types absorb in the 10–12.5 μ region (71, 508). It would be unwise to assign such a band in the spectrum of an unknown compound to the peroxide linkage, however, unless there were strong supporting evidence.

Briner and coworkers (73, 123, 124, 127, 136, 144, 145, 146, 147, 148) have done considerable work on Raman spectra, dipole moments, and other physical properties of "ozonides." In most cases, they were not dealing with pure products. Heats of combustion and formation of certain pure ozonides have been determined (115, 116). Other physical properties have been reported by Rieche and coworkers (470).

C. CONVERSION OF PEROXIDIC OZONOLYSIS PRODUCTS TO USEFUL NONPEROXIDIC PRODUCTS

Peroxidic ozonolysis products have potential use as polymerization and condensation catalysts (397, 439). More generally, however, they are converted immediately to such substances as aldehydes, ketones, or carboxylic acids, either for the purpose of analysis or identification of the starting materials or as a method for the synthesis of useful substances.

Until recently the high cost of ozone production and the low yields associated with the ozonolysis reaction made the use of ozone in industrial syntheses impractical. Two factors have changed this picture: the development of large-scale ozone-producing equipment (13, 287) and a greater understanding of the theory of ozonation, resulting in higher yields of products.

Four methods have been used in the conversion of peroxidic to nonperoxidic ozonolysis products. These are oxidation, reduction, hydrolysis, and thermal decomposition. Oxidation and reduction are broad general reactions important to all branches of chemistry. A discussion of their mechanism is beyond the scope of this review. That which can be said about the mechanism of the other two types will be found under the respective headings.

1. *Oxidation*

The oxidative decomposition of peroxidic ozonolysis products has become of considerable importance in the synthesis of carboxylic acids. Three general methods have been used most often.

The most economical method on a large scale utilizes oxygen, usually catalyzed by ozone or metal salts (41, 172, 248, 323, 386, 541). An Australian patent indicates that Emery Industries, the first company to employ ozone on a tonnage basis for synthesis, uses this method to produce azelaic (CDXIIa) and pelargonic (CDXIId) acids after ozonolysis of oleic acid (CDXIa) diluted with pelargonic acid (248, 386). Another patent describes the synthesis of ω-aminononanoic acid (CDXIIc) by the ozonolysis of oleonitrile (CDXIb), followed by oxidative decomposition to CDXIIb and reduction of CDXIIb to CDXIIc (172). Other examples are shown in table 7.

TABLE 7

Examples of oxidative conversions

No.	Product	Yield	Compound Ozonized	Solvent	Method of Decomposition	References
		per cent				
1......	Adipic acid	73	Cyclohexene	Methanol	O_2-O_3-formic acid	(41)
2......	Heptanoic acid	83	1-Octene	Methylene chloride + acetic acid	O_2-O_3-acetic acid	(386)
3......	Hendecanoic acid	77	1-Dodecene	Acetic acid	O_2-O_3-acetic acid	(386)
4......	ω-Aminononanoic acid	25	Oleylamine	Chloroform	Air-manganese catalyst-HCl	(445)
5......	Pinonic acid	40-60	Pinene	Acetic acid + chloroform	O_2–O_3	(262, 311)
6......	Adipic acid	85	Cyclohexene	Methanol	H_2O_2-formic acid	(40, 41)
7......	Phthalic acid	88	Naphthalene	Methanol	H_2O_2-formic acid	(48, 49)
8......	Quinolinic acid	92	8-Hydroxyquinoline	Acetic acid	H_2O_2-acetic acid	(374)
9......	Diphenic acid	65	Phenanthrene	Methanol	H_2O_2-NaOH	(38)
10......	Adipic acid	86	Cyclohexene	Acetic acid	Peracetic acid	(590)
11......	Lauric acid	94	1-Tridecene	Chloroform	Ag_2O-NaOH	(17)
12......	Hendecanoic acid	93	1-Dodecene	Pentane	Ag_2O-NaOH	(18)

$$CH_3(CH_2)_7CH{=}CH(CH_2)_7G \qquad HOOC(CH_2)_7G$$

CDXI CDXII

a: $G = COOH$. b: $G = C{\equiv}N$. c: $G = CH_2NH_2$. d: $G = CH_3$. e: $G = CHO$.

Another method employs hydrogen peroxide or a per acid. Hydrogen peroxide has been used with water only (190, 391, 395) or in combination with sodium hydroxide (38, 528), acetic acid (311, 553), acetic acid and sulfuric acid (296, 604), or formic acid (40, 41, 48). Formic acid is a superior solvent for these oxidations, owing to shorter reaction times and rapid decomposition of excess hydrogen peroxide (40, 41). The actual oxidizing agent probably is performic acid. Peracetic acid has been used effectively in several cases (590, 606, 607). Examples of these reactions are shown in table 7.

The third important method utilizes silver oxide suspended in sodium hydroxide solution (17, 18, 19, 20, 21, 458, 607). Examples are given in table 7. Other possible oxidizing agents are mentioned in the review by Long (380). Recent examples include potassium permanganate (79, 183, 536) and chromic acid (590).

It should be noted that rearrangements and overoxidation often occur in varying degrees when these methods are used (607) (Section II,C,2). Nevertheless, high yields have been obtained (table 7).

2. Reduction

The review by Long (380) lists many reducing agents for the conversion of peroxidic ozonolysis products to aldehydes and ketones. Sodium or potassium iodide (37, 38, 208, 211), zinc or magnesium and water or acetic acid (233, 296, 307, 322, 520, 564), and catalytic reduction (36, 297, 530, 537, 597) appear to be used most frequently. Others are sodium bisulfite (135, 467), sulfur dioxide (595), stannous chloride (517), Raney nickel (72, 189), and formaldehyde (517). Sodium bisulfite is useful in cases where one of the reduction products is an aldehyde and it is necessary to separate it from another product (467).

Catalytic reduction has been used in the synthesis of ω-aminononanoic acid (CDXIIc). The peroxidic ozonolysis product of oleic acid (CDXIa) was reduced catalytically in two steps to CDXIIc (173, 446). The second step involved reduction of CDXIIe in the presence of ammonia. Similarly, hexamethylenediamine, $H_2N(CH_2)_6NH_2$, has been obtained by the ozonolysis of cyclohexene (245, 264, 471).

Stoll and Rouvé (530) report that catalytic reduction often goes only about 70 per cent to completion and that acids and other rearrangement products are obtained in appreciable amounts. These competing reactions of the zwitterion (VI) often can be minimized by reducing at low temperatures with such reagents as sodium iodide (compounds 2 and 3, table 8).

Under the category of syntheses of aldehydes and ketones comes the ozonolysis step or steps in the manufacture of cortisone. Several ozonolyses which have been or conceivably could be used in the partial synthesis of cortisone are in the literature (75, 80, 81, 82, 170, 177, 179, 180, 215, 216, 298, 299, 301, 302, 303, 304, 305, 327, 328, 369, 370, 371, 372, 385, 503, 516, 517, 518, 554). The

TABLE 8

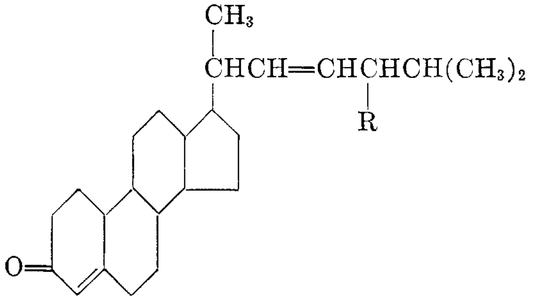
Examples of reductive and hydrolytic conversions

No.	Product	Yield	Compound Ozonized	Solvent	Method of Decomposition	References
		per cent				
1......	Adipaldehyde	54	Cyclohexene	Methanol	Catalytic reduction	(261)
2......	2,2′-Biphenyldicarboxaldehyde	84	Phenanthrene	Methanol	Sodium iodide	(38)
3......	Camphenilone	75	Camphene	Methanol	Sodium iodide	(37)
4......	2,6-Heptanedione	74	1,2-Dimethylcyclopentane	Carbon tetrachloride	Catalytic reduction	(209)
5......	1-Propanol and 1-pentanol	87	3-Octene	Hexane	$LiAlH_4$	(279)
6......	1-Pentanol	89	2-Heptene	Hexane	$LiAlH_4$	(279)
7......	1-Heptanol	93	1-Octene	Hexane	$LiAlH_4$	(279)
8......	Benzaldehyde	93	Stilbene	Methanol + methylene chloride	Steam	(386, 534)
9......	Benzaldehyde	87	Styrene	Methanol + methylene chloride	Steam	(386, 534)
10......	Anisaldehyde	92	Anethole	Methanol + methylene chloride	Steam	(386, 534)
11......	Piperonal	87	Isosafrole	Methanol + methylene chloride	Steam	(386, 534)
12......	Phthalaldehydic acid	87	Naphthalene	Methanol	Heat in methanol	(48, 49)
13......	2-Formyl-2′-biphenylcarboxylic acid	69	Phenanthrene	Methanol	Heat in methanol	(38, 52)
14......	4-Formyl-5-phenanthrenecarboxylic acid	89	Pyrene	Carbon tetrachloride	Pyridine decomposition	(50)

most interesting of these is a part of the conversion of ergosterol or stigmasterol to progesterone (215, 216, 303, 304, 327, 328, 503), which is both a sex hormone and a cortisone intermediate (503). It involves the selective ozonolysis of the side-chain double bond rather than the nuclear double bond of 4,22-ergostadien-3-one (CDXIIIa) or 4,22-stigmastadien-3-one (CDXIIIb). This occurs to give 3-ketobisnor-4-cholen-22-al (CDXIV) in 94 per cent yield in the presence of pyridine, but only in 82 per cent yield in the absence of pyridine (503, 516, 517). This promotion by pyridine of the selectivity of attack by ozone probably is the result of complex formation (e.g., CDXVI) between ozone and either pyridine or pyridine oxide (from the ozonation of pyridine) (515, 516, 517). The electrophilic character of the ozone molecule is thereby diminished and only the more electron-rich double bond can react with it (516, 517).

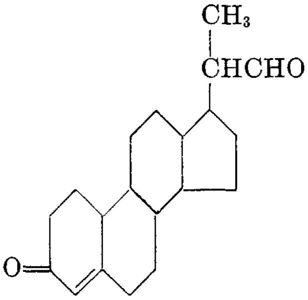
Pyridine also functions as a unique reducing agent in these reactions. In the presence of pyridine (one mole per mole of steroid) two moles of aldehyde (both CDXIV and CDXV) were produced during the ozonolysis, whereas in the absence of pyridine only one mole of aldehyde was produced (516, 517). The probable explanation is an attack of pyridine (CDXVIII) on the zwitterion (CDXVII) to produce pyridine oxide (CDXXII) and the aldehyde (CDXXI) via CDXIX or CDXX (516, 517).

Phenylhydrazine, hydroxylamine, and similar substances have been used as reducing agents for peroxidic ozonolysis products (36, 286, 329, 456, 578). In some instances the ozonolysis was carried out in the presence of 2,4-dinitrophenylhydrazine; the phenylhydrazone precipitated as the reaction proceeded (95, 362, 488). Apparently the phenylhydrazone was less reactive toward ozone than the original compound (*cf.* Section VI).

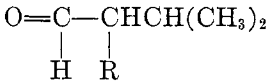


CDXIII

a: R = CH_3
b: R = C_2H_5

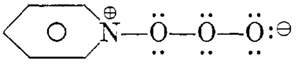


CDXIV

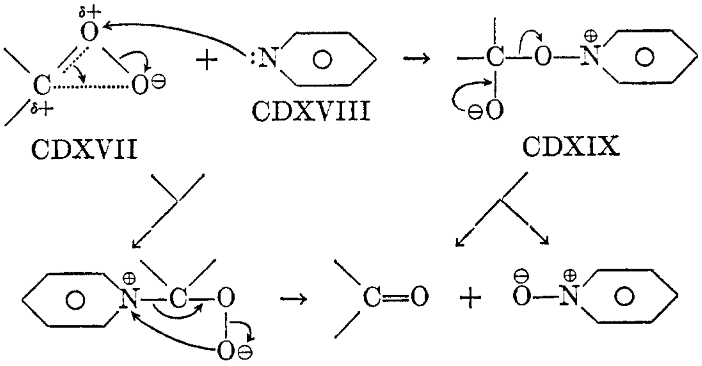


$$\underset{\displaystyle H}{O{=}\overset{|}{C}}{-}\underset{\displaystyle R}{\overset{|}{C}}HCH(CH_3)_2$$

CDXV



CDXVI



CDXVII CDXVIII CDXIX

CDXX CDXXI CDXXII

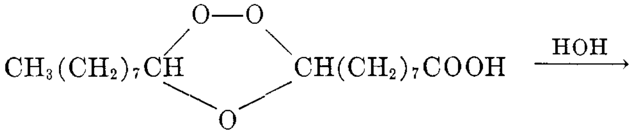
Reagents which have been used to reduce peroxidic ozonolysis products to alcohols have been lithium aluminum hydride (279, 310, 366, 456, 561, 597), sodium borohydride (451, 597), Grignard reagents (523, 597), and methyllithium (597). Some lithium aluminum hydride reductions are shown in table 8, along with some reductions to aldehydes and ketones.

3. Hydrolysis

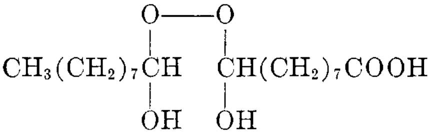
Hydrolysis generally is not as good a method for converting peroxidic to nonperoxidic ozonolysis products as are the oxidative and reductive methods. Either yields are low (282, 396, 550), or else, in those cases where reduction yields aldehydes and oxidation yields acids, hydrolysis produces a mixture of the two (77, 104, 121, 135, 239, 318, 416). Nevertheless, high yields of aromatic aldehydes have been obtained by ozonolysis of the desired olefin in a methylene chloride–methanol mixture, followed by rapid steam distillation (479, 534) (table 8). The method failed in attempted syntheses of aliphatic aldehydes.

Rieche and coworkers (470) have proposed that the first step in the hydrolysis of ozonides is cleavage of the ether bridge. The evidence presented was isolation of the dihydroxy peroxides CDXXIX and CDXXX from ozonolysis of the ozonide (CDXXIII) of oleic acid. The proposed route for the formation of the dihydroxy peroxides was CDXXIII → CDXXIV → (CDXXV + CDXXVI + CDXXVII + CDXXVIII) → CDXXIX + CDXXX. None of the mixed dihydroxyperoxide (CDXXIV) was isolated. Rieche and coworkers (470) stated that whenever a hydroxy hydroperoxide (such as CDXXVI or CDXXVII) is brought together with an aldehyde other than that to which it can be reduced (e.g., CDXXVII can be reduced to CDXXV), exchange reactions occur so that only symmetrical dihydroxy peroxides result (e.g., CDXXVII + CDXXVIII ⇄ CDXXIV ⇄ CDXXV + CDXXVI, followed by CDXXV + CDXXVII ⇄ CDXXIX, and CDXXVI + CDXXVIII ⇄ CDXXX).

The hydrolysis of alkoxy hydroperoxides (IX) should be analogous to that of hemiacetals.



CDXXIII

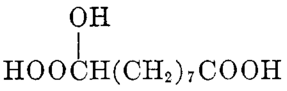


$$\begin{array}{cc} \text{O} & \!\!\text{—O} \\ | & | \\ \text{CH}_3(\text{CH}_2)_7\text{CH} & \text{CH}(\text{CH}_2)_7\text{COOH} \\ | & | \\ \text{OH} & \text{OH} \end{array}$$

CDXXIV

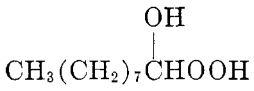
$CH_3(CH_2)_7CHO$

CDXXV



$$\overset{\text{OH}}{\text{HOOCH}}(\text{CH}_2)_7\text{COOH}$$

CDXXVI

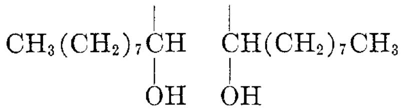


$$\text{CH}_3(\text{CH}_2)_7\overset{\text{OH}}{\text{CHOOH}}$$

CDXXVII

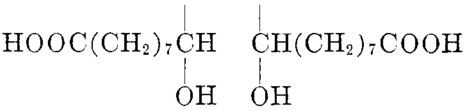
$OHC(CH_2)_7COOH$

CDXXVIII



$$\begin{array}{cc} \text{O} & \!\!\text{—O} \\ | & | \\ \text{CH}_3(\text{CH}_2)_7\text{CH} & \text{CH}(\text{CH}_2)_7\text{CH}_3 \\ | & | \\ \text{OH} & \text{OH} \end{array}$$

CDXXIX



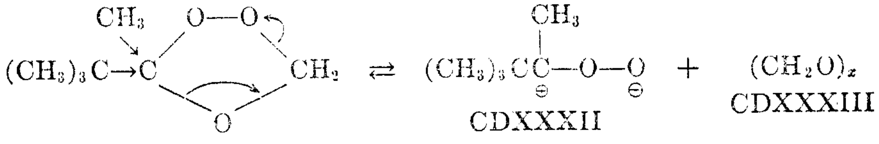
$$\begin{array}{cc} \text{O} & \!\!\text{—O} \\ | & | \\ \text{HOOC}(\text{CH}_2)_7\text{CH} & \text{CH}(\text{CH}_2)_7\text{COOH} \\ | & | \\ \text{OH} & \text{OH} \end{array}$$

CDXXX

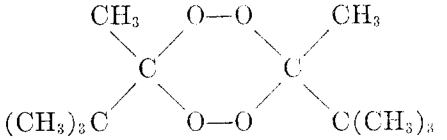
4. Decomposition

Thermal decompositions of peroxidic to nonperoxidic ozonolysis products, like hydrolysis, usually give mixtures (98, 135). In some cases, however, good yields of desired products have been obtained. Examples are phthalaldehydic acid from naphthalene (example 12, table 8) and 2-formyl-2′-biphenylcarboxylic acid (example 13, table 8) and its methyl ester from phenanthrene (Section IV,C). Oftentimes so-called abnormal products are obtained by thermal decompositions of peroxidic ozonolysis products (Section II,C,2).

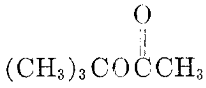
The ozonide (CDXXXI) of 2,3,3-trimethyl-1-butene decomposes slowly to produce formaldehyde polymers (CDXXXIII), the dimeric peroxide CDXXXIV, and *tert*-butyl acetate (CDXXXV) (207). Both CDXXXIV and CDXXXV arise from zwitterion CDXXXII, the ester (CDXXXV) by rearrangement (Section II,C,2). The following mechanism was proposed (207).



CDXXXI CDXXXII CDXXXIII



CDXXXIV

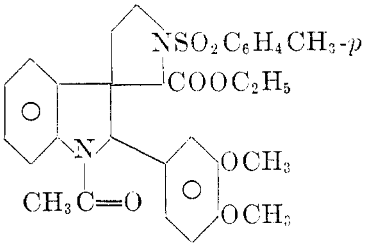


$(CH_3)_3CO\overset{\overset{O}{\|}}{C}CH_3$

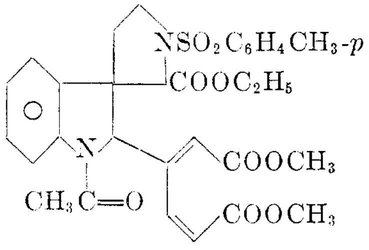
CDXXXV

5. Ozonolysis step in synthesis of strychnine

Ozonolysis played an important role in the total synthesis of strychnine (600). The ozonolysis step was conversion of CDXXXVI to CDXXXVII. The bond of the aromatic ring which was activated by the methoxy groups (CDXXXVI) was more reactive toward ozone than were the olefinic double bonds of the product (CDXXXVII).



CDXXXVI



CDXXXVII

D. USE OF OZONE IN ANALYSIS

The classical use of ozone has been in the proof of structure of olefins. A variety of illustrations were given in the review by Long (380). Many examples continue to appear in the literature. A recently important application has to do with the structures of various synthetic rubbers and other polymers and copolymers. Considerable information has been gained from the ozonolysis reaction concerning the extent to which a given diene polymerizes by 1,4- or by 1,2-addition, the extent to which head-to-head or head-to-tail polymerization occurs, whether a systematic or completely random distribution of monomers is produced in the polymer during copolymerization, and which of the multiple bonds of a given polyfunctional monomer is involved in the polymerization (4, 5, 6, 16, 253, 308, 309, 344, 345, 346, 390, 395, 460, 463, 551, 606). Ozone has also been used in the study of the deterioration of rubber (542) and in determinations of the degree of unsaturation in polymers (464, 465, 474).

Boer and Kooyman (87) have used ozone as a titrimetric agent for the quantitative determination of olefinic unsaturation. Other authors have measured the rate of absorption of ozone by various olefinic, acetylenic, aromatic, and polyfunctional compounds, and mixtures thereof, and report that it is possible to identify the type of compound or mixture being ozonized by the shape of its absorption curve (602, 603).

Identification of nonperoxidic ozonolysis products often is a difficult problem, especially where mixtures are obtained. Chromatographic techniques have been described for the separation and identification of carboxylic acids (56, 63, 64, 65, 69, 97, 306, 324, 348, 393, 417, 444, 462, 568, 608) and of aldehydes and ketones (174, 175, 251, 274, 314, 453). Acids have been separated by fractional extraction techniques (394). Special techniques have been developed for the quantitative determinations of formaldehyde (1, 55, 83, 212, 237, 319, 332, 349, 426, 428, 499), acetone (46, 359, 536), and other simple aldehydes and ketones (300), but the precision of the methods is not great.

E. MISCELLANEOUS USES

Ozone has been used for many years in various European cities (e.g., Paris, France) for the purification of water (270, 281, 363, 547). The city of Philadelphia in Pennsylvania also uses this method (68). Ozone is reported to be very effective against bacteria and to decrease color, bad taste, odor, and the ammonia and organic matter content of water (68, 281, 288, 363, 547).

Processes have been developed for the destruction of oxidizable wastes in industrial waters. For example, ozone has been shown to be effective in destroying phenols (431, 432) and cyanides (340, 500).

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