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Stereospecificity in Ozonide and Cross-Ozonide Formation

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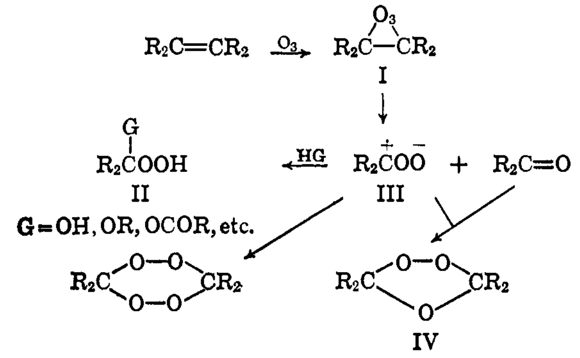
Abstract: Additional data are presented in regard to stereospecificity in ozonide and cross-ozonide formation, as evidenced by *cis–trans* ratios. The effect of solvent, temperature, and concentration changes on these ratios and other aspects of ozonolysis are discussed. It is shown that the results herein presented, as well as those from other laboratories, are explicable on the basis of a refined Criegee mechanism, involving the stereoselective decomposition of *cis* and *trans* initial ozonides to isomeric *syn* and *anti* zwitterions and the stereoselective recombination of these with aldehydes to give final ozonides.

The proposal (1949–1953) of the Criegee mechanism[2–4] for the classical ozonolysis reaction not only placed the reaction on a sound theoretical basis, but greatly stimulated research in the field, of both a theoretical and a practical nature. The mechanism is outlined in Scheme I. The evidence for the Criegee mechanism and its key zwitterionic intermediate III is most convincing. It includes: (1) interception of the zwitterion III by participating solvents to give substituted hydroperoxides II, or with reactive foreign aldehydes to give ozonides other than that of the olefin itself;[4] (2) the formation of the same ozonide from two structurally different olefins which, however, yield the same zwitterion and carbonyl moieties;[4] (3) the formation of cyclic oxyhydroperoxides from olefins having a properly placed hydroxy functional group;[5] and (4) the formation of cross ozonides[6] from unsymmetrical olefins.[7–11]

Scheme I



plus polymeric peroxides and ozonides

Early, however, facts began to accumulate which were difficult to explain on the basis of the simple Criegee mechanism outlined in Scheme I, necessitating the realization that either there is another mechanism for ozonide IV formation (possibly an intramolecular rearrangement of the initial ozonide) competing with the Criegee mechanism,[12] or else the Criegee mechanism needs refinement. These observations include: (1) the early failure of Criegee[13] to find cross ozonides upon ozonolysis of either 3-heptene or a mixture of 3-hexene and 4-octene, possibly because he was not using concentrated enough solutions or high enough temperatures;[8] (2) the findings of Briner and coworkers[14] that *cis* and *trans* isomers of 1-arylpropenes do not give the same proportions of ozonide on the one hand and aldehydes and polymeric peroxides on the other hand; (3) the finding that *cis* and *trans* olefins not only give different ozonide–polymeric peroxide ratios, but often different *cis–trans* ozonide ratios;[10,15–21] (4) the recent important and exciting discovery that even

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[1] To whom inquiries concerning this paper should be directed.

[2] R. Criegee and G. Wenner, *Ann.*, **564**, 9 (1949).

[3] R. Criegee, *ibid.*, **583**, 1 (1953).

[4] P. S. Bailey, *Chem. Rev.*, **58**, 925 (1958).

[5] (a) A. Rieche and M. Schulz, *Chem. Ber.*, **98**, 3623 (1965); (b) A. Rieche, M. Schulz, and D. Becker, *ibid.*, **98**, 3627 (1965).

[6] The term "normal ozonide" is used to describe the parent ozonide obtained from ozonolysis of an olefin. For an unsymmetrical olefin it is the unsymmetrical ozonide, whereas the two symmetrical ozonides obtained are termed "cross ozonides." See ref 7.

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

[8] G. Riezebos, J. C. Grimmelikhuysen, and D. A. Van Dorp, *Rec. Trav. Chim.*, **82**, 1234 (1963).

[9] O. S. Privett and E. C. Nickell, *J. Am. Oil Chemist's Soc.*, **41**, 72 (1964).

[10] O. Lorenz and C. R. Parks, *J. Org. Chem.*, 30, 1976 (1965).

[11] Earlier references to cross ozonides also appear, but their significance was not emphasized: (a) M. Indo, *Nippon Kagaku Zasshi*, **80**, 537 (1959); *Chem. Abstr.*, **55**, 4404 (1961); (b) T. Vrbaski and R. J. Cvetanovic, *Can. J. Chem.*, **38**, 1063 (1960); (c) O. Lorenz and C. R. Parks, *Rubber Chem. Technol.*, **36**, 201 (1963).

[12] P. S. Bailey, S. B. Mainthia, and C. J. Abshire, *J. Am. Chem. Soc.*, **82**, 6136 (1960).

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

[14] (a) E. Briner, E. Dallwigk, and M. Ricca, *Helv. Chim. Acta*, **41**, 1390 (1958); (b) E. Briner and M. Ricca, *ibid.*, **41**, 2178 (1958); (c) E. Briner and S. Fliszar, *ibid.*, **42**, 1310, 2063 (1959).

[15] R. Criegee, S. S. Bath, and B. von Bornhaupt, *Chem. Ber.*, **93**, 2891 (1960).

[16] G. Schröder, *ibid.*, **95**, 733 (1962).

[17] P. Kolsaker, *Acta Chem. Scand.*, **19**, 223 (1965).

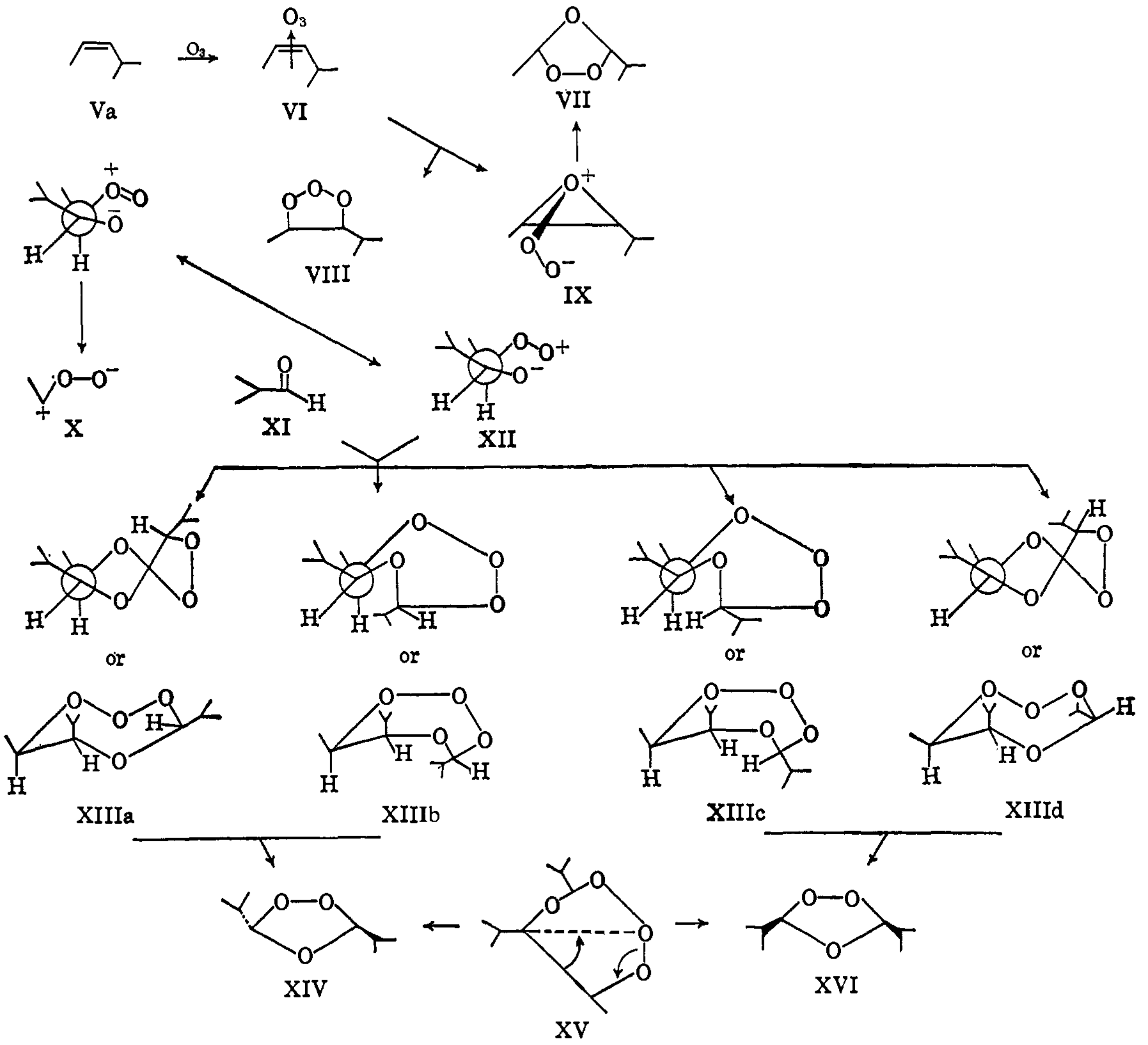
[18] F. L. Greenwood and B. J. Haske, *Tetrahedron Letters*, 631 (1965).

[19] R. W. Murray, R. D. Youssefyeh, and P. R. Story, *J. Am. Chem. Soc.*, **88**, 3143 (1966).

[20] F. L. Greenwood, *ibid.*, **88**, 3146 (1966).

[21] R. W. Murray, R. D. Youssefyeh, and P. R. Story, *ibid.*, **89**, 2429 (1967).

Scheme II. *cis* Olefins



the *cis–trans* ratios of cross ozonides obtained from *cis* and *trans* unsymmetrical olefins often differ.[19-21]

In their principal paper on stereospecificity in cross-ozonide formation, Murray, Youssefyeh, and Story[21] state that the observed dependence of *cis–trans* ratios for cross ozonides on olefin geometry "*is inconsistent with the Criegee zwitterion mechanism in which the zwitterion precursor to ozonide should give the same ozonide cis–trans ratios for both olefin stereoisomers in both normal and cross ozonides.*" In order to explain the stereochemistry of cross-ozonide formation, these authors[21] propose a new mechanism, illustrated in Schemes II and III. Although they suggest that "the observed *cis–trans* ratio is—the net result of contributions from several pathways" in which the Criegee zwitterion pathway is retained as "*a possible contributing pathway,*" Murray, *et al.*,[21] base their arguments on examples for which they state that the mechanisms of Schemes II and III make "the dominant contributions to the observed ratio with other pathways making smaller contributions."

In the principal mechanism of Schemes II and III, Story, Murray, and Youssefyeh[21,22] propose that an aldehyde molecule XI attacks the initial ozonide VIII (*via* XII) to give an adduct XIII, the preferred conformation of which determines the predominant stereochemical course of ozonide (XIV or XVI) formation (*via* XV). According to the conformational analysis of these authors,[21,22] conformation XIIIc of Scheme II would be favored in the case of *cis* olefins, since it contains only H–H nonbonded repulsions, but there would be no preference among conformations XIXa–d for *trans* olefins in Scheme III. Thus, the *cis–trans* ratio of ozonides produced by this mechanism should be approximately unity from *trans* olefins but greater than unity from *cis* olefins. Scheme II includes the suggestion that highly hindered *cis* olefins form normal ozonides[6] *via* an intramolecular rearrangement of a α complex IX rather than by either the Criegee mechanism or the main mechanism of Schemes II and III.

To our minds, the Story–Murray–Youssefyeh (SMY) proposal[21,22] is an unsatisfying explanation of results accumulating from various laboratories for the following reasons. First, whereas we agree with their conformational analysis in regard to *cis* olefins (preferred conformation XIIIc of the intermediate, Scheme II), we reach a different conclusion from theirs in regard to *trans* olefins (Scheme III). Our study of models indicates that conformation XIXd of Scheme III would be favored, because it, like conformation XIIIc of Scheme II, contains only H–H nonbonded repulsions. Therefore, the aldehyde displacement mechanism predicts a predominant formation of a *cis* ozonide XVI from a *trans* as well as from a *cis* olefin. This is contrary to

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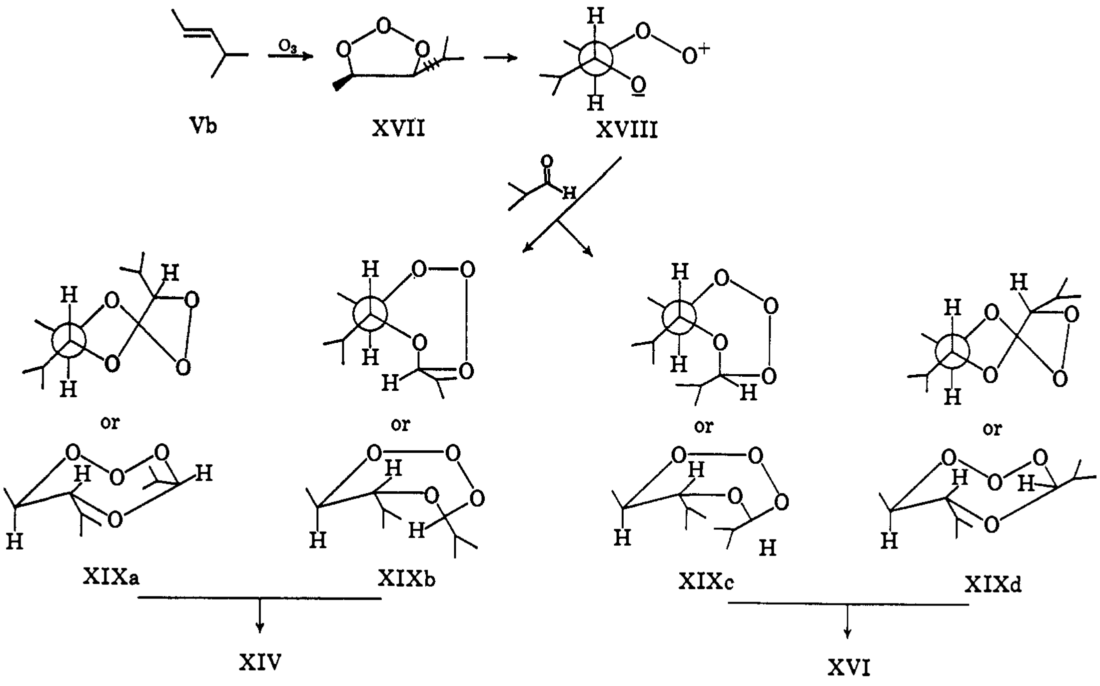
[22] P. R. Story, R. W. Murray, and R. D. Youssefyeh, *J. Am. Chem. Soc.*, **88**, 3144 (1966).

Scheme III. *trans* Olefins



fact, at least with ozonides having large substituents. Our results with *cis*- and *trans*-4-methyl-2-pentenes (Table III, experiments 1 and 9) show, for example, predominantly *cis* ozonide from *cis* olefin and *trans* ozonide from *trans* olefin. Second, it appears to us somewhat unlikely that a σ complex (IX, Scheme II) would rearrange to an ozonide rather than lose molecular oxygen and produce an epoxide, or similar products containing only one oxygen atom of the ozone molecule. The latter certainly is the case with substances which have bulky groups attached to one carbon atom of the double bond.[23] Third, as stated by the authors themselves, the SMY mechanism can at best be only one of several possible routes to ozonides, competing with the Criegee mechanism,[21] rather than being a unifying concept in itself. For example, the mechanism does not explain the striking stereochemical results obtained upon ozonolysis of *trans*-1,2-di-*t*-butylethylene at −78° (Table II, experiments 8 and 9).

In the present paper we intend to show that stereospecificity in both normal and cross-ozonide formation, as well as other known facts concerning the ozonolysis reaction, is consistent with the Criegee mechanism, provided that certain refinements are made upon it, and that the SMY proposal is, therefore, unnecessary. The principal refinements are fourfold. First, ozone adds to a double bond in a *cis*, stereospecific manner (1,3-dipolar cycloaddition[24]) to give an initial ozonide with a five-membered, nonplanar, 1,2,3-trioxolane ring.[25] Second, as the initial ozonide decomposes, the zwitterion and carbonyl moieties remain attracted to each other, much like an ion pair, predominantly recombining to a normal ozonide[6] unless they are separated because of the polarity of the solvent, a relatively high reaction temperature, or contact with other species in a concentrated reaction mixture. Third, the Criegee zwitterion (or carbonyl oxide) can exist in isomeric *syn* (XXI) and *anti* (XXIII) forms which, especially in the case of hindered olefins, are produced in preferential proportions, depending on whether the initial ozonide has the *cis* or the *trans* configuration. Fourth, the combination of a zwitterion and an aldehyde (or ketone) is, generally, a 1,3-dipolar cycloaddition[24] and occurs to some extent stereospecificially, depending on the configuration of the zwitterion and the preferred conformation of the final ozonide. The last two refinements require further amplification.

Criegee[26] has already called attention to the probability of *syn* and *anti* forms of a zwitterion. It seems likely that the pertinent π bond orders of these species would be great enough that equilibration between them would be incomplete, or even nonexistent, under the low-temperature conditions of most ozonolyses and given the rapidity with which zwitterions combine with aldehydes. A pertinent analogy is the recent observation of *syn* and *anti* forms of protonated aldehydes, ketones, and carboxylic acids at low temperatures.[27] Thus it is reasonable that different initial ozonide isomers should give different ratios of zwitterion isomers and that these, in turn, should combine with aldehydes to give different *cis*–*trans* ozonide ratios. We now proceed to a consideration of the stereochemistry of these decompositions and recombinations.

Scheme IV shows the initial ozonides (XX and XXV) resulting from generalized *trans* and *cis* olefins, their preferred stereochemical fates in decomposing to *syn* and *anti* zwitterions and aldehydes, and the preferred stereochemical recombinations of these to final ozonides. Although the initial ozonides are represented in the half-chair conformation, analogous to tetrahydrofuran and ethylene carbonate,[28] any nonplanar

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[23] P. S. Bailey and A. G. Lane, *J. Am. Chem. Soc.*, **89**, 4473 (1967).

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

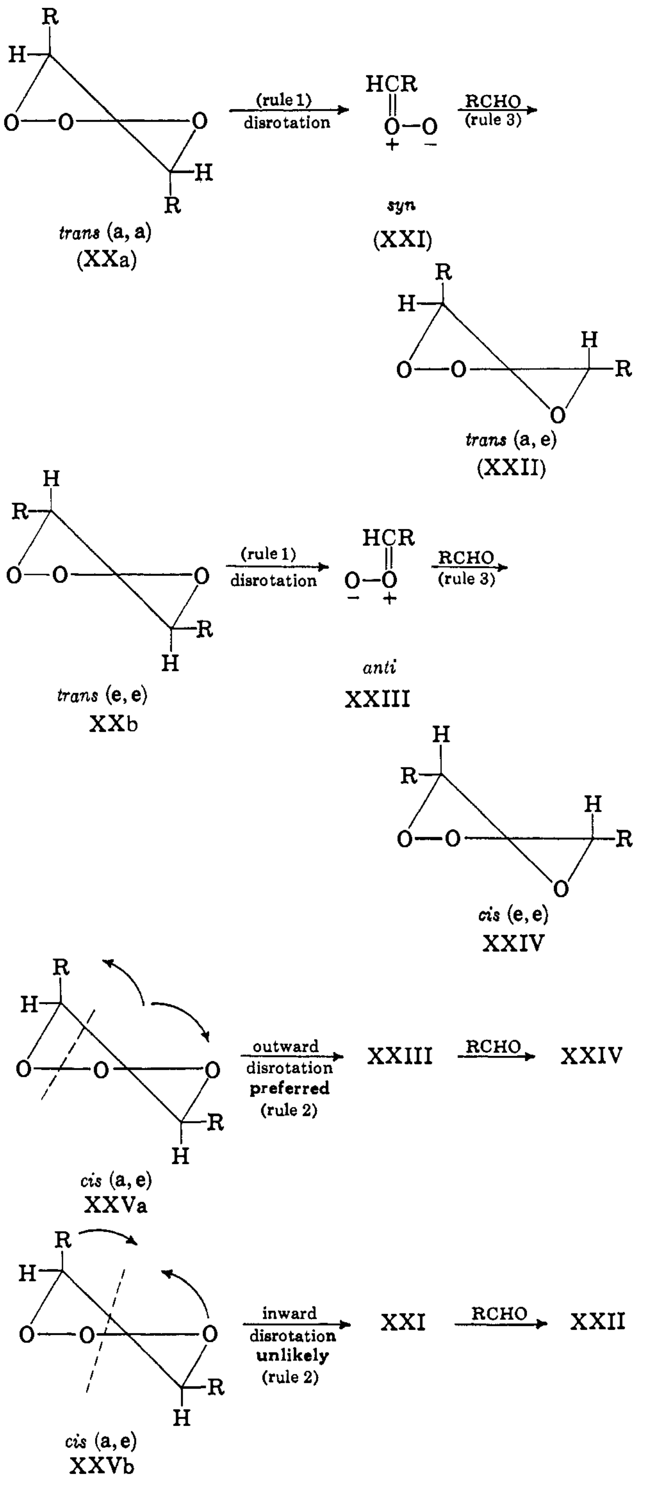
[25] P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *J. Am. Chem. Soc.*, **88**, 4098 (1966).

[26] R. Criegee in "Peroxide Reaction Mechanisms," J. O. Edwards, Ed., Interscience Publishers, Inc., New York, N. Y., 1962, p 29.

[27] M. Brookhart, G. C. Levy, and S. Winstein, *J. Am. Chem. Soc.*, **89**, 1735 (1967).

[28] (a) E. E. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 251; (b) F. V.

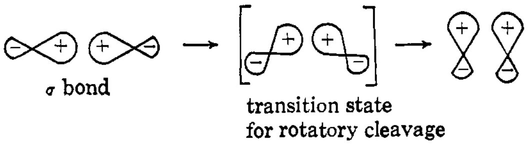
Scheme IV



model of the ring could lead to similar predictions. The conformations of the initial and final ozonides used in Scheme IV were chosen so as to minimize torsional strain involving the C–H and C–R bonds, *i.e.*, placing as many carbon atoms as possible in positions maximally staggered. In our representation of the half-chair, the rear two atoms are most nearly staggered, as shown to be true with ethylene carbonate.[28b]

The stereochemical transformations depicted in Scheme IV can be formulated into three general rules. The first is that *equatorial substituents are preferentially converted into anti and axial substituents into syn zwitterions.* This is due to the fact that equatorial bonds are approximately *trans* and axial bonds are more nearly *cis* to two ring bonds, one of which is always the oxygen–oxygen bond that will become part of the zwitterion. Thus, in order to incorporate an equatorial substituent into a *syn* zwitterion or an axial substituent into an *anti* zwitterion, the cleavage would have to be accompanied by isomerization of the incipient zwitterion moiety. In Scheme IV, therefore, initial ozonide XXa would give the *syn* zwitterion XXI predominantly, initial ozonide XXb would give the *anti* zwitterion XXIII predominantly, and initial ozonide XXV presumably could give either, since it has both an equatorial and an axial substituent.

Rule 2 is that an *equatorial substituent is incorporated into a zwitterion moiety in preference to an axial substituent.* Assuming concerted oxygen–oxygen and carbon–carbon cleavages, the carbon-carbon cleavage must be rotatory in order for the R and H groups to orient one *syn* and one *anti* to the oxygen–oxygen bond. Attention needs to be centered only on the local symmetry of the carbon–carbon bond in the inherently unsymmetrical cleavage transition state. In general, rotatory σ-bond cleavages should be preferentially disrotatory because of the fact that both the σ bond and the disrotated transition state have a plane of symmetry (see following diagram). In the conrotated transition state, bonding is cut off sharply and antibonding interactions are introduced. Of the two disrotatory processes, inward rotation should be sterically less favorable than outward rotation of the substituents. In the case of a *cis* initial ozonide incorporation of a substituent into the zwitterion would require an inward rotation if it were axial, but an outward rotation if it were equatorial. Hence XXV should produce predominantly the *anti* zwitterion, as shown by XXVa → XXIII.



The third rule is that *aldehydes preferentially interact with anti zwitterions so as to orient bulky substituents diequatorially (cis) and with syn zwitterions to orient bulky substituents into an equatorial,axial(trans) conformation.* By the converse of rule 1, the *anti* zwitterion should preferentially install its substituent in an equa-

Table I. Predicted Stereochemical Course of Ozonide Formation with Olefins Possessing Bulky Substituents

Olefin config	Initial ozonide Config	Initial ozonide Conform[a]	Predominant zwitterion config	Predominant final ozonide Config	Predominant final ozonide Conform[a]
cis	*cis*	a,e	*anti*	*cis*	e,e
trans	*trans*	a,a[b]	*syn*	*trans*	a,e
trans	*trans*	e,e	*anti*	*cis*	e,e

[a] Half-chair conformation is assumed with following axial and equatorial positions of substituents. [b] Axial,axial relationship of substituents should be preferred with large substituents.

Brutcher, Jr., T. Roberts, S. J. Barr, and N. Pearson, *J. Am. Chem. Soc.*, **81**, 4915 (1959).

Table II. Ozonolyses of Symmetrical Olefins

Expt	R in RCH=CHR	Config	Solvent	Concn, *M*	Temp, °C	Ozonide *cis*:*trans*	Total ozonide yield, %	Ref[a]
1	*t*-Butyl	*cis*	Pentane	0.3	−75	70:30	82[b]	16
2				0.3	−75	70:30	82[c]	
3				0.2	RT[d]	[e]	64	[f]
4			$CFCl_3$	0.1	−105	55:45	[e]	
5			Et_2O	0.1	−75	[e]	77	[f]
6			AcOEt	0.15	−75	[e]	57	[f]
7			CH_2Cl_2	0.15	−75	[e]	27	[f]
8		*trans*	Pentane	0.3	−75	28:72	51	
9				0.3	−75	0:100	58	16
10				0.1	−75	[e]	47	[f]
11				0.1	RT[d]		0	[f]
12			Et_2O, AcOEt or CH_2Cl_2	0.15	−75		0	[f]
13			$CFCl_3$ or acetone	0.1	−95 or −110		0	
14	Isopropyl	*cis*	Pentane	1	−70	66:34	85	21
15				1	−75	62:38	[e]	
16		*trans*		1	−70	53:47	47	21
17				1	−75	45:55	52	
18				2	−78	25:75	60	10
19	Et	*cis*		1	−70	53:47	81	21
20				0.2	−30	48:52	88	20
21			Et_2O	0.2	−70	38:62	80	20
22		*trans*	Pentane	1	−70	53:47	49	21
23				0.2	−70	[e]	10	18
24				0.2	−30	41:59	22	18, 20
25			CH_2Cl_2	0.2	−30	46:54	24	20
26			Et_2O	0.2	−30	34:66	44	20
27				0.2	−70	33:67	42	20
28				0.2	−110	34:66	36	20
29	CH_3	*cis*	Pentane	1	−75	34:66	[e]	
30				1	−70	39:61	48	21
31			Butane	0.2	−30	35:65	72	20
32			Me_2O	0.2	−70	29:71	62	20
33		*trans*	Pentane	1	−70	38:62	36	21
34			Butane	0.2	−30	34:66	36	20
35			Me_2O	0.2	−70	30:70	34	20

[a] If no reference is given, the result comes from the present study. [b] Yield independent of olefin concentration. [c] Ozone–nitrogen rather than ozone–oxygen was used. [d] Room temperature of laboratory where experiment performed. [e] Not determined. [f] G. Schroeder, Dissertation, Karlsruhe, 1959.

torial position in the final ozonide, causing the aldehyde substituent also to assume, predominantly but not entirely, an equatorial position, since this avoids interaction with the orbitals of unshared electron pairs[29] as well as with the axial hydrogen. Thus, more *cis* than *trans* ozonide should be formed from an *anti* zwitterion. Also, by the converse of rule 1, the *syn* zwitterion should place its substituent axially, thus strongly encouraging the aldehyde substituent to enter equatorially in order to avoid 1,3-diaxial interactions between the substituents, which would be much more serious than interactions with unshared electron pairs. Hence, the *trans* ozonide should be formed in excess.

The predictions arising from the foregoing rules are summarized in Table I. A *cis* olefin with bulky substituents should yield a final ozonide with a *cis–trans* ratio greater than one. The prediction for a *trans* olefin depends on the position of the axial,axial–equatorial,equatorial equilibrium in the initial ozonide. With very bulky substituents the axial,axial conformation should be preferred since interference between the gauche substituents in the equatorial,equatorial conformer should be greater than interference between the *trans* substituents and the relevant oxygen lone pairs in the axial,axial conformer.

Tables II and III show stereochemical results from ozonolysis studies carried out in this and other laboratories. We now intend to show that these results are compatible with the generalizations of Table I and the other refinements of the Criegee mechanism already outlined.

As has already been observed by Murray, *et al.*,[21] the *cis–trans* ratios of the ozonides of various olefins are strongly influenced by the bulk of the substituents attached to the double bond. There is very little difference in the *cis–trans* normal ozonide ratios obtained from the *cis* and *trans* isomers of 2-butene (Table II, experiments 29–35), 3-hexene (Table II, experiments 19, 21, 22, 26–28), 2-pentene (Table III, experiments 14–19), 2-hexene (Table III, experiments 20, 21), or 4-methyl-2-pentene (Table III, experiments 1, 2, 5, 9, 10, 12), provided the comparison is made in the same solvent. Neither is there much difference in the *cis–trans* ratio of 2-butene ozonide, whether it is produced as a normal or as a cross ozonide in a hydrocarbon solvent (*cf.* Table II, experiments 30, 33, and Table III, experiments 1, 3, 9–11, 14, 15, 17, 18, 20, 21). On the other hand, the *cis–trans* ratio of an ozonide with two

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(29) *Cf.* S. A. Barker, E. J. Bourne, R. M. Pinkard, M. Stacey, and D. A. Whiffen, *J. Chem. Soc.*, 3232 (1958).

Table III. Ozonolyses of Unsymmetrical Olefins

Expt	R and R^1 in RCH=CHR^1	Config	Solvent	Concn, *M*	Temp, °C	Pair A[a]		Pair B[a]		Pair C[a]		Total ozonide yield,[c] %	Ref[d]
						%[b]	*c*:*t*	%[b]	*c*:*t*	%[b]	*c*:*t*		
1	*i*-Pr; CH$_3$	*cis*	Pentane	1	−75	11	71:29	86	48:52	3	43:57	*e*	
2				1	−70	19	66:34	69	49:51	12	49:51	86	21
3[f]				1	−30	20	66:34	72	50:50	8	43:57	*e*	
4[f]				2.5	−75	20	63:37	70	46:54	10	42:58	*e*	
5			AcOEt	1	−75	30	57:43	58	47:53	12	34:66	*e*	
6[f]				1	0	27	60:40	59	51:49	14	40:60	*e*	
7			CH$_2$Cl$_2$	1	−75	31	71:29	56	63:37	13	56:44	*e*	
8[f]				1	0	24	62:38	58	54:46	18	49:51	*e*	
9		*trans*	Pentane	1	−75	12	40:60	85	46:54	3	31:69	*e*	
10				1	−70	11	50:50	83	48:52	6	38:62	66	21
11				1	−30	17	46:54	77	52:48	6	41:59	*e*	
12			AcOEt	1	−75	17	49:51	75	48:52	8	32:68	*e*	
13			CH$_2$Cl$_2$	1	−75	25	60:40	60	55:45	15	41:59	*e*	
14	Et; CH$_3$	*cis*	Pentane	1	−70	14	56:44	68	42:58	18	44:56	91	21
15			Butane	0.2	−30	9	52:48	87	42:58	4	44:56	83	20
16			Me$_2$O	0.2	−70	22	40:60	53	34:66	25	29:71	80	20
17		*trans*	Pentane	1	−70	8	41:59	82	38:62	10	32:68	56	21
18			Butane	0.2	−30	15	42:58	80	40:60	5	32:68	35	20
19			Me$_2$O	0.2	−70	17	40:60	52	36:64	31	27:73	46	20
20	Pr; CH$_3$	*cis*	Pentane	1	−70	*g*	*e*	*e*	41:59	16	43:57	72[g]	21
21		*trans*		1	−70	*g*	*e*	*e*	40:60	11	39:61	53[g]	21
22	*t*-Bu; CH$_3$	*cis*		1	−70	3	74:26	88	54:46	9	46:54	81	21
23		*trans*		1	−70	*g*	*e*	*e*	30:70	*g*	*e*	32[g]	21
24	*t*-Bu; Et	*cis*		1	−70	11	82:18	77	67:33	12	62:38	84	21
25		*trans*		1	−70	*g*	*e*	*e*	29:71	*g*	*e*	16[g]	21

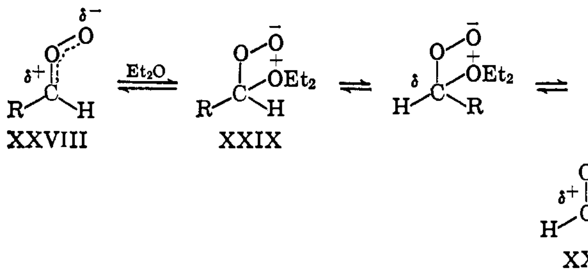
[a] Pair A is the higher molecular weight cross-ozonide pair, pair B is the normal ozonide pair, and pair C is the lower molecular weight cross-ozonide pair. [b] This represents per cent of each ozonide in the mixture of ozonides. [c] This is the actual yield of the mixture of ozonides. [d] If no reference is given, the result comes from the present work. [e] Not determined. [f] Ozone–nitrogen rather than ozone–oxygen was used. [g] An ozonide qualitatively, but not quantitatively, determined.

bulky groups varies greatly as to whether it comes from a *cis* or a *trans* olefin. These facts are consistent with the mechanism of Scheme IV. In the case of smaller substituents (R = Me or Et) there may be but little axial,axial conformer in the *trans* initial ozonide. As a result, little *syn* zwitterion would be produced from either the *cis* or the *trans* initial ozonide, and both would yield similar ozonide ratios, although, of course, not necessarily in the same total yield. Where at least one R group is *t*-butyl or isopropyl the axial,axial conformation becomes more popular and the *syn* zwitterion is produced in appreciable amounts from the *trans* initial ozonide. In these cases the ozonide *cis–trans* ratios differ appreciably. It is interesting that in one case, 2-butene, the *cis–trans* ozonide ratio is less than one even from the *cis* olefin isomer. It may well be that the *trans* ozonide (and the transition state leading to it) is more stable for very small substituents regardless of the zwitterion configuration. Already when R = ethyl the effect vanishes.

The *cis–trans* ratios of the ozonides of olefins with large substituents, such as 1,2-di-*t*-butylethylene (Table II, experiments 1, 8, 9; Table III, experiments 22 and 24), 1,2-diisopropylethylene (Table II, experiments 14, 15, 17, 18; Table III, experiments 1 and 9), 4,4-dimethyl-2-pentene (Table III, experiments 22 and 23), and 5,5-dimethyl-3-hexene (Table III, experiments 24 and 25) fit well the predictions of Table I. For example, *cis*-1,2-di-*t*-butylethylene produced an ozonide with a 70:30 *cis–trans* ratio (Table II, experiments 1 and 2), while the *trans* olefin afforded an ozonide with a 28:72 *cis–trans* ratio (Table II, experiment 8); Schröder[16] reported 100% *trans* (Table II, experiment 9). The 1,2-diisopropylethylenes, with slightly lower steric requirements, gave *cis–trans* ozonide ratios of 62:38 for the *cis* olefin (Table II, experiment 15) and 45:55 for the *trans* olefin (Table II, experiment 17).

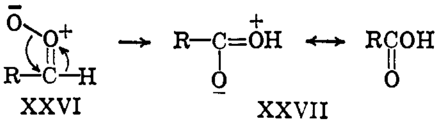
The effect of solvent changes on the *cis–trans* ozonide ratios from *cis* and *trans* olefins is also interesting. In each case the *cis–trans* ratio tends to be higher in pentane and methylene chloride, especially the latter, than in ether or ethyl acetate, with both normal and cross ozonides (*cf.* Table II, experiments 20 and 21; Table II, experiments 24, 25, 26; Table II, experiments 29–32; Table II, experiments 33–35; Table III, experiments 1, 5, 7; Table III, experiments 12 and 13; Table III, experiments 14–16; Table III, experiments 6 and 8). These findings may reflect a partial equilibration of the zwitterions under certain conditions. In most of the cases cited, both *syn* and *anti* zwitterions should be produced, with the latter perhaps being favored. It is not known at the present time whether the *syn* or the *anti* zwitterion is the more stable, although one intuitively might expect the latter to be. Perhaps, in pentane and methylene chloride, especially the latter since it is more polar, some isomerization of *syn* to *anti* zwitterion occurs. This tendency may be less, however, in ether and ethyl acetate due to a stabilizing solvation effect. This solvation effect may also be the explanation for other differences observed in Tables II and III between results with ethyl acetate and methylene chloride as solvents.

An alternative explanation is that some isomerization of *anti* to *syn* zwitterion occurs in ethyl acetate or ether solvent, perhaps *via* the mechanism depicted by XXVIII → XXIX → XXX, which involves the nucleophilic properties of these two solvents. By analogy to allylic anions,[30] where the *cis* isomer appears to be the more stable, the *anti* zwitterion may in some cases be the labile isomer. If, however, the kinetically produced *cis–trans* ratio from decomposition of an initial ozonide is richer in *anti* isomer than is the thermodynamic mixture, an enrichment in *syn* content could occur, even if the *anti* isomer were the more stable of the two. At the present time we cannot make a definitive choice between these explanations of this interesting solvent effect.


XXVIII XXIX XXX

One of the most striking observations from the data of Tables II and III and other data, as has previously been discussed,[18,21] is that *cis* olefins give higher yields of ozonides than do *trans* olefins (*cf.* Table II, experiments 1, 8, 9, 14, 16, 19, 22, 30, 33, and Table III, experiments 2, 10, 14, 17, 20–25). Greenwood and Haske[18] have suggested that this is due to the greater stability of the *trans* initial ozonide, causing it to build up to greater concentrations than the *cis* initial ozonide and, thus, be more vulnerable to side reactions. We, too, consider this a likely contributing factor. The side reactions could include attack by other species, resulting in polymeric ozonides or peroxides.[31] As an explanation for the greater stability (*i.e.*, slower unimolecular cleavage) of a *trans* than a *cis* initial ozonide (and of those with larger than of those with smaller *trans* substituents), we suggest the following. In a disrotatory cleavage of either the axial,axial or the equatorial,equatorial conformer of the *trans* initial ozonide, one of the substituents must rotate inward. This is likely to encounter steric repulsions which should be especially strong when the substituent is bulky. In contrast, the *cis* initial ozonide may avoid this by rotating both substituents outward in the disrotatory cleavage. As a consequence, the rate of unimolecular decomposition of a *trans* initial ozonide should be retarded in comparison to that of a *cis*. The foregoing is especially appealing as an explanation for the extraordinary stability of the initial ozonide of *trans*-1,2-*t*-butylethylene.

Another factor which could play a role in the greater production of ozonide by *cis* than by *trans* olefins is the difference in reactivity of the isomeric zwitterions. The *syn* zwitterion should, according to our predictions, be produced in greater amounts from *trans* than from *cis* olefins (Table I). It appears likely from several standpoints that this zwitterion undergoes wasteful side reactions more readily than does its *anti* counterpart. First, cycloaddition between the *syn* zwitterion and an aldehyde is hindered since the zwitterion must place its substituent axially in the transition state leading to the final ozonide. The nonbonded repulsions in such a transition state must be perceptively larger than those in the transition state derived from the *anti* zwitterion, in which the substituent assumes an equatorial position. Second, the *syn* zwitterion should be more susceptible, sterically, than the *anti* zwitterion to the stepwise, noncyclic mode of attack involved in polymerization.[32] Finally, the *syn* zwitterion should be more susceptible to a Beckmann-like rearrangement to an acid (XXVI → XXVII).


XXVI XXVII

Another interesting observation is that the ozonide yield from *cis* olefins usually is somewhat lower with polar than with nonpolar solvents (Table II, experiments 1, 5, 6, 7, 19–21, 31, 32).[33] This is understandable on the basis that in polar solvents, the polar zwitterion and aldehyde moieties, from decomposition of the initial ozonide, more readily diffuse apart, thus increasing the opportunity for side reactions of the zwitterion, such as polymerization, to occur at the expense of geminate recombination of aldehyde and zwitterion fragments to an ozonide. In contrast to this, available examples show that the ozonide yield from *trans* olefins is actually greater with polar than with nonpolar solvents (Table II, experiments 23–27, and Table III, experiments 18 and 19), except with *trans*-1,2-di-*t*-butylethylene where no ozonide was obtained with polar solvents (Table II, experiments 8, 9, 12, 13). This is also understandable on the basis of the ideas already presented. Decomposition of the initial ozonide to the polar zwitterion and carbonyl moieties is enhanced by polar solvents. In the case of *trans* initial ozonides with small substituents, the main effect is to decrease the chances of side reactions occurring through the attack of outside species (such as zwitterions or aldehydes) on the initial ozonide and, therefore, actually to increase ozonide formation. The initial ozonide of *trans*-1,2-di-*t*-butylethylene is unique, however. First, attack by outside species is sterically inhibited and does not occur to any appreciable extent whether the solvent is polar or nonpolar. Second, the proportion of *syn* to *anti* zwitterion should be greater from this olefin than any other, and the *syn* zwitterion, as discussed earlier, should be much more susceptible to various side reactions than to 1,3-dipolar cycloaddition with the aldehyde to give an ozonide. It is curious that ozonide yields tend to be lower in methylene chloride than in ethyl acetate (which has a greater dipole moment) or in ether (Table II, experiments 5, 6, 7, 25, 26). It appears futile at this time to speculate on whether this is associated with the acidity, the solvating power, the nucleophilicity, or some other property of the solvent.

Further evidence that an increase in solvent polarity encourages the separation of the zwitterion and carbonyl moieties, allowing them to react independently at the

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(30) S. Bank, A. Schriesheim, and C. A. Rowe, Jr., *J. Am. Chem. Soc.*, 87, 3245 (1965).

(31) N. A. Milas and I. Belic, *Vestn. Sloven. Kem. Drustva*, 10, 37 (1963). These authors have shown that such peroxides are complex, involving both the zwitterion and the carbonyl moieties in various proportions.

(32) In this respect it is noteworthy that the reaction between two zwitterions should, by application of a Woodward–Hoffmann rule, be stepwise ($8 = 4n$ π electrons): R. Hoffmann and R. B. Woodward, *J. Am. Chem. Soc.*, 87, 2046 (1965). This is a logical first step in one route to polymeric peroxides.

(33) Such effects have also been observed with methyl oleate.[9,34]

(34) O. S. Privett and E. C. Nickell, *J. Am. Oil Chemists' Soc.*, 43, 393 (1966).

Table IV. Ozonolyses[a] in the Presence of Added Aldehyde

Expt	R in $RCH{=}CHR$	Config	RCHO added, R	Pair A[b] %	Pair A[b] *c*:*t*	Pair B[b] %	Pair B[b] *c*:*t*	Other prod	Total ozonide yield,[c] %
1	*i*-Pr	*trans*	*i*-Pr		48:52			[d]	51
2	*i*-Pr	*cis*	*i*-Pr		68:32			[e]	82
3	*i*-Pr	*cis*	Me	36[f]	61:39	64[f]	52:48	[g]	[g]
4	*t*-Bu	*trans*	*t*-Bu		30:70				60

[a] Ozonolyses were carried out on pentane solutions 1 *M* with respect both to the olefin and the aldehyde at −75°, usually using about 0.75 mol equiv of ozone. [b] A is the normal ozonide pair and B is the ozonide pair incorporating the aldehyde with different R group. [c] This is total ozonide yield based on amount of ozone reacting. [d] 1.1 mol equiv of aldehyde was recovered, indicating it is a product of the reaction. A large amount (1.8 g from 2.6 g of olefin and 1.6 g of aldehyde) of polymeric peroxide was obtained. [e] In comparison to footnote *d*, 1.1 mol equiv of aldehyde was recovered and 1.2 g of polymer was produced. [f] Per cent of each ozonide in mixture of ozonides. [g] Not determined.

expense of geminate recombination, comes from ozonation of unsymmetrical olefins. An increase in solvent polarity increases the ratio of cross to normal ozonide yield (Table III, experiments 1, 5, 7, 9, 12, 13, 15, 16, 18, 19).[33] A point of passing interest is that the larger cross ozonide usually is produced in greater amounts than the smaller (Table III, experiments 1–13, 15, 18). This probably reflects a more facile polymerization of small zwitterions.

There are very little data available concerning the effect of temperature changes (all other factors constant) on ozonide yields. However, temperature increases lowered the ozonide yield with both *cis*- and *trans*-1,2-di-*t*-butylethylenes, and the effect was greater with the *trans* isomer (Table II, experiments 1, 3, 10, 11). On the other hand, Greenwood[18,20] observed a small increase in ozonide yield at higher temperatures with *trans*-3-hexene (Table II, experiments 23, 24, 26–28). These results are explicable on the same basis as the solvent effects just discussed. As the temperature increases, the decomposition rate of the initial ozonide increases, the dispersion of the resulting zwitterion and carbonyl moieties becomes more extensive, and independent side reactions of the zwitterion tend to increase at the expense of geminate recombination of the zwitterion and aldehyde fragments. This effect is especially important with *trans* initial ozonides having large substituents, since the resulting *syn* zwitterions undergo side reactions more readily than 1,3-dipolar cycloaddition. With *trans* initial ozonides having smaller substituents, however, the faster decomposition at higher temperature decreases the opportunity for side reactions at the initial ozonide stage, and results in a slight elevation of ozonide yield. Further evidence for the greater dispersion of the zwitterion and aldehyde moieties at elevated temperatures comes from the observation that in nonpolar solvents the ratio of cross to normal ozonides from unsymmetrical olefins increases as the temperature increases (Table III, experiments 1, 3, 10, 11).[35] This effect is not observed with polar solvents (Table III, experiments 5, 6, 7, 8), with which the cross to normal ozonide ratio is already greater than with nonpolar solvents.

At higher olefin concentrations the ratio of cross to normal ozonides, from unsymmetrical olefins, is increased (Table III, experiments 1 and 4).[35] This is to be expected since geminate recombination should be reduced either by interception of one of the moieties of a zwitterion–aldehyde pair by the opposite member of another close-by zwitterion–aldehyde pair or by the increased polarity of the medium. Increased concentration would also be expected to increase the yield of polymeric by-products at the expense of total ozonide yield.

We have carried out several ozonolyses of olefins in the presence of an equimolar quantity of an aldehyde (Table IV). In these experiments there were only small effects both in regard to the *cis–trans* ratios of the ozonides produced and the ozonide yields (*cf.* Table IV, experiment 1, and Table II, experiment 17; *cf.* Table IV, experiments 2 and 3, and Table II, experiments 14 and 15, also Table III, experiment 1, pair B; *cf.* Table IV, experiment 4, and Table II, experiment 8). It appears to us that if the SMY mechanism were competing with the Criegee mechanism to any appreciable extent, an excess of aldehyde should increase the degree to which the reaction course follows the SMY mechanism. Thus, the ozonide yield should increase, and, according to our conformational analysis of the SMY mechanism, the *cis–trans* ratio of the final ozonide from the *trans* olefins should increase. This did not happen. Although recent experiments with oxygen-18-labeled acetaldehyde appear to confirm that the SMY mechanism operates in the presence of excess aldehyde,[36] these results are questionable, since the mechanisms of the ozonide decompositions employed are not known.

Experimental Section

Materials. ***cis*-1,2-Di-*t*-butylethylene** was made by catalytic reduction of 1,2-di-*t*-butylacetylene[3,37] and purified on a spinning-band column, bp 144°. *trans*-1,2-Di-*t*-butylethylene was either made by ultraviolet light isomerization of the *cis* isomer in the presence of a trace of iodine or was purchased from Chemical Samples Co. and purified on a spinning-band column, bp 125°. *cis*- and *trans*-4-Methyl-2-pentenes and *cis*- and *trans*-2,5-dimethyl-3-hexenes were purchased from Chemical Samples Co. in 99% purity. *cis*-2-Butene was obtained from Union Carbide Corp. and Freon 11 ($CFCl_3$) from Du Pont. *n*-Pentane was Matheson Coleman and Bell spectrograde; methylene chloride was Fisher Certified Grade, and ethyl acetate was Baker anhydrous reagent.

Ozonolysis Procedure. The ozonation set-up and procedures, using either ozone–oxygen or ozone–nitrogen, are described in earlier publications.[38] In initial experiments, results from ozone–nitrogen and ozone–oxygen were compared and found not to be appreciably different. Thereafter, ozone–oxygen streams of known

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(35) See also ref 8.

(36) P. R. Story, C. E. Bishop, J. R. Burgess, J. B. Olson, R. W. Murray, and R. D. Youssefyeh, paper presented at the International Oxidation Symposium, San Francisco, Calif., Aug 28–Sept 1, 1967.

(37) G. F. Hennion and T. F. Banigan, Jr., *J. Am. Chem. Soc.*, **68**, 1203 (1946).

(38) (a) P. S. Bailey, *ibid.*, **78**, 3811 (1956); (b) P. S. Bailey, *J. Org. Chem.*, **22**, 1548 (1957); (c) P. S. Bailey and A. M. Reader, *Chem. Ind.* (London), 1063 (1961); (d) A. M. Reader, P. S. Bailey, and H. M. White, *J. Org. Chem.*, 30, 784 (1965).

ozone content between 3 and 6% by weight were employed. The ozonolyses were run to about 75% completion on solutions of concentrations and at temperatures shown in Tables II–IV.

With the experiments included in Table III, only the *cis–trans* ratios and the relative yields of normal and cross ozonides, but not actual total ozonide yields, were determined, by direct injection on the gas chromatograph. In some cases *cis–trans* ratios were verified by nmr.

In most of the other cases a 25-ml solution of the olefin was ozonized. The solvent, unreacted starting material, and volatile products were removed under reduced pressure and condensed in a cold trap. This was diluted to a definite volume with pentane and analyzed by vpc. The residue was diluted with pentane and the ozonide determined both for yield and *cis–trans* ratio by vpc or nmr. Yields were generally based on the ozone reacting. In some instances, the ozonides were then removed by distillation and the yield of polymeric peroxides obtained by weight. The procedures were the same whether or not the ozonolyses were carried out in the presence of an added aldehyde.

Gas Chromatography. Ozonide *cis–trans* ratios and relative yields of cross and normal ozonides were determined on an Aerograph A-90-P3 gas chromatograph, using a 20 ft × $^3/_8$ in. column packed with 20% cyanosilicone fluid on Chromosorb P; injector temperature 63°, column temperature 68°, detector temperature 190°, flow rate 150 cc/min. Peak areas were determined by a K and E compensating polar planimeter, making three successive determinations on each of three separate injections. In some cases determinations were made on two or more separate ozonolysis mixtures; the values shown in Tables II–IV are average values. Checks made in this way and with solutions of *cis* and *trans* ozonides of known concentrations, as well as by means of nmr, showed the determinations to have a maximum variation of ±0.5 for a given ozonolysis reaction mixture, or ±2.0 for different ozonolysis reaction mixtures. In those cases where total ozonide yields were determined by vpc (*cis*- and *trans*-1,2-diisopropylethylenes) peak areas were compared with those of standard solutions of the ozonides. *cis* and *trans* ozonide assignments were based on the *cis* isomer having the longer vpc retention time, as done by previous investigators.[16,21]

Unreacted olefin and aldehyde determinations were done with an F & M Model 500 gas chromatograph equipped with a disk integrator, and using a 20 ft × 0.25 in. column packed with 20% Carbowax 20M on Chromosorb P; yields were determined by comparing with standard solutions of the known compounds.

Nmr spectra were obtained with a Varian Associates A-60 spectrometer. *cis–trans* ozonide ratios were determined by integrating the methine hydrogen peak areas. These were τ 4.68 (*cis*-2-butene ozonide), 4.72 (*trans*-2-butene ozonide), 5.18 (*cis*-di-*t*-butylethylene ozonide), and 5.25 ppm (*trans*-di-*t*-butylethylene ozonide). The total yields of the di-*t*-butylethylene ozonides and of pivaldehyde were also determined by nmr; the integrated *t*-butyl proton peak areas were compared with that of a known amount of *t*-butyl bromide. These were τ 8.23 (*t*-butyl bromide), 8.95 (pivaldehyde), and 9.04 ppm (*cis* and *trans* ozonides).

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Chemistry of Cyclopropanols. VI. Cleavage by Electrophilic Halogen

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Abstract: It has been shown that both *cis,trans*- and *trans,trans*-2,3-dimethyl-1-phenylcyclopropanols and their corresponding acetates react stereospecifically with a variety of brominating agents to form bromo ketones with complete *inversion* of configuration at the site to which the bromine becomes attached. Thus the *cis,trans* isomer gives only *erythro*-α-methyl-β-bromobutyrophenone and the *trans,trans* isomer gives exclusively the corresponding *threo* isomer. Chlorinating agents react with both cyclopropanols and the same 50:50 mixture of *threo*- and *erythro*-chloro ketones is produced from either isomer. The direction of ring opening with halogenating agents has been studied for 1,2,2-trimethylcyclopropanol and *trans*-2-phenyl-1-methylcyclopropanol and compared with the direction found for ring opening with protons. Halogenating agents are more specific with both compounds, giving exclusively 1,3 bond breaking in the former compound and exclusively 1,2 bond breaking in the latter. This is to be contrasted with openings with protons in which 1,3 bond breaking predominates (75–25% and 60–40%, respectively).

The acid- and base-catalyzed isomerization reactions of *trans*-2-phenyl-1-methylcyclopropanol to 3-phenyl-2-butanone and 4-phenyl-2-butanone were extensively explored in an earlier study.[1] The base-catalyzed reaction was assigned an SE1 mechanism based on the observation that, in deuterated solvents, 4-deuterio-4-phenyl-2-butanone was formed from the optically active cyclopropanol with inversion of configuration at the benzylic carbon atom. The exclusive C-1–C-2 bond cleavage may be rationalized by assuming that an intermediate cyclopropoxide ion rearranges, with ring opening, to produce the more stable carbanion. The acid-catalyzed reaction was assigned an SE2 mechanism based on the formation of 4-deuterio-4-phenyl-2-butanone, in deuterated solvent, in which the stereochemistry of the benzylic carbon atom had been retained. In contrast to the base-catalyzed reaction, however, this material accounted for only 40% of the product mixture, the remainder being 4-deuterio-3-phenyl-2-butanone resulting from C-1–C-3 bond cleavage (see Figure 1). This product ratio suggests that the potential stability of charge at the benzylic position is not the determining factor in directing ring opening under acidic conditions. In order to examine the possible steric requirements of the reaction, the concept of replacing the protonating species by elec-

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(1) C. H. DePuy, F. W. Breitbeil, and K. R. DeBruin, *J. Am. Chem. Soc.*, **88**, 3343 (1966).