Formation and Structure of Ozonides

ROBERT L. KUCZKOWSKI

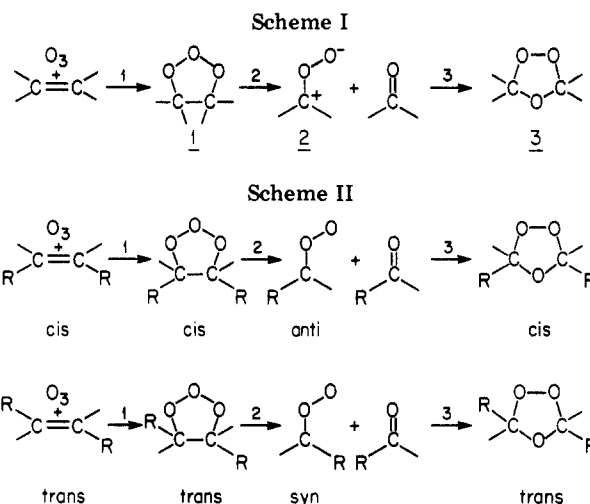*Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48109*

Received July 12, 1982 (Revised Manuscript Received October 18, 1982)

Our interest in ozonides (1,2,4-trioxolanes) was stimulated by an Account by R. W. Murray dealing with the mechanism of ozonolysis.[1] This made us aware that detailed information on the structures of small ozonides was nonexistent and could be a fruitful research area for a microwave spectroscopist. After commencing a structural investigation of ethylene ozonide,[2] we realized that ^{18}O tracer studies could expand this project into a more comprehensive study dealing with the mechanism of ozonide formation as well. This was prompted by certain ^{18}O tracer studies on more complex systems that had questioned the classical (Criegee) mechanism of ozonolysis.[3]

The ability to probe both structural and mechanistic details via microwave spectroscopy (MWS) originates in the rotational isotope effect, i.e., the shifts in rotational transitions upon isotopic substitution. Thus, an ozonide structure can be deduced if these shifts or, more correctly, the rotational moments of inertia are available from enough isotopic species. At the same time, mechanistic insights can be obtained by locating the site of enrichment from a synthesis with labeled reactants. This isotopic specificity is apparent in Figure 1 where selected $J = 1 \rightarrow 2$ rotational transitions for various ^{16}O, ^{18}O, and D_1 species of ethylene ozonide are illustrated. Usually there is no ambiguity as to the origin of the transitions since the magnitude of the isotope shifts are distinctive and predictable even with only an approximately correct structural model,[4a] This Account will describe recent mechanistic and structural studies on ozonides[4b] with an underlying theme that especially highlights results employing isotopic data analyzed by MWS and other techniques.

Mechanism of Ozonide Formation

A three-step mechanism (Scheme I) was formulated by R. Criegee over the period 1949–1957 to describe the ozonolysis of alkenes in solution.[5,6] This "bare bones" proposal describes the formation of a relatively unstable primary ozonide (1), which cleaves to an aldehyde (or ketone) and a carbonyl oxide (2), often called the Criegee intermediate or zwitterion. Recombination of the carbonyl compound and 2 produces the final ozonide (3). A variety of data supported this proposal including isolation of 1, or its glycol derivative for some systems, trapping of 2 by foreign aldehydes or reactive solvents, and isolation of 3 and other products such as peroxide dimers of 2. In the late 1960s, this mechanism was scrutinized when questions arose from ^{18}O labeling experiments[3] and especially regarding new stereochemistry data.[1,6] For example, it became apparent that

Robert Kuczkowski was born in Buffalo, NY, where he received a B.S. degree from Canisius College in 1960. The Ph.D. was obtained from Harvard University followed by postdoctoral research at the National Bureau of Standards. He joined the faculty at Michigan in 1966 where his research in structural chemistry, heterogeneous catalysis, and ozonide chemistry usually incorporates some microwave spectroscopy.

Scheme I

Scheme II

cis-(or *trans*-) alkenes with bulky alkyl substituents usually resulted in more cis (or trans) final ozonide; i.e., the reaction was stereoselective.

Following a seminal paper in 1968,[7] the incorporation of stereochemistry into the Criegee mechanism was further developed during the 1970s. This subject was recently reviewed,[6,8] and a detailed analysis would be lengthy. Therefore, only a brief overview will be given here.

The most thoroughly developed proposal views the Criegee reaction as a sequence of concerted $(2\pi_s + 4\pi_s)$ cycloaddition–reversion steps (Scheme II). Accordingly, step 1 is a 1,3 cycloaddition with retention of the alkene configuration in the primary ozonide. This decomposes in step 2 via a 1,3 cycloreversion to give a syn or anti carbonyl oxide. Another 1,3 cycloaddition occurs in step 3 with a preferred configuration for the final ozonide. It is worthwhile to recognize that the proposal for the *cis*- or *trans*-alkene, particularly steps 2 and 3, refers to the dominant pathway to the ozonide since only occasionally is the one ozonide isomer obtained.

The stereospecificity in step 1 has been established from primary ozonide data for nine cases.[9] In steps 2

(1) R. W. Murray, *Acc. Chem. Res.*, 1, 313 (1968).

(2) C. W. Gillies and R. L. Kuczkowski, *J. Am. Chem. Soc.*, 94, 6337 (1972).

(3) (a) P. R. Story, C. E. Bishop, J. R. Burgess, R. W. Murray, and R. D. Youssefyeh, *J. Am. Chem. Soc.*, 90, 1907 (1968). (b) R. W. Murray and R. Hagen, *J. Org. Chem.*, 36, 1103 (1971). (c) P. R. Story, J. A. Alford, J. R. Burgess, and W. C. Ray, *J. Am. Chem. Soc.*, 93, 3042 (1971).

(4) (a) The intensities of the transitions in Figure 1 have been arbitrarily equalized. In actual spectra they would be weighted by the isotopic abundance and other well-understood factors. (b) The term ozonides will refer to 1,2,4-trioxolanes (alternatively, 1,2,4-trioxacyclopentanes or final ozonides). The less stable 1,2,3-trioxolanes will be specifically called primary ozonides.
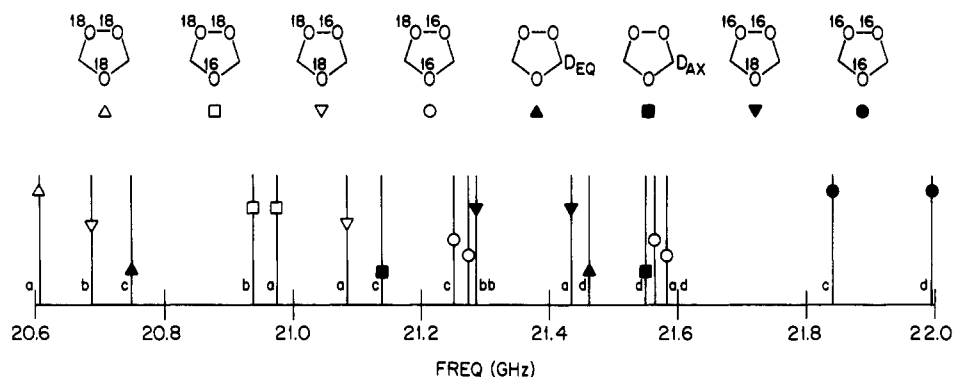
(5) R. Criegee, *Angew. Chem., Int. Ed. Engl.*, 14, 745 (1975).

(6) P. S. Bailey, "Ozonation in Organic Chemistry", Vol. 1, Academic Press, New York, 1978.

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

(8) R. L. Kuczkowski in "1,3-Dipolar Cycloadditions", A. W. Padwa, Ed., Wiley, New York, in press.

Figure 1. Selected $J = 1 \rightarrow 2$ microwave transitions for the d_1 (axial), d_1 (equatorial), and the six ^{16}O, ^{18}O species of ethylene ozonide between 20 600 and 22 000 MHz.[4a] The transition labels are a ($1_{01} \rightarrow 2_{02}$), b ($1_{11} \rightarrow 2_{12}$), c ($1_{11} \rightarrow 2_{02}$), and d ($1_{01} - 2_{12}$). The actual instrumental resolution is better than 1 MHz.

and 3 it is based on cis/trans final ozonide ratios, and the explanation is more complex. The rationale focuses on transition states and considers substituent interactions, the principle of least motion, syn vs. anti stability, and the Hammond postulate. This has been developed by Bailey et al.[7,10] and Kuczkowski et al.[11] They provided essentially equivalent analyses that differ in some details such as certain transition-state conformations. More recently, estimates of reaction energetics and transition states from thermochemical and ab initio calculations have also argued that the ozonide formation occurs by concerted reactions steps.[12,13] These four analyses together provide the best current description of the concerted Criegee proposal.[8]

Nevertheless, there are certain data that are difficult to incorporate into the concerted mechanism, such as anomalous stereochemical results, variability in cis/trans ozonide ratios with conditions, poorly understood solvent effects, and puzzling examples where ozonide formation is suppressed. This has prompted suggestions that steps 2 and 3 may be nonconcerted in some cases (or a competitive pathway) and could occur with some stereochemical control.[14,15]

In summary, recent research on the mechanism of ozonolysis has been directed at better understanding the details of the "bare bones" Criegee mechanism. Among the areas to receive attention in this Account will be the structure–reactivity of the Criegee intermediate, the question of concerted vs. nonconcerted reaction steps, stereochemistry, solvent effects, and the extension of the mechanism to halogenated alkenes.

Carbonyl Oxide 2. This species is central to the mechanism of ozonolysis, and it is curious that it has never been clearly detected spectroscopically in situ. It has been the subject of several MO calculations that

Scheme III
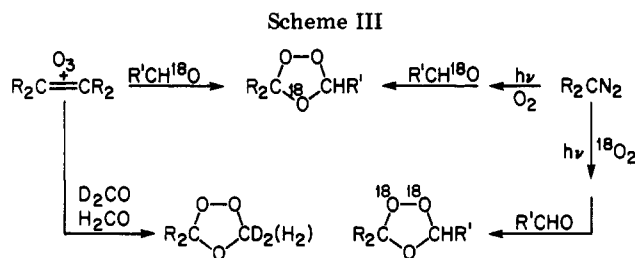
characterize it by a singlet diradical wave function similar to that for isoelectronic ozone.[13d,14,16] This is equivalent to an electron density distribution represented by the valence-bond structure 4 rather than a
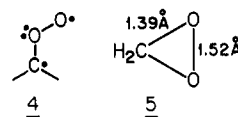
zwitterionic form such as 2 preferred by Criegee. The diradical character suggests the possibility of nonconcerted reactivity patterns.[14] The calculations also show that the dioxirane isomer (5) is considerably more stable (~ 25–35 kcal) than the carbonyl oxide form. In fact, dioxirane has been identified in the gas phase from the in situ reaction between ozone and ethylene condensed on the walls of a MW spectrometer cell, and its structural parameters have been determined.[17] Nevertheless, the early results of Criegee and the more recent experiments point solidly to the carbonyl oxide isomer as the reactive intermediate participating in ozonide formation in solution reactions.

Trapping experiments and product analysis have been the tranditional methods for studying the carbonyl oxide moiety. Recent isotopic labeling experiments have provided insights as illustrated in Scheme III. Ozonolyses in the presence of added ^{18}O-enriched aldehydes for a variety of systems[18] have shown conclusively by using MWS (e.g., Figure 1) and mass

(9) (a) P. S. Bailey, T. M. Ferrell, A. Rustaiyan, S. Seyhan, and L. E. Unruh, *J. Am. Chem. Soc.*, **100**, 894 (1978). (b) P. S. Bailey, J. A. Thompson, and B. A. Shoulders, *ibid.*, **88**, 4098 (1966). (c) L. J. Durham and F. L. Greenwood, *Chem. Commun.*, 843 (1967); *J. Org. Chem.*, **33**, 1629 (1968); *Chem. Commun.*, 24 (1968).

(10) P. S. Bailey and T. M. Ferrell, *J. Am. Chem. Soc.*, **100**, 899 (1978).

(11) R. P. Lattimer, R. L. Kuczkowski, and C. W. Gillies, *J. Am. Chem. Soc.*, **96**, 348 (1974).

(12) P. S. Nangia and S. W. Benson, *J. Am. Chem. Soc.*, **102**, 3105 (1980).

(13) (a) D. Cremer, *J. Chem. Phys.*, **70**, 1898 (1979); (b) *ibid.*, **70**, 1911 (1979); (c) *ibid.*, **70**, 1928 (1979). (d) D. Cremer, *J. Am. Chem. Soc.*, **101**, 7199 (1979); (e) *ibid.*, **103**, 3619 (1981); (f) *ibid*, **103**, 3627 (1981); (g) *ibid.*, **103**, 3633 (1981).
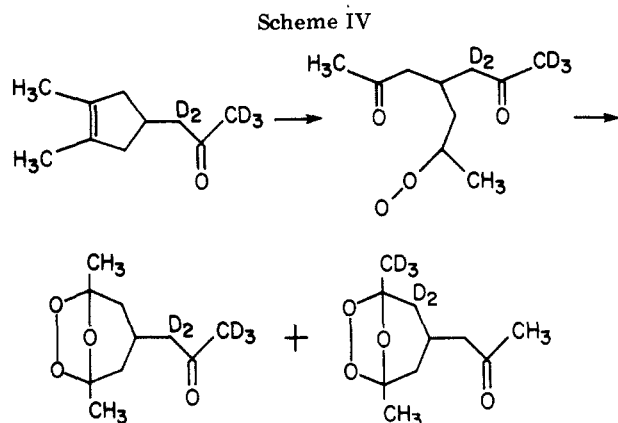
(14) L. B. Harding and W. A. Goddard III, *J. Am. Chem. Soc.*, **100**, 7180 (1978).

(15) (a) R. W. Murray and R. Hagen, *J. Org. Chem.*, **36**, 1098 (1971); (b) J. Su and R. W. Murray, *ibid.*, **45**, 678 (1980); (c) V. Ramachandran and R. W. Murray, *J. Am. Chem. Soc.*, **100**, 2197 (1978).

(16) (a) T.-K. Ha, H. Kühne, S. Vaccani, and Hs. H. Günthard, *Chem. Phys. Lett.*, **24**, 172 (1974); (b) G. Karlström, S. Engström, and B. Jönnson, *ibid.*, **67**, 343 (1979); (c) K. Yamaguchi, S. Yabushita, T. Fueno, S. Kato, K. Morokuma, and S. Iwata, *ibid.*, **71**, 563 (1980).

(17) R. D. Suenram and F. J. Lovas, *J. Am. Chem. Soc.*, **100**, 5117 (1978).

(18) (a) C. W. Gillies and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **94**, 7609 (1972). (b) C. W. Gillies, R. P. Lattimer, and R. L. Kuczkowski, *ibid.*, **96**, 1536 (1974). (c) R. P. Lattimer and R. L. Kuczkowski, *ibid.*, **96**, 6205 (1974). (d) K. L. Gallaher and R. L. Kuczkowski, *J. Org. Chem.*, **41**, 892 (1976). (e) D. P. Higley and R. W. Murray, *J. Am. Chem. Soc.*, **98**, 4526 (1978). (f) S. Fliszár and J. Carles, *ibid.*, **91**, 2637 (1969). (g) J. Castonguay, M. Bertrand, J. Carles, S. Fliszár, and Y. Rousseau, *Can. J. Chem.*, **47**, 919 (1969).

Scheme IV

Table I
Kinetic Secondary Isotope Effect for Ethylene
and Fraction of Ethylene-d_2 Ozonide (Cross-Ozonide)
from Ozonolysis of C_2H_4/C_2D_4 Mixtures ($\approx 1/1$)
in Various Solvents[20]

solvent	μ, D[a]	k_H/k_D[b]	cross-fraction[c]	T, °C
neat	0.0	0.93	0.08 (3)	−126
i-C_4H_{10}	0.13	0.96	0.027 (14)	−116
CF_3Cl	0.51	0.94	0.107 (22)	−116
CF_2BrH	1.31	0.94	0.372 (23)	−116
CF_2ClH	1.42	0.95	0.384 (20)	−116
CF_3H	1.65	0.92	0.387 (15)	−116
CF_2H_2	1.97	0.94	0.362 (10)	−116

[a] Solvent dipole moment. [b] Normalized KSIE ratio for ethylene on a per deuterium basis at 25 °C. [c] Cross-fraction = oz-d_2/(oz-d_0 + oz-d_2 + oz-d_4).

spectrometry that the label appears exclusively at the ether site in the ozonide. These data supplant earlier work that argued that some [18]O label appeared in the peroxy bridge.[3] Reappraisal of several of these earlier studies[18c-e] indicated that degradation processes or the mass spectrometry technique for determining the site of enrichment were misleading. While specific labeling at the ether site is consistent with the carbonyl oxide isomer (step 3 in Schemes I or II), it is troublesome for a dioxirane isomer. Dioxirane would seem to be more likely to add an aldehyde after breakage of its weak O–O linkage. The [18]O label should then appear at the peroxide site in the ozonide.

A novel synthesis of an ozonide sans ozone is described in Scheme III from photolysis of a diazo compound.[18e,19] This produces R_2C, a carbene, which adds O_2 to give R_2COO and subsequently an ozonide. With [18]O in either the aldehyde or the O_2 it is possible to produce the appropriately labeled ozonide consistent with step 3 of the Criegee mechanism.

Scheme III also illustrates H_2CO/D_2CO competition for the Criegee intermediate. When HDC=CHD was used, the H_2CO/D_2CO kinetic secondary isotope effect (KSIE) was determined as $k_H/k_D = 0.891$ (30) from the relative amounts of the ethylene-d_1 and -d_3 ozonide.[20] This inverse KSIE is consistent with a cycloaddition in step 3 with partial transformation of the sp^2 carbon atom of formaldehyde to sp^3 in the transition state. This KSIE is more difficult to reconcile with a stepwise radical transition state recently considered involving ·CH_2OCH_2OO· in which a bond is first formed to the formaldehyde oxygen atom with development of a radical center at the formaldehyde carbon atom.[14]

A noteworthy trapping experiment involved sidechain deuteration of a cyclopentyl system (Scheme IV).[21] The two possible ozonides were found in equal amounts. This implies that the carbonyl oxide did not prefer the keto group produced during ozonolysis and must have a sufficient lifetime to randomly react with either one.

These types of experiments, along with the stereochemical data mentioned earlier that suggest *syn–anti* isomerism in the carbonyl oxide, have given considerable insight into the Criegee intermediate but do not completely resolve whether it is better described as a

zwitterion or as a singlet diradical since the ozonide formation may well be consistent with either species. Conversion to the more stable dioxirane isomer is not a factor, presumably due to the kinetic stability of the carbonyl oxide formed in solution. Barriers for conversion of H_2COO to dioxirane have been estimated as 17–27 kcal.[16a,22] It has also been suggested that solvent effects may considerably stabilize the carbonyl oxide form and help account for a reactivity pattern appropriate to a 1,3 dipole in spite of the diradical character proposed for an isolated carbonyl oxide.[14]

Cross-Ozonide Formation and Solvent Effects. Cross-ozonide production is expected according to the Criegee mechanism, and this phenomena can be explored by using tracers. A recent example involves the use of mixtures of C_2D_4 and C_2H_4. It was found that

$$CD_2=CD_2 + CH_2=CH_2 \xrightarrow{O_3} D_2COOCD_2O,$$

$$H_2COOCH_2O, \ D_2COOCH_2O \ (cross \ ozonide)$$
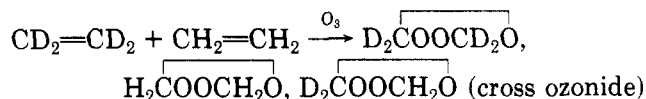
C_2D_4 reacted significantly faster than C_2H_4.[20] In a variety of solvents the ratio k_H/k_D was 0.945 (15) (Table I). This inverse KSIE for ozone addition to ethylene indicates a transition state with transformation of an sp^2 carbon atom to sp^3. The value of the isotope effect is plausible for a concerted addition process, and other [2 + 3] and [2 + 4] cycloadditions have yielded similar KSIE ratios.

The amount of the cross-ozonide (ethylene ozonide-*3,3-d_2*) is listed in Table I for several solvents. This sheds light on the effect of the solvent cage. The increase in the fraction of cross-ozonide indicates a reduced cage effect in polar solvents. The amount of cross-fraction would be 0.5 for complete scrambling. However, KSIE effects in the overall reaction probably lower the statistical ratio to about 0.36–0.45 or close to the observed values based on a rough model that estimates KSIE effects in the three-step concerted Criegee mechanism.[20] Therefore, the amount of ozonide formed outside the original solvent cage can vary from below 10% to at least 90% as solvent polarity changes. This behavior indicates considerable solvent stabilization of the two polar species produced upon primary ozonide decomposition.

Haloalkenes. Since ozonides have been difficult to isolate from haloalkenes, a mechanistic picture of their solution reaction with ozone has been more difficult to establish. Another limitation has been a reduced re-

(19) (a) R. W. Murray and A. Suzui, *J. Am. Chem. Soc.*, **93**, 4963 (1971); **95** 3343 (1973); (b) R. W. Murray and D. P. Higley, *ibid.*, **95**, 7886 (1973); **96**, 3330 (1974).

(20) G. D. Fong and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **102**, 4763 (1980).

(21) R. Criegee, A. Banciu, and H. Keul, *Chem. Ber.*, **108**, 1642 (1975).

(22) (a) L. A. Hull, *J. Org. Chem.*, **43**, 2780 (1978); (b) G. Karlström and B. O. Ross., *Chem. Phys. Lett.*, **79**, 416 (1981).

Table II
Product Analysis from Ozonolysis of Fluoroalkenes[a]

alkene	normal ozonide	cross ozonide	aldehyde	epoxide	cyclopropane	ref
C_2H_3F	33-45%	EtOz,[b] 1-3% F_2Oz,[b] 1%	HCOF, 36-40% H_2CO, 1%			24
H_2CCF_2	20%	EtOz (minor)	F_2CO (major)			25, 26
cis-HFC=CFH	6-30%, c/t ≈ 10/90		HCOF, 30-45%	6-16%, c/t ≈ 30/1	$C_3H_3F_3$, ~0.3% (cis,cis and cis,trans)	27
trans-HFC=CFH	3-14% c/t ≈ 10/90		HCOF, 33-50%	3-10%, c/t ≈ 1/20	$C_3H_3F_3$, ~0.5% (cis,trans)	27
HFCCF₂	13% (major)	F_2Oz (minor)	HCOF (major) F_2CO (major)	major		27
F_2CCF_2	trace		F_2CO, 10-60%	5-15%	trace (≤2%)	27, 28

[a] Selected results; yields vary with solvent. Nonvolatile residues are also formed although the yields are small or zero for the F_3 and F_4 alkenes under some conditions. [b] EtOz = ethylene ozonide; F_2Oz = 3,5-difluoro-1,2,4-trioxacyclopentane.

Table III
Ozonolysis of Mixtures Containing Two Alkenes or Alkene and Aldehyde

reaction	alkene	added alkene or aldehyde	labeled products[a]	ref
1	C_2H_3F	DCOF	FOz (70% d_1), F_2Oz (80% d_1)	30
2	CHFCHF	DCOF	F_2Oz (58% d_1)	30
3	C_2H_4	HCOF	FOz (2%), EtOz (98%)	30
4	CHFCHF	$H_2C^{18}O$	FOz (^{18}O at ether)	31
5	CHFCHF	C_2H_4	EtOz (54%), FOz (5%), F_2Oz (15%)	30
6	C_2H_3F	C_2D_3F	FOz (d_n statistical mixture)	30
7	CHFCHF	$H_2^{13}CO$	FOz (^{13}C enriched)	31
8	C_2H_3F	$^{18}O_3$, HC^{16}OF	FOz (enriched in $\overline{CH_2^{18}O^{18}OCHF^{16}O}$)	31
9	CH_2CF_2	$^{18}O_3$, C^{16}OF₂	*g*-F_2Oz (enriched in $\overline{CH_2^{18}O^{18}OCF_2^{16}O}$)	32

[a] FOz = vinyl fluoride ozonide; EtOz = ethylene ozonide; F_2Oz = 3,5-difluoro-1,2,4-trioxacyclopentane; *g*-F_2Oz = 3,3-difluoro-1,2,4-trioxacyclopentane. Relative enrichment in parenthesis except rxn 3 and 5 (relative yields).

activity toward ozone. For example, the $C_2H_xCl_{4-x}$ series shows a decrease in the ozone rate of attack by a factor of 25 ($x = 3$) to 25 000 ($x = 0$) compared to ethylene.[23] The halogen presumably deactivates the double bond toward electrophilic attack by ozone.

The fluoroethylene series has recently been investigated in some detail and shows similarities and differences from alkylethylenes. The products upon ozonolysis are listed in Table II.[24-28] It is apparent that all six alkenes can lead to final ozonides although the amounts decline to trace quantities with complete fluorination. Four of the six possible cross-ozonides have also been identified, at least under certain conditions. The formation of large amounts of CHFO and CF_2O are consistent with a Criegee cleavage mechanism but suggest a reduced reactivity between the carbonyl oxide and CHFO or CF_2O.

The ozonide products formed from the mixtures in Table III, many involving isotopic labels, are further evidence for the Criegee mechanism. Reactions 1 and 2 indicate that both the H_2COO and HFCOO species are produced. However, inspection of yields combined with the labeling data suggests that cleavage to H_2COO and HCOF is the preferred process for vinyl fluoride

(probably 70–95%). Reactions 3–5 and 7 also indicate that H_2CO is better than HCOF at cycloaddition with a carbonyl oxide. From reaction 6 it is evident that a cage effect is not prevalent. Reactions 4, 8, and 9 show that the oxygen in the added aldehyde appears at the ether site in the ozonide. The results of reaction 9 and others involving CH_2CF_2 are also consistent with the Criegee mechanism.

It is apparent that fluorine substitution leads to another reaction pathway since the four alkenes without a CH_2 moiety lead to stereospecific epoxide and cyclopropane formation. The mechanism of these two processes, i.e., the source of the oxygen atom and the carbenes, CHF or CF_2, which add across the alkene double bond is still unclear although labeling experiments apparently eliminate carbene addition to an aldehyde.[27a] In contrast to these halolakenes, epoxide or other "partial cleavage" products from ozonolysis of non-haloalkenes are usually associated with steric factors that seem to block normal ozone 1,3 cycloaddition to the double bond.[29]

Another difference from alkylalkenes is the high stereospecificity observed in the formation of the *cis*- and *trans*-difluoroethylene ozonide. A cis/trans ratio of about 1/10 to 1/20 is observed from either *cis*- or *trans*-HFC=CHF or as the cross-ozonide from C_2H_3F and probably C_2F_3H. This suggests the formation of predominantly the syn-HFCOO isomer that would be

(23) D. G. Williamson and R. J. Cvetanović, *J. Am. Chem. Soc.*, **90**, 4248 (1968).

(24) (a) R. P. Lattimer, U. Mazur, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **98**, 4012 (1976); (b) U. Mazur, R. P. Lattimer, A. Lopata, and R. L. Kuczkowski, *J. Org. Chem.*, **44**, 3181 (1979).

(25) C. W. Gillies, S. P. Sponseller, and R. L. Kuczkowski, *J. Phys. Chem.*, **83**, 1545 (1979).

(26) J. W. Agopovich and C. W. Gillies, *J. Am. Chem. Soc.*, **102**, 7572 (1980).

(27) (a) C. W. Gillies, *J. Am. Chem. Soc.*, **97**, 1276 (1975); **99**, 7239 (1977). (b) J. W. Agopovich and C. W. Gillies, *ibid.*, **104**, 813 (1982).
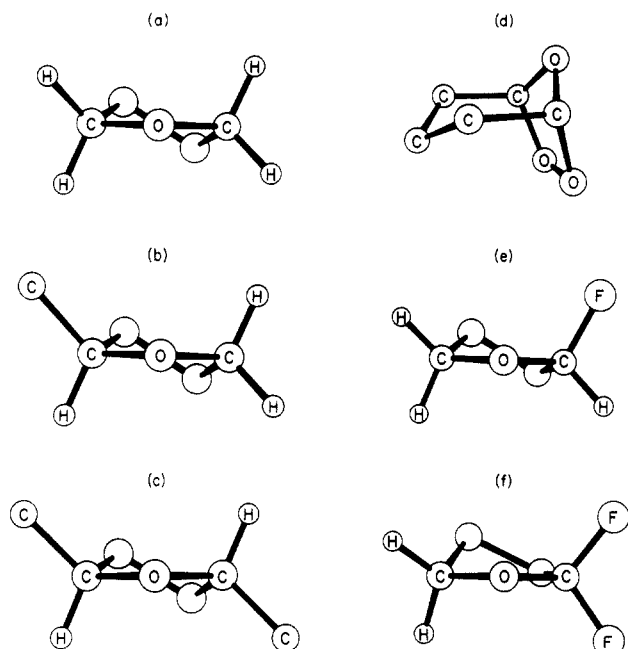
(28) F. Gozzo and G. Camaggi, *Chim. Ind. (Milan)*, **50**, 197 (1968).

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

(30) U. Mazur and R. L. Kuczkowski, *J. Org. Chem.*, **44**, 3185 (1979).

(31) K. W. Hillig II, R. P. Lattimer, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **104**, 988 (1982).

(32) K. W. Hillig II and R. L. Kuczkowski, *J. Phys. Chem.*, **86**, 1415 (1982).

Figure 2. Ozonide conformations: (a) ethylene ozonide,[33] (b) propylene ozonide,[11] (c) *trans*-butene ozonide,[11] (d) cyclopentene ozonide,[39] (e) vinyl fluoride ozonide,[31] (f) vinylidene fluoride ozonide.[32]

expected if an anomeric interaction influences the cleavage of the primary ozonide[8,27] (cf. the discussion of the structure of vinyl fluoride ozonide below). Alternatively, the cycloaddition of HFCOO and HFCO may be preferentially trans, due to fluorine repulsions, regardless of the configuration of the carbonyl oxide. Calculations[13g] suggest that both of these factors probably contribute.

Structures of Ozonides

This section will focus on the conformational results from selected MWS studies and a series of ab initio calculations by D. Cremer.[13] Such data are important for understanding properties and reactivity. They provide insight into the conformation of the ground state, the rigidity of the ring, and barriers to planarity or pseudorotation, i.e., the dynamics of the ozonide ring. Since the ultimate goal of the ozonide chemist is to describe the dynamics of the ozonolysis reaction, these results can provide some guidance when one speculates about reaction profiles and transition-state conformations.

At the outset, it is useful to imagine that the five atoms which comprise the ozonide ring might assume either a planar geometry or one of several possible twisted or envelope forms. Ring substituents may lead to less symmetric forms, and low barriers to conformational interchange may complicate the picture, but such idealized conformations are a useful starting point. In the ensuing discussion the peroxy and ether oxygens with be referred to as O_p and O_e, respectively.

The MW results for six ozonides are illustrated in Figure 2. Ethylene ozonide (EtOz, Figure 2a) is the prototype and has a conformation described as the twisted O_p–O_p.[2,33] The most significant element is the

C_2 symmetry and the large associated C–O_p–O_p–C dihedral angle of 49.2°. This ring twisting leads to nonequivalent axial and equatorial sites for the hydrogen atoms evident in the d_1 MW spectra (Figure 1). The MW and IR spectra showed no effects from pseudorotation, and the two ring-motion vibrational modes were estimated to be about 190 and 350 cm^{-1}.[2,34] The ab initio calculations also concluded that EtOz is a fairly rigid species.[13a] The barriers to pseudorotation and inversion through the planar form were estimated to be 3 kcal and 4–6 kcal, respectively. Of course, these barriers are low on the NMR time scale which may be the reason why the proton spectrum of EtOz appears as a singlet even at fairly low temperatures.[24b]

Because of the pronounced O_p–O_p twist it is attractive to infer that the same interactions that lead to the stable gauche form in H_2O_2 are operative in the ozonide ring. Cremer described this as arising from C–O_p bond dipole repulsions, which promote a twist, and oxygen p-type lone-pair interactions on both the O_p and O_e which stabilize the twisted form. Considering lone-pair effects, the overall stabilization is dominated by a lowering of the two highest π-type HOMOs, which favor twisting over envelope puckering or the planar form.[13a,b]
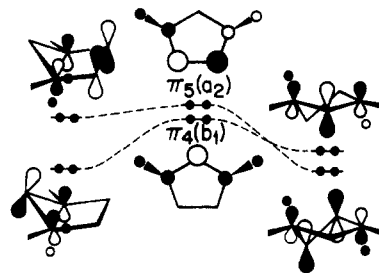
The MW spectra for *cis*- and *trans*-ethylene ozonide-d_2 were used to establish clearly that the stereochemistry observed in ozonolysis of *cis*- (*trans*-) alkenes resides in the stereochemical properties of the substituent and does not partly arise from some intramolecular rearrangement process between the primary ozonide and the final ozonide. The latter possibility is unlikely based on ozonolysis of *cis*- or *trans*-HDC= CHD in a nonpolar solvent. Both gave a final ozonide cis/trans ratio of 1.00 (4), i.e., complete stereorandomization.[20] NMR observation of the ozonolysis of *cis*- or *trans*-1-deuterio-1-hexene showed a similar result.[35]

Propylene (PrOz, Figure 2b) and *trans*-2-butene ozonide (*trans*-BuOz, Figure 2c) have the same conformation as EtOz and comparable rigidity.[11,13c,36] A preference by the Me substituents for the equatorial position was observed. For example, the twisted isomers with axial Me groups for PrOz and *trans*-BuOz were not detected by MW spectroscopy and are predicted to be 1–2 kcal higher in energy.[13c] The equatorial preference can be rationalized in terms of molecular mechanics by postulating a decrease in unfavorable gauche and across-the-ring interactions for Me_{eq} compared to Me_{ax}. The MO calculations suggested that stabilization also arises from a favorable π-type ring interaction with Me at the equatorial site.

Of course, it is implicit in a stereochemical study that the cis and trans ozonides can be distinguished. *trans*-BuOz is the fifth system for which the configu-

(33) (a) R. L. Kuczkowski, C. W. Gillies, and K. L. Gallaher, *J. Mol. Spectrosc.*, **60**, 361 (1976); (b) U. Mazur and R. L. Kuczkowski, *ibid.*, **65**, 84 (1977).
(34) H. Kühne and Hs. H. Günthard, *J. Phys. Chem.*, **80**, 1238 (1976).

(35) R. W. Murray and G. J. Williams, *J. Org. Chem.*, **34**, 1896 (1969).
(36) R. P. Lattimer, C. W. Gillies, and R. L. Kuczkowski, *J. Am. Chem. Soc.*, **95**, 1348 (1973).

Ozonide Structure

ration has been unambiguously established.[37] It is satisfying that the MW results concur with the previous assignment that was based on the usual but more equivocal procedure of assigning the trans configuration to the isomer with the shorter GC retention time.[38]

MW analysis[39] of the bicyclic ozonides obtained from cyclobutene and cyclopentene (Figure 2d) failed to confirm the suggestion from some PE data[40] that the forces leading to the O_p-O_p twist conformation in the simpler ozonides might also be evident in these more constrained systems. Both ozonides have a plane of symmetry (C_s symmetry). Clearly it is possible to force the ozonide moiety into the diaxial or ether oxygen (O_e) envelope form given the constraints imposed by a bicyclic ring system.

Vinyl fluoride ozonide (FOz, Figure 2e) has a conformation intermediate between a pure twist (as in EtOz) and an O_H envelope.[31] Furthermore, the fluorine occupies an axial position and the C_F-O_p and C_F-O_e bonds decrease about 0.03 Å from those of EtOz. These contrasts are a manifestation of the anomeric effect.[41] A simple model for this electronic interaction emphasizes the overlap between a p-type oxygen lone pair with the empty σ^*_{CF} providing a mechanism for a shorter C–O bond and a longer C–F bond ($d(CF) = 1.37$Å).[31,41] MO calculations basically support this model and estimate that the equatorial conformer is higher in energy by 3 kcal.[13g] This preference for an axial fluorine led to the initial inference that a similar propensity may occur in the transition state of the fluoroalkene primary ozonide decomposition step (cf. above).[27a]

The conformation of vinylidene fluoride ozonide (F_2Oz, Figure 2f) has an even more pronounced distortion from EtOz. In fact, it is better described as an O_p envelope conformer.[32] The results imply that the ozonide ring adjusts to place two *gem*-fluorines in a pseudoaxial orientation with somewhat similar ring interactions. Nevertheless, other effects such as the C–O bond dipole repulsions still result in nonplanarity of the ring. It is also curious that the conformation resembles the envelope form proposed as a transition state for the 1,3-cycloaddition reaction between a carbonyl species and the Criegee intermediate.[11,42] Recent

results indicate that *cis*-difluoroethylene ozonide possesses an O_e envelope conformation (resembling the bicyclic ozonide, Figure 2d) with both fluorines in a diaxial orientation.[43]

In summary, several types of ground-state conformations have been observed. The MO calculations estimate that the less stable conformations are modestly higher ($\sim$1–5 kcal) for simple ozonides and that low pseudorotation barriers provide transient accessibility to a variety of conformations. This structural diversity implies that a complex interplay exists between ring strain and dipole–dipole, lone–pair, and substituent interactions, resulting in the most stable form. Extending this to reaction dynamics, the mechanistic chemist should be cautious when considering possible transition states for formation (or decomposition) of ozonides since perhaps no single conformation is overwhelmingly preferred on energetic grounds for many systems. This also seems to be implied by the stereoselectivity of the reaction and its sensitivity to solvent, temperature, and other reaction parameters. Competition from nonconcerted reaction paths may also be a factor.

This Account has highlighted some recent insights obtained regarding ozonides. Yet, informed observers recognize that much still remains obscure since the reaction process producing ozonides (as well as poorly understood non-ozonide products) is fundamentally more complex than perhaps intimated by our selection of examples. The pragmatic goal of rationalizing the full diversity of reaction details via the idealized model in Scheme II has not actually been achieved. The lofty dream of obtaining a more dynamic model that describes how species approach and interact, how energy is localized and dissipated in bond breakage/formation processes, and how the solvent may participate at the intermolecular level remains in the future, although progress has been made. Still it is clear that the Criegee mechanism, with embellishments added from subsequent findings, is a compelling descriptor of much ozonolysis phenomena. It remains the reference point for new work.

(37) The others are (a) diisopropylethylene (R. W. Murray, R. D. Youssefyeh, and P. R. Story, *J. Am. Chem. Soc.*, 88, 3655 (1966)) and (b) stilbene, 1,4-dichloro-2-butene, and 1,4-dibromo-2,3-dimethyl-2-butene (R. Criegee and H. Korber, *Chem. Ber.*, 104, 1807 (1971)).

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

(39) D. G. Borseth, Ph.D. Thesis, University of Michigan, 1982.

(40) P. Rademacher and W. Elling, *Liebigs Ann. Chem.*, 1979, 1473.

(41) (a) S. Wolfe, M-H. Whangbo, and D. J. Mitchell, *Carbohydr. Res.*, 69, 1 (1979). (b) A. D. Lopata and R. L. Kuczkowski, *J. Am. Chem. Soc.*, 103, 3304 (1981).

(42) A. Eckell, R. Huisgen, R. Sustmann, G. Wallbillich, D. Grashey, and E. Spindler, *Chem. Ber.*, 100, 2192 (1967).

(43) K. W. Hillig II and R. L. Kuczkowski, unpublished work.