

The Mechanism of Ozonolysis

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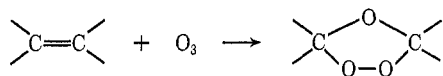
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The reaction of ozone with olefins was apparently first studied in 1855 by Schönbein,¹ who reported that ozone and ethylene react to give carbonic acid, formaldehyde, and formic acid. The first ozonide was isolated by Houzeau in 1873² as a white, amorphous, explosive product from the reaction of ozone with benzene. From these beginnings interest in this reaction and its products has grown so that ozonolysis is now recognized as perhaps the most versatile method for oxidative cleavage of the double bond.

Several reviews have appeared which are pertinent to the subject of this account, and the reader is referred to them for background information. Long³ and, more recently, Bailey⁴ have written extensive reviews on organic ozone chemistry. More specialized reviews have been given by Bischoff and Rieche,⁵ Criegee,⁶ and Menyailo and Pospelov.⁷

The term ozonolysis is used here to describe that reaction of ozone with a double bond which leads to cleavage of that bond. The terms ozonization and ozonozation are more general and include all the reactions of ozone with other materials. Interest in the ozonolysis reaction falls conveniently into three general areas: use of ozone to locate unsaturation in structure determinations, use of the reaction synthetically, that is, to convert unsaturation into ketones, aldehydes, alcohols, or acids, and, finally, study of the mechanism of the reaction. This last area is the subject of this account.

Considered formally, the over-all reaction is an unusual one in that the three oxygen atoms of ozone are somehow inserted into a carbon-carbon double bond to give a cyclic compound, an *ozonide*, with one ether and one peroxy bridge between the two carbon atoms origi-



nally bearing the unsaturation. Hydrolytic or reductive cleavage of the ozonide to aldehydes, ketones, alcohols, etc., is beyond the scope of the present discussion.

All of the mechanistic proposals made for the ozonolysis reaction accept the idea first suggested by Stau-

dinger⁸ in 1925 that ozone first adds to the double bond to give an unstable adduct or *molozonide*, as he called it. This unstable adduct then somehow goes on to give the normal ozonide. A number of points relative to the over-all mechanism require attention. These include (a) the nature of the initial attack of ozone on the double bond, (b) the nature and structure of the initial adduct, (c) the process or processes by which the initial adduct is converted to ozonides and other products, and (d) the influence of olefin geometry and substituents, solvent, temperature, concentration, and other reaction variables on points a-c.

I. The Nature of the Initial Attack and the Structure of the Initial Adduct

The questions whether the ozonolysis reaction is free radical or ionic in nature are answered by the observation of Criegee⁶ that ozonolysis of styrene gave no polystyrene. All mechanistic proposals which have been made have been ionic in nature.

Wibaut and coworkers first suggested^{9,10} that the initial attack of ozone on the double bond was electrophilic in character, and evidence has accumulated that this is probably the case.⁹⁻¹⁷ Huisgen considers the formation of the initial adduct to be an example of a 1,3-dipolar cycloaddition reaction.¹⁸ This kind of a reaction would lead to a five-membered 1,2,3-trioxolane ring structure (2) for the initial adduct.

Recent evidence on the structure of the initial adduct suggests that it is indeed the result of a one-step *cis* addition of ozone to the double bond. Criegee and Schröder¹⁹ have shown that the initial adduct formed between ozone and *trans*-di-*t*-butylethylene is a crystalline material which can be reduced to the racemic diol. This important observation indicates that this initial adduct was formed by *cis* addition of ozone and that it still had one carbon-carbon bond intact. Greenwood

(8) H. Staudinger, *Ber.*, **58**, 1088 (1925).

(9) J. P. Wibaut, F. L. J. Sixma, L. W. F. Kampschmidt, and H. Baer, *Rec. Trav. Chim.*, **69**, 1355 (1950).

(10) J. P. Wibaut and F. L. J. Sixma, *ibid.*, **71**, 761 (1952).

(11) L. W. F. Kampschmidt and J. P. Wibaut, *ibid.*, **73**, 431 (1954).

(12) F. L. J. Sixma, *ibid.*, **71**, 1124 (1952).

(13) F. L. J. Sixma, H. Boer, and J. P. Wibaut, *ibid.*, **70**, 1005 (1951).

(14) F. L. J. Sixma and J. P. Wibaut, *ibid.*, **71**, 473 (1952).

(15) C. R. Noller, J. F. Carson, H. Martin, and K. S. Hawkins, *J. Am. Chem. Soc.*, **58**, 24 (1936).

(16) T. I. Temnikova, Z. A. Baskova, and M. A. Khaimova, *Sb. Statei Obshch. Khim.*, **2**, 874 (1954); *Chem. Abstr.*, **49**, 6889 (1955).

(17) T. Vrbaski and R. J. Cvetanović, *Can. J. Chem.*, **38**, 1053 (1960).

(18) R. Huisgen, *Angew. Chem. Intern. Ed. Engl.*, **2**, 565, 633 (1963).

(19) R. Criegee and G. Schröder, *Chem. Ber.*, **93**, 689 (1960).

(1) C. F. Schönbein, *J. Prakt. Chem.*, **66**, 282 (1855).

(2) A. Houzeau, *Compt. Rend.*, **76**, 572 (1873).

(3) L. Long, Jr., *Chem. Rev.*, **27**, 437 (1940).

(4) P. S. Bailey, *ibid.*, **58**, 925 (1958).

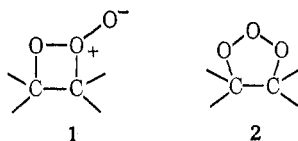
(5) C. Bischoff and A. Rieche, *Z. Chem.*, **5**, 97 (1965).

(6) R. Criegee, *Record Chem. Progr. (Kresge-Hooker Sci. Lib.)*, **18**, 111 (1957).

(7) A. T. Menyailo and M. V. Pospelov, *Usp. Khim.*, **36**, 662 (1967).

has shown that the initial adduct in the cases of several other *trans* olefins can be reduced to the diol.^{20,21} Again, the structures of the diols formed indicated that the addition of the olefin was stereospecific. No cases of reduction of the initial adduct to diol have been reported for *cis* ozonides.

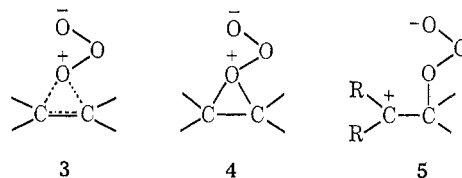
While their reduction results were consistent with both the four-membered ring structure **1**, proposed earlier by Staudinger,⁸ and the five-membered ring structure **2**, both Criegee and Greenwood preferred type **2**.



The next step in elucidating the structure of the initial adduct was the significant observation by Bailey, Thompson, and Shoulders²² that the nmr spectrum of this adduct, again in the case of *trans*-di-*t*-butylethylene, showed a single methine proton absorption. Thus, at least in this case, the 1,2,3-trioxolane structure **2** is the correct one since the methine protons are not equivalent in structure **1**. Durham and Greenwood²³ have made similar observations for a number of other *trans* olefins. The latter authors have also provided convincing evidence that the initial adduct is indeed a precursor to normal ozonide by observing simultaneous decay of initial adduct nmr absorption and appearance of normal ozonide absorption, using the oscilloscope of the nmr spectrometer. More recently Durham and Greenwood²⁴ have obtained the nmr spectra of the elusive initial adducts from several *cis* olefins. In these cases lower temperatures (-130°) were required to obtain the spectra, and even under these conditions the initial adduct was being converted to normal ozonide.

There are several cases in which it seems likely that the initial adduct does not have structure **2**, cases in which one of the ozonolysis products is the epoxide derived from the olefin.²⁵⁻²⁸ Sometimes the epoxide is the major ozonolysis product, particularly from 1-olefins in which one side of the double bond is heavily substituted.^{25,26,28} Although the epoxide product may derive from the five-membered ring structure **2**, it seems more likely that the precursors in these cases must have a different structure. One possibility is a π (**3**) or σ (**4**) complex²⁷⁻²⁹ which eliminates molecular

oxygen to give the epoxide. It has also been suggested²⁸ that the intermediate adduct may be an unbalanced, open σ complex, **5**, which is prevented from closing to **2** because of steric hindrance.



Several additional observations bear on this point. While it is not possible to detect retention of olefin stereochemistry in the reactions of 1-olefins which give high yields of epoxides, in those few cases where an internally unsaturated olefin has given epoxide the olefin stereochemistry was retained.²⁷ Such an observation is consistent with structures **3** and **4** and may not be inconsistent with structure **5** depending upon the relative rates of closure to epoxide and rotation about the carbon-carbon single bond. The literature contains a number of cases in which ozonolysis leads to cleavage not of the olefinic bond but of the adjacent carbon-carbon single bond. It seems possible that these cases also involve an initial adduct of structure type **3**, **4**, or **5**.

Finally, there is the observation²⁸ that oxygen is evolved during the production of epoxide product from sterically hindered 1-olefins. It has recently been suggested³⁰ that this oxygen and that produced in a variety of similar reactions in ozone chemistry ought to have singlet multiplicity. In one such case, the oxidation of triphenyl phosphite to the corresponding phosphate,³¹ it has actually been shown that the oxygen evolved undergoes typical singlet oxygen reactions.^{30,32}

II. Conversion of the Initial Adduct into Normal Ozonide

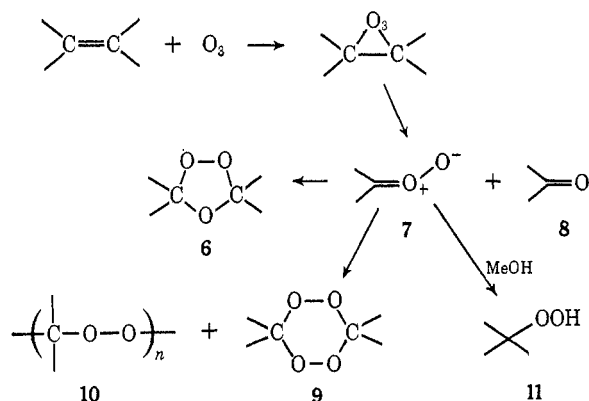
A. Some Proposals for the Mechanism. A successful complete mechanism for the ozonolysis reaction must describe in as great detail as possible how the initial adduct, generally **2**, but sometimes perhaps **3**, **4**, or **5**, proceeds to normal ozonide **6**. Several suggestions have been made. Leffler³³ and Milas^{34,35} made proposals which involved preliminary heterolysis of an oxygen-oxygen bond followed by rearrangement to ozonide without further fragmentation of the adduct.

The most extensive proposal for the ozonolysis mechanism was given by Criegee,^{6,36} based on several years of work by himself and his coworkers. According to the original Criegee proposal the initial adduct underwent a heterolysis to give a zwitterion with one carbon-

- (20) F. L. Greenwood, *J. Org. Chem.*, **29**, 1321 (1964).
 (21) F. L. Greenwood, *ibid.*, **30**, 3108 (1965).
 (22) P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Am. Chem. Soc.*, **88**, 4098 (1966).
 (23) L. J. Durham and F. L. Greenwood, *Chem. Commun.*, 843 (1967).
 (24) L. J. Durham and F. L. Greenwood, *ibid.*, 24 (1968).
 (25) P. D. Bartlett and M. Stiles, *J. Am. Chem. Soc.*, **77**, 2806 (1955).
 (26) R. Criegee, *Advances in Chemistry Series*, No. 21, American Chemical Society, Washington, D. C., 1959, p 133.
 (27) R. W. Murray, R. D. Youssefieh, and P. R. Story, *J. Am. Chem. Soc.*, **89**, 2429 (1967).
 (28) P. S. Bailey and A. G. Lane, *ibid.*, **89**, 4473 (1967).
 (29) P. R. Story, R. W. Murray, and R. D. Youssefieh, *ibid.*, **88**, 3144 (1966).

- (30) R. W. Murray and M. L. Kaplan, *ibid.*, **90**, 537 (1968).
 (31) Q. E. Thompson, *ibid.*, **83**, 846 (1961).
 (32) R. W. Murray and M. L. Kaplan, *ibid.*, **90**, 4161 (1968).
 (33) J. Leffler, *Chem. Rev.*, **45**, 385 (1949).
 (34) N. A. Milas in "The Chemistry of Petroleum Hydrocarbons," Vol. II, B. T. Brooks, S. S. Kurtz, Jr., C. E. Boord, and L. Schmerling, Ed., Reinhold Publishing Corp., New York, N. Y., 1955, p 399.
 (35) N. A. Milas, P. Davis, and J. T. Nolan, Jr., *J. Am. Chem. Soc.*, **77**, 2536 (1955).
 (36) R. Criegee in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, New York, N. Y., 1962, p 29.

carbon bond intact. This was later amended to a synchronous decomposition of the initial adduct to give zwitterion **7** and a carbonyl compound **8**. This path was chosen because it afforded an opportunity to explain the formation of both ozonide and nonozonide products.³⁶ The proposal then postulated formation of normal ozonide by recombination of **7** and **8**. Depending upon the structure of the olefin and other reaction conditions, the zwitterion **7** might dimerize to diperoxides **9** or polymerize to give polymeric peroxides **10**. In reactive solvents, here illustrated with methanol, **7** can be diverted to a new product such as the methoxyhydroperoxide **11**. This mechanism has been successful in explaining most of the accumulated experimental data.



B. Recent Experimental Data. We now discuss some more recent experimental data and consider what they mean in terms of the mechanism. Strong evidence for the intermediacy of zwitterion **7** was found by Criegee⁶ when he showed that addition of a foreign aldehyde, that is, an aldehyde not derivable from the olefin being ozonized, leads to the formation of a new ozonide which incorporates the foreign aldehyde and the zwitterion.

The formation of normal ozonide upon ozonolysis will obviously depend upon the nature of the carbonyl and zwitterion fragments involved. When the carbonyl compound is an aldehyde, ozonide formation occurs smoothly. For some time it was believed that simple ketones, such as acetone, would not react with zwitterions to give ozonides.^{6,37} This conclusion was apparently based on the failure of tetramethylethylene to give an ozonide. Ozonolysis of this olefin gave only acetone, acetone diperoxide, and polymeric peroxide.⁶ The latter two products presumably are formed because acetone is too unreactive to recombine with the zwitterion which is then left to other fates. That the general conclusion is incorrect was shown by the observation of two new ozonides when pentene-2 was ozonized in the presence of an excess of acetone.³⁸ These ozonides were those of 2-methylpentene-2 and 2-methylbutene-2 and, formally at least, represent the addition of acetone to the two aldehydic zwitterions expected as intermediates in this ozonolysis. Moreover, com-

bination of a simple ketone with a ketonic zwitterion has recently been observed by Criegee:³⁹ ozonolysis of tetraphenylethylene in acetone solution gave a 74% yield of crystalline 1,1-diphenyl-2,2-dimethylethylene ozonide.

Simple ketones containing negative substituents react readily to give ozonides; an example is *trans*-1,4-dibromo-2,3-dimethylbutene-2.⁴⁰ Likewise the bifunctional ketone zwitterions which are produced intramolecularly from cyclic olefins readily cyclize to give ozonides, as in the case of 1,2-dimethylcyclopentene.⁴¹

According to the Criegee mechanism, unsymmetrical olefins ought to give two zwitterions and two carbonyl compounds and, if both scission and recombination are statistical, the three possible ozonides should be formed in a 1:2:1 ratio. The three are two symmetrical ozonides and the ozonide of the parent olefin, with the latter statistically favored. The two symmetrical ozonides are referred to as cross-ozonides. When he failed to find the cross-ozonides in the ozonolysis of heptene-3, Criegee postulated that the zwitterion and carbonyl fragments were formed and recombined in a solvent cage, thus preventing cross-recombination.

The ozonides from symmetrically disubstituted olefins are capable of existing as *cis-trans* pairs. Criegee postulated that operation of his zwitterion-carbonyl recombination mechanism should give the same *cis-trans* ozonide distribution from *cis* and *trans* olefin stereoisomers and reported this to be the case for a number of olefin pairs. In 1962 Schröder⁴² reported the important observation that *cis*- and *trans*-1,2-ditbutylethylenes do not give the same ozonide *cis-trans* distribution. His paper was equally important for its demonstration that gas-liquid partition chromatography could be used to handle ozonides.

In 1963 the prediction of the Criegee mechanism relative to cross-ozonide formation was realized when two groups reported that ozonolysis of methyl oleate gave the three expected pairs (*cis-trans*) of ozonides.^{43,44} Shortly thereafter a similar finding was reported for the simple olefin, pentene-2; that is, the ozonide *cis-trans* pairs from butene-2, pentene-2, and hexene-3 were all obtained.⁴⁵ These results were obtained using the pure olefin as reactant and glpc to separate the products. The earlier failure of Criegee to obtain cross-ozonides in the case of heptene-3 could now probably be attributed to the olefin concentration used. This view was confirmed by a plot of the ratio of normal ozonides to cross-ozonide *vs.* olefin concentration (Figure 1) which showed that cross-ozonide formation decreases with dilution. At the concentration of olefin normally used

(39) R. Criegee, private communication.

(40) R. Criegee, S. S. Bath, and B. V. Bornhaupt, *Chem. Ber.*, **93**, 2891 (1960).

(41) R. Criegee and G. Lohaus, *ibid.*, **86**, 1 (1953).

(42) G. Schröder, *ibid.*, **95**, 733 (1962).

(43) G. Riezebos, J. C. Grimmelikhuyzen, and D. A. Van Dorp, *Rec. Trav. Chim.*, **82**, 1234 (1963).

(44) O. S. Privett and E. C. Nickell, *J. Am. Oil Chemists Soc.*, **40**, 22 (1963).

(45) L. D. Loan, R. W. Murray, and P. R. Story, *J. Am. Chem. Soc.*, **87**, 737 (1965).

(37) R. Huisgen, *Angew. Chem.*, **75**, 604 (1963).

(38) R. W. Murray, P. R. Story, and L. D. Loan, *J. Am. Chem. Soc.*, **87**, 3025 (1965).

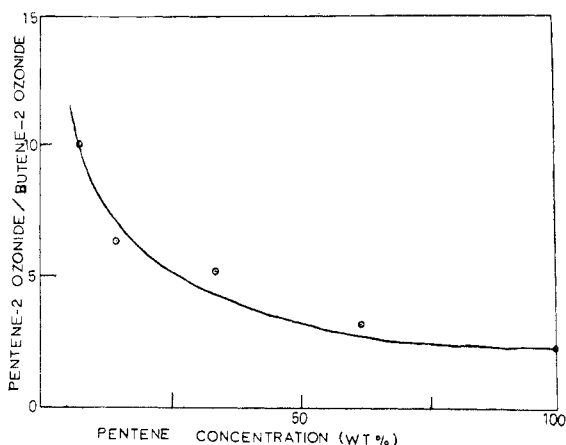


Figure 1. Effect of pentene-2 concentration on ozonide distribution.

in ozonolysis the predominant product is the parent ozonide of the unsymmetrical olefin.

Following Schröder's observation, a number of instances were reported in which the ozonide *cis:trans* ratio obtained was different from the *cis* and *trans* olefin isomers of a stereochemical pair.⁴⁶⁻⁵⁰ In 1966 the startling observation that the ozonide *cis:trans* ratio in cross-ozonides was also a function of the starting olefin geometry was reported.⁴⁸ Similar observations have since been made for a number of unsymmetrical olefins.^{27,49}

It is also possible to study the formation of an unsymmetrical cross-ozonide from pairs of symmetrical olefins which are ozonized simultaneously. Criegee had attempted to obtain an unsymmetrical cross-ozonide from hexene-3 and octene-4 but found no evidence of its being produced.⁶ However, more recently ozonolysis of these two olefins has been demonstrated to give a good yield of heptene-3 ozonide.⁵¹

Two other general trends could be discerned in the results described to this point. One was that *cis* olefins consistently gave a higher yield of ozonide than their corresponding *trans* isomers. Greenwood and Haske have presented a plausible explanation for this dependence of yield on olefin geometry, based on the relative stabilities of the initial adducts.⁴⁹

Secondly, in those cases where *cis* and *trans* olefin stereoisomers gave different ozonide *cis:trans* ratios, the *cis* isomer gave a higher percentage of *cis* ozonide. Furthermore, this tendency seemed itself to be related to the bulk of the groups present in the *cis* isomer. Thus *cis*-di-*t*-butylethylene gave a 70:30 *cis:trans* ozonide ratio whereas its *trans* isomer gave 100% *trans* ozonide.⁴² Likewise in the case of diisopropylethylene, the *cis* isomer gave ozonide in a 66:34 *cis:*

Table I
Normal Ozonide Stereoisomers from *trans* Olefins

OLEFINS	CIS	TRANS	TOTAL YIELD ^a OF OZONIDES
	29	71	16 ^b
	30	70	32 ^b
	53	47	47
	53	47	49
	48	52	66
	40	60	53 ^b
	38	62	56
	38	62	36

a. IT SHOULD BE NOTED THAT FOR UNSYMMETRICAL OLEFINS THIS FIGURE INCLUDES THE YIELDS OF CROSS OZONIDE.

b. YIELD OF ONE OR BOTH CROSS OZONIDES COULD NOT BE DETERMINED.

trans ratio while the *trans* isomer gave 53:47.⁴⁸


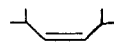
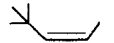
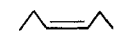
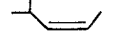
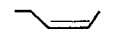
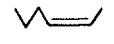
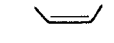
On the basis of these observations it was decided to study in detail the effect of substituent size on the ozonide *cis-trans* distribution in a series of *cis* and *trans* olefins. First, however, it was necessary to find a reliable way of making ozonide stereoisomer assignments. The assignments mentioned heretofore were made on the basis of a number of experimental correlations including various combinations of glpc, nmr, infrared, tlc, and chemical reactivity data. In fact the correlations used were quite reasonable ones. Thus the *cis* configuration was assigned to the isomer with the longer glpc retention time or lower R_f value, etc.

An unequivocal assignment of ozonide configuration was finally made by taking advantage of the fact that the *trans* isomer of a symmetrical ozonide must be a *d,l* pair.⁵² The two ozonides obtained in the ozonolysis of diisopropylethylene were treated with less than the stoichiometric amount of brucine in an attempt at kinetic resolution in the true *trans* isomer. The ozonides were then reisolated and analyzed for optical activity. Only one of the ozonide isomers developed optical activity, and this isomer could, therefore, be unequivocally assigned the *trans* configuration.⁵² In fact the assignment made earlier in this case on the basis of glpc, nmr, and infrared data was the correct one. Ozonide configurational assignments made on the basis of such experimental correlations could now be used with more confidence.

(46) P. Kolsaker, *Acta Chem. Scand.*, **19**, 223 (1965).
 (47) O. Lorenz and C. R. Parks, *J. Org. Chem.*, **30**, 1976 (1965).
 (48) R. W. Murray, R. D. Youssefyeh, and P. R. Story, *J. Am. Chem. Soc.*, **88**, 3143 (1966).
 (49) F. L. Greenwood and B. J. Haske, *Tetrahedron Letters*, 631 (1965).
 (50) F. L. Greenwood, *ibid.*, **88**, 3146 (1966).
 (51) R. W. Murray and G. J. Williams, *Advances in Chemistry Series*, American Chemical Society, Washington, D. C., in press.

(52) R. W. Murray, R. D. Youssefyeh, and P. R. Story, *J. Am. Chem. Soc.*, **88**, 3655 (1966).

Table II
Normal Ozonide Stereoisomers from *cis* Olefins

OLEFINS	CIS	TRANS	TOTAL YIELD ^a OF OZONIDES
	67	33	84
	66	34	85
	54	46	81
	53	47	81
	49	51	86
	42	58	91
	41	59	72
	39	61	48

a. IT SHOULD BE NOTED THAT FOR UNSYMMETRICAL OLEFINS THIS FIGURE INCLUDES THE YIELDS OF CROSS OZONIDE.

The results of the ozonolysis of a series of *cis* and *trans* olefins in which the substituent size has been varied are shown in Tables I and II.²⁷ In the *cis* series there is a clear dependence of the parent olefin ozonide *cis:trans* ratio on the substituent size. In keeping with the earlier observations, the correlation is that increasing substituent size increases the percentage of *cis* ozonide. The *trans* series shows a similar correlation to a point. Increasing the substituent size also increases the percentage of *cis* ozonide produced until one of the substituents becomes *t*-butyl, at which point the products suddenly contain a higher percentage of *trans* ozonide.

We now consider the effect of other reaction variables on the ozonolysis reaction, particularly as re-

flected in ozonide *cis:trans* ratios. Tables III and IV contain data from the ozonolysis of *cis*- and *trans*-diisopropylethylenes in a variety of solvents.⁵³ The results indicate a pronounced effect of solvent on ozonide *cis-trans* distribution as well as some effect on the yields obtained. For both the *cis* and *trans* isomers the more nucleophilic solvents, ethyl acetate and ethyl ether, gave substantially higher percentages of *trans* ozonide, with the effect being more pronounced for the *trans* olefin. Greenwood has also observed the formation of higher percentages of *trans* ozonides in ether solvents.⁵⁰ The fact that use of methylene chloride as solvent causes little change in the ozonide ratio from either olefin stereoisomer suggests that the solvent effect has more to do with the nucleophilicity than the polarity of the solvent.^{50,53} More data in a variety of solvents are needed before a definite statement can be made on this point.

The effect of solvent on yield is also evident. For the *cis* isomer the yields are all about 83% except in methylene chloride where the yield is substantially lower. The *trans* isomer, on the other hand, shows a substantially higher yield in ether solvent.

The ozonide distribution and yield are also a function of the olefin concentration, as shown in Figures 2 and 3.⁵³ At higher olefin concentrations, that is, above ~1.5 M, the ozonide distribution is constant, but different, for the *cis* and *trans* isomers of diisopropylethylene. At lower olefin concentrations the ozonide *cis-trans* distribution changes in the direction of a greater percentage of *trans* ozonide from both the *cis* and *trans* olefins. In addition the *trans* olefin apparently shows a maximum in the percentage of *trans* ozonide (Figure 2) at low olefin concentrations. Actually, more data at very high dilution are needed in order to verify this observation.

The yield data in Figure 3 indicate that there is an optimum concentration of olefin insofar as yield is concerned. As seen before, the *cis* olefin gives a higher yield of ozonide than the *trans* under all concentration conditions. A comparison of Figures 2 and 3 suggests that the process which causes the decrease of yield after the maximum is reached is also associated with the change in the ozonide distribution in the direction of a lower percentage of *trans* ozonide. This further implies that there may be two general pathways to ozonide, one of which becomes dominant at higher olefin concentrations. The latter pathway would then be associated with the production of ozonides containing a lower percentage of *trans* ozonide. At the same time it apparently permits nonozonide-producing reactions to compete and thus leads to a decreasing yield of ozonide. The two general pathways could be as simple as a cage *vs.* noncage competition or perhaps something more complex including the possibility of two distinct precursors to ozonide formation. Again additional data are required before a final conclusion can be drawn on this point.

Table III
Ozonide Stereoisomers from *cis*-1,2-Diisopropylethylene

Solvent	Solvent dipole moment	Ozonide %		Total yield of ozonides, %
		<i>trans</i>	<i>cis</i>	
Pentane	0	34.0	66.0	83.8
CH ₂ Cl ₂	1.55	36.9	63.1	57.7
Ethyl acetate	1.81	46.6	53.4	81.2
Ethyl ether	1.15	44.3	55.6	84.1

Table IV
Ozonide Stereoisomers from *trans*-1,2-Diisopropylethylene

Solvent	Solvent dipole moment	Ozonide %		Total yield of ozonides, %
		<i>trans</i>	<i>cis</i>	
Pentane	0	47.3	52.7	46.8
CH ₂ Cl ₂	1.55	50.8	49.2	55.6
Ethyl acetate	1.81	64.5	35.5	57.4
Ethyl ether	1.15	64.7	35.3	73.1

(53) R. W. Murray, R. D. Youssefyeh, G. J. Williams, and P. R. Story, *Tetrahedron*, **24**, 4347 (1968).

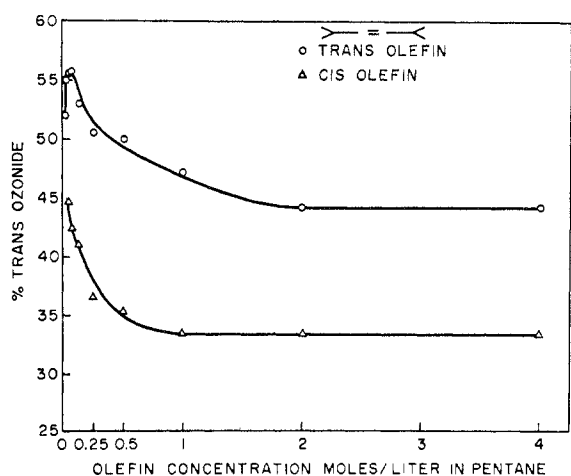


Figure 2. The percentage *trans* ozonide obtained from *cis*- and *trans*-1,2-diisopropylethylenes as a function of concentration.

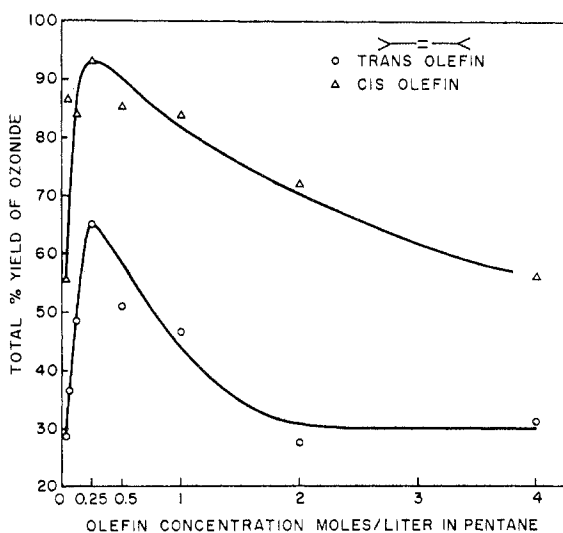


Figure 3. Ozonide yield as a function of concentration for *cis*- and *trans*-1,2-diisopropylethylenes.

C. Additional Proposals for the Mechanism. The Criegee mechanism has been successful in coordinating and explaining a large amount of the literature data on the ozonolysis reaction. This mechanism makes no provision for stereochemical effects,^{6,54} however, and some alternative proposals need to be considered either as modifications to the Criegee scheme or possibly as competing pathways. Two such proposals have been made. Prompted by their results indicating a dependence of cross-ozonide *cis:trans* ratio on olefin geometry, Story, Murray, and Youssefieh put forth an additional proposal for the mechanism in the form of a working hypothesis.^{27,29,55} More recently Bauld, *et al.*, have also made some new proposals regarding the mechanism which they regard as a refined Criegee mechanism.⁵⁶ Both proposals are more involved than the original Criegee proposal, but recent data on the ozonol-

ysis reaction require that more complex schemes be considered.

The working hypothesis of Story, *et al.*, suggests that, in addition to the Criegee pathway to ozonide, at least one other pathway might be important under certain reaction conditions. Essentially this other pathway involves the reaction between aldehyde and the initial olefin-ozone adduct. The aldehyde could be added aldehyde or that generated in the reaction *via* the Criegee pathway. The proposal further suggests that the ozonide *cis:trans* ratios observed experimentally may be the result of more than one contributing pathway, each of which may contribute a different ozonide *cis:trans* ratio. It was felt that the direct reaction between aldehyde and initial adduct provided a means by which the stereochemistry of the olefin could operate to give different ozonide *cis:trans* ratios. The hypothesis contains the additional proposal that the initial adduct, probably with a structure approximated by **3** or **4**, could proceed directly to ozonide in a stereospecific or at least stereoselective manner. This possibility was seen as most likely to occur in a *cis* olefin with large substituents which would resist the transition to structure **2**; the change from sp^2 to sp^3 hybridization would increase steric interaction between substituents in the olefin. This additional proposal is admittedly speculative, but at present cannot be rigidly excluded and is only invoked under special circumstances in the total proposal.

A number of points must be kept in mind when considering this working hypothesis. The scheme requires reaction between aldehyde and initial adduct and thus would only be expected to play an important role under reaction conditions where both species are present. While the scheme makes predictions regarding relative tendencies toward *cis* or *trans* ozonide production, it cannot make predictions about the absolute value of the ratio of these two isomers. Since it is postulated that this kind of reaction is occurring along with others, including the Criegee pathway, the resultant *cis:trans* ratios will depend on the percentage contribution of each path as well as the individual *cis:trans* ratio contribution. Comparison of predictions of this scheme with experiment, therefore, requires careful consideration of a number of factors for the precise case under consideration. It may be that as more data become available this process of prediction will become simpler or, alternatively, that parts of the scheme may have to be modified or discarded.

The main elements of the scheme are shown in Figure 4 for a specific *cis* olefin. Addition of ozone to the olefin gives either the five-membered ring adduct **12** or the σ complex **13**, with the latter perhaps also being a precursor to **12** under special circumstances. Heterolysis then occurs at an oxygen-oxygen bond in **12** to give the zwitterion **14**. The zwitterion **14** can cleave further to give an aldehyde and the Criegee zwitterion **15**. Zwitterion **15** may then combine with the 2-methylpropanal to give ozonide **16** with some *cis:trans* ratio. Alternatively, **14** may react with aldehyde to give a new

(54) P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958); see p 936.

(55) R. W. Murray, *Trans. N. Y. Acad. Sci.*, **29**, 854 (1967).

(56) N. L. Bauld, J. A. Thompson, C. E. Hudson, and P. S. Bailey, *J. Am. Chem. Soc.*, **90**, 1822 (1968).

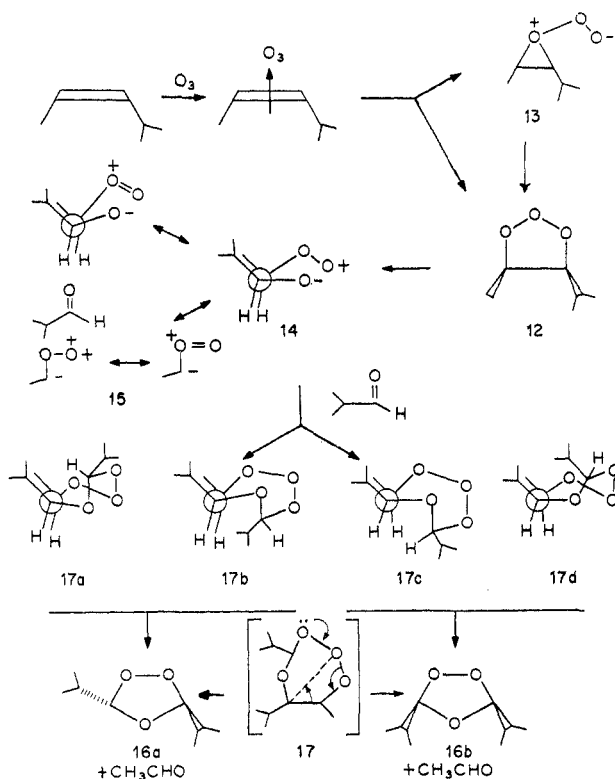


Figure 4. Schematic of proposed mechanism for *cis*-4-methylpentene-2.

intermediate or transition state, **17a-d**, which has two configurational and four conformational possibilities. It may also be that the original cleavage of **12** is induced or assisted by the aldehyde in a path which leads directly to **17**.

Structure **17** provides a means for an aldehyde interchange to occur to give the ozonide **16a,b** and the other aldehyde (acetaldehyde in this example). Examination of models suggests that production of ozonide in this way may permit steric and stereochemical effects in the olefin to influence the *cis-trans* distribution in the ozonide. Thus it appears that in this case conformer **17c** should be preferred because it contains only H-H nonbonded interactions. Since this conformer is a precursor to *cis* ozonide one would expect that more *cis* than *trans* ozonide would be produced by this interchange reaction. Provided also that this pathway is a significant one, the final ozonide *cis-trans* ratio in ozonide **16** might be in favor of more *cis*. A similar analysis starting with the *trans* olefin leads to the conclusion that the aldehyde-interchange reaction should not show any great preference for *cis* or *trans* ozonide or at least that any preference shown will not be as great as in the *cis* case.

There is no question that the working hypothesis of Story, Murray, and Youssefyeh is an involved scheme, although the underlying proposal of a reaction between aldehyde and initial ozonide would probably be considered a reasonable possibility by most workers in the field. It has the virtue of permitting olefin stereochemistry and steric factors to influence ozonide *cis:trans* ratios. What has been lacking is sufficient ex-

perimental data to be able to distinguish one kind of reaction pathway from another.

Recently three reports have appeared which bear on this last point. Taking advantage of the fact that the aldehyde oxygen is incorporated differently into the ozonide depending upon whether the ozonide is formed from the aldehyde-initial adduct path or the Criegee path, Story, *et al.*,⁵⁷ have used ¹⁸O-labeled aldehyde to prepare an ozonide. Reference to Figure 4 and the Criegee mechanism schematic given above will show that the aldehyde-interchange mechanism puts ¹⁸O into the peroxide bridge of the ozonide, specifically at the oxygen atom adjacent to the original carbonyl carbon atom of the incorporated aldehyde. The Criegee mechanism, on the other hand, puts the ¹⁸O label only in the ether bridge of the ozonide. The method used then calls for reduction of the ozonide and determination of ¹⁸O distribution in the ozonide from its distribution in the alcohols produced. Some experiments to determine which ozonide oxygen is lost upon lithium aluminum hydride reduction have also been completed.⁵⁸ The case studied was the ozonolysis of *trans*-diisopropylethylene in the presence of labeled acetaldehyde. The methyl isopropyl ozonide so produced was then examined for ¹⁸O distribution. Because of the possibility that the results may have been affected by a steric effect in the ozonide the reduction was carried out both by lithium aluminum hydride and by methyllithium.

The results from the hydride reduction suggest that 32% of the ozonide was formed by a pathway which placed O¹⁸ in the ether oxygen bridge, presumably the Criegee pathway, and 68% of the ozonide was formed by a path which placed ¹⁸O in the peroxide bridge. The results are consistent with the aldehyde-interchange path described above, but do not exclude other possibilities. Use of methyllithium as reducing agent showed 23% of the ozonide with ¹⁸O in the ether bridge and 77% with label in the peroxide bridge. The difference between the two types of reduction is presumably due to a small steric effect which should operate in opposite directions in the two types of reduction. Strictly speaking the results apply only to conditions where excess aldehyde is present. They do suggest, however, that more complex ozonide-forming mechanisms may be operating under the usual ozonolysis conditions.

Results of a similar approach using ¹⁸O labeling have also been reported by Fliszar, *et al.*⁵⁹ The system studied was the ozonolysis of *cis*- and *trans*-stilbene in the presence of added benzaldehyde containing ¹⁸O. In this work an analysis of mass spectral fragmentation pattern was used to determine the location of the ¹⁸O in the ozonide. The results of the experiments, according to the authors, show that ¹⁸O is incorporated mostly at the ether oxygen except at low temperature where some 10% of the ¹⁸O may have been incorporated

(57) P. R. Story, C. E. Bishop, J. R. Burgess, R. W. Murray, and R. D. Youssefyeh, *J. Am. Chem. Soc.*, **90**, 1907 (1968).

(58) C. E. Bishop and P. R. Story, *ibid.*, **90**, 1905 (1968).

(59) S. Fliszar, J. Carles, and J. Renard, *ibid.*, **90**, 1364 (1968).

in the peroxide bridge. The authors conclude that either the Criegee mechanism or a new mechanistic proposal which is a variation of the aldehyde-interchange reaction is equally compatible with the ^{18}O distribution found.

Another major attempt to provide a mechanistic scheme which takes account of olefin stereochemistry has been given by Bailey, *et al.*⁵⁶ Basic to this scheme is a revival of the idea originally discussed by Criegee³⁶ that the Criegee zwitterion can exist as *syn* and *anti* isomers. The proposal by Bailey, *et al.*, is a comprehensive one which defines conditions which would lead to a different *syn-anti* zwitterion distribution as well as proposing that *syn* and *anti* zwitterions can react with aldehydes to give different ozonide *cis:trans* ratios. The separate existence of *syn* and *anti* zwitterions under the usual low-temperature conditions of ozonolysis is certainly conceivable. While at present no information is available on the barrier to interconversion of these two forms, the nmr results reported by Winstein, *et al.*,⁶⁰ on protonated aldehydes and carboxylic acids at low temperatures suggest that the *syn* and *anti* forms may not be rapidly interconverting, at least at low temperatures.

The Bailey proposal starts with a consideration of the factors which determine the best conformation of the initial adduct. The proposal also assumes concerted decomposition of the adduct and then specifies three rules which operate to determine the final ozonide *cis:trans* ratio. In summary, the rules are (1) equatorial substituents in the initial adduct preferentially become *anti* to the terminal oxygen and axial substituents *syn* in the zwitterions, (2) an equatorial substituent is incorporated into a zwitterion moiety in preference to an axial substituent, and (3) in their reactions with aldehydes *anti* zwitterions preferentially give *cis* ozonide and *syn* zwitterions give *trans* ozonide. The last conclusion is based on a consideration of the preferred conformation in the final ozonide. The rules then lead to several predictions for the ozonolysis reaction, as follows. A *cis* olefin with bulky substituents should yield a final ozonide with a *cis:trans* ratio greater than unity. For *trans* olefins the prediction will depend upon the conformation of the initial ad-

duct. With very bulky substituents a predominance of *syn* zwitterion and hence *trans* final ozonide is predicted. With less bulky substituents the *trans* olefin should give more *anti* zwitterion and hence more *cis* ozonide. The authors feel that these predictions are consistent with the available experimental data.

The over-all proposal is an interesting one and should stimulate experimental activity to determine some of the unknowns which are essential to the scheme, for example, the position of the *syn-anti* equilibrium under various experimental conditions. One might also expect that some temperature should be reached at which the *syn-anti* distribution would be the same from isomeric *cis* and *trans* olefins, and thus that the ozonide *cis:trans* ratio should be the same. At present there are few data available regarding temperature effects on ozonide distributions. Needed also is some indication that the application of conservation of symmetry arguments is valid, that is, evidence as to whether the initial adduct decomposes in a stepwise or concerted manner.

At this time it is difficult to come to any definite conclusions regarding a complete mechanism of ozonolysis other than that it is more complicated than originally thought. The several proposals which have been put forth to provide a mechanism consistent with more recent experimental data require careful consideration of a number of individual factors. While this makes them difficult to use in any specific case, they will undoubtedly serve the purpose of guiding further experimental work. Sufficient evidence is available to suggest that the mechanism is sensitive to a number of experimental factors. More work of this kind is needed and can be expected. More kinetic data on reactions of simple alkenes is certainly needed. Additional work using isotopic labeling could prove valuable in unraveling the intricacies involved in going from initial adduct to final ozonide.

Most of the work referred to here in which I am a coauthor is the result of a collaborative effort with Professor P. R. Story when he and I were colleagues at Bell Telephone Laboratories. We were fortunate to have as coworkers Drs. L. D. Loan, R. D. Youssefyeh, and G. J. Williams, each of whom made significant contributions to the over-all program. In my subsequent efforts in this area I have had the very talented assistance of Dr. R. Hagen and Mr. M. L. Kaplan.

(60) M. Brookart, G. C. Levy, and S. Winstein, *J. Am. Chem. Soc.*, **89**, 1735 (1967).