

Mechanism of Ozonolysis. A More Flexible Stereochemical Concept¹

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Abstract: The Bauld–Bailey stereochemical refinement of the Criegee ozonolysis mechanism and the Kuczkowski modification thereof are compared and contrasted. The rationale behind the Bauld–Bailey scheme has been further elucidated, and additional concepts, such as kinetic vs. thermodynamic control of primary ozonide decomposition, have been added. This makes possible a more flexible stereochemical modification of the carbonyl oxide mechanism and provides a foundation from which is attained a greater understanding than previously possible of the differences in cis–trans ozonide ratios observed with olefins under a variety of conditions. This includes very low vs. medium low temperatures, slow vs. fast warm-up of the ozonolysis reaction mixture, and results with substituted ethylenes with large vs. those with small substituents. Of special interest is the predominance of cis ozonide obtained from ozonolysis of trans-1,2-diisopropylethylene in isopentane at $-150\text{ }^{\circ}\text{C}$ followed by a slow warm-up.

The Criegee mechanism for the ozonolysis of alkenes,^{2,3} first suggested nearly 30 years ago,⁴ has provided the foundation upon which a greater and greater understanding and utilization of the classical reaction is continuing to develop. The key concept of the Criegee mechanism is the intermediacy of a carbonyl oxide (usually described as a zwitterion) in the major route to ozonides and other peroxidic ozonolysis products.

For a period of time serious doubt was cast upon this concept because of findings that cis and trans isomeric olefins generally provide different ratios of peroxidic (and accompanying nonperoxidic) ozonolysis products.⁵ The original, basic, Criegee mechanism² predicted the contrary since the same pair of carbonyl oxide zwitterion and carbonyl moieties were formulated as intermediates in either case. Most important in this respect was the discovery that cis and trans isomeric olefins generally yield different ratios of cis and trans final ozonides (1,2,4-trioxolanes); this not only applies to symmetrical olefins and their ozonides, but also to both “normal” and “cross” ozonides of unsymmetrical olefins.^{5–9} Some of the most pertinent data are gathered in Table I.

These results, of course, spawned new mechanisms,^{6,12} all of which have since been discarded or shown to be inconsequential.^{13,14} The principal one of these, an aldehyde-exchange mechanism,⁶ was shown to play no significant role by means of novel and definitive oxygen-18 studies.¹³ In addition, the elegant studies of Criegee,¹⁵ regarding competitions in intramolecular ozonide formation, made just before his death, render untenable any general route to ozonide not involving a carbonyl oxide as the principal intermediate.

Thus, there remains for consideration today two stereochemical refinements of the Criegee carbonyl oxide mechanism, namely, the Bauld–Bailey⁹ scheme and the Kuczkowski¹¹ modification of it, both of which utilize as the fundamental rationale for stereoselectivity in ozonide formation the concept of syn and anti stereoisomers of the carbonyl oxide intermediate. The possibility of syn and anti carbonyl oxide zwitterions was suggested initially by Criegee,¹⁶ but Bauld, Bailey et al.⁹ were the first to use the notion in regard to ozonide stereochemistry.

The purpose of the present paper is to compare and contrast the Bauld–Bailey⁹ and Kuczkowski¹¹ schemes and to expand the Bauld–Bailey concept into a stereochemical modification of the carbonyl oxide mechanism which has the flexibility necessary to rationalize not only the data of Table I but, also, the new data presented in the accompanying paper,¹⁷ which neither of the present schemes can accommodate.

The data of Table I show that cis olefins generally afford a

higher percentage of cis ozonide than do trans olefins. In many cases the cis–trans ozonide ratio is greater than unity for cis olefins and less than unity for trans olefins. This is especially true for symmetrical olefins with large substituents and for the larger cross ozonides of unsymmetrical olefins. It should be emphasized, however, that little information is available as to whether a “slow” or a “fast” warm-up was employed with the examples of Table I. Murray and Hagen¹⁸ have shown that this makes a considerable difference, and, as noted in the accompanying paper,¹⁷ their findings have been verified¹⁹ and expanded upon in our laboratory.

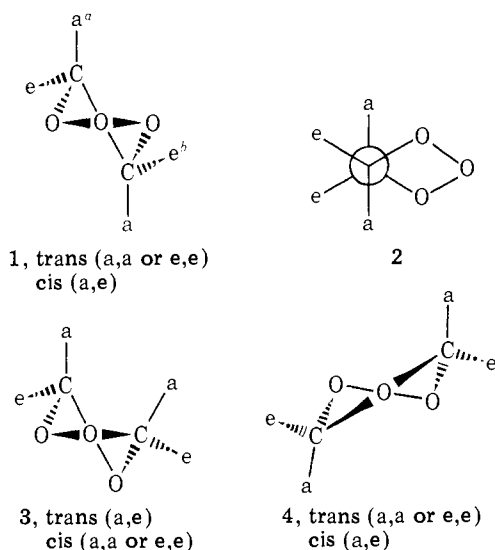
The Bauld–Bailey Concept. In their 1968 paper, Bauld, Bailey et al.⁹ laid down some fundamental principles upon which both their scheme and the 1974 Kuczkowski¹¹ scheme are based. First, all three stages in ozonide formation are concerted,²⁰ stereospecific, or selective, one-step, orbital-symmetry-allowed reactions, namely, 1,3-dipolar cycloaddition of ozone to an olefin (a cis addition) to give a 1,2,3-trioxolane primary ozonide, 1,3-dipolar cycloreversion of the primary ozonide to carbonyl oxide and carbonyl moieties, 1,3-dipolar cycloaddition of the latter two moieties to a 1,2,4-trioxolane final ozonide. Second, the reactions involving the primary and final ozonides require nonplanar geometries, either in the starting materials or the transition states. Although one particular set was chosen to illustrate the principles involved and to formulate a set of rules for a working hypothesis, it was explicitly stated that any nonplanar model with definite axial and equatorial substituents could lead to similar predictions.⁹ The validity of this statement has been amply demonstrated by the Kuczkowski scheme, itself. Third, cis and trans primary ozonides decompose in a stereoselective manner from preferred conformations (or via preferred transition-state geometries) to anti and syn carbonyl oxides which, in turn, recombine with the aldehyde moiety in a stereoselective manner to yield cis and trans final ozonides. Fourth, equatorial and axial substituents on the primary ozonide ring preferentially incorporate into anti and syn carbonyl oxides, respectively, and these, in turn, tend to afford cis and trans final ozonides, respectively. Fifth, the steric effects which control these preferences are substituent–substituent, substituent–ring–bond, and substituent–oxygen lone-pair repulsions.

The Bauld–Bailey scheme, as originally proposed,⁹ selected a C–C half-chair, **1** or **2**, as the reactive conformation of the primary ozonide, and a C–O half-chair, **3**, for the conformation of the final ozonide. These were chosen because each afforded reasonably well-defined equatorial and axial substituent positions. Three rules were then postulated to account for the stereoselectivity of ozonide formation. Following the original

Table I. Stereoselectivity of Ozonide Formation

Expt	R and R' in RCH=CHR'	Confign	Ozonide cis-trans ratios ^a			Total ozonide yield, %	Ref
			Pair A ^b	Pair B ^b	Pair C ^b		
1	R = R' = <i>t</i> -Bu	Cis ^c		70:30		82	7, 9
2	R = R' = <i>t</i> -Bu	Trans ^c		28:72		51	9
3	R = R' = <i>i</i> -Pr	Cis		66:34		85	6
4	R = R' = <i>i</i> -Pr	Cis		62:38		<i>d</i>	9
5	R = R' = <i>i</i> -Pr	Trans		53:47		47	6
6	R = R' = <i>i</i> -Pr	Trans		45:55		52	9
7	R = R' = Et	Cis		53:47		81	6
8	R = R' = Et	Trans		53:47		49	6
9	R = R' = Me	Cis		39:61		48	6
10	R = R' = Me	Trans		38:62		36	6
11	R = <i>i</i> -Pr; R' = Me	Cis	71:29	48:52	43:57	<i>d</i>	9
12	R = <i>i</i> -Pr; R' = Me	Trans	40:60	46:54	31:69	<i>d</i>	9
13	R = <i>t</i> -Bu; R' = Me	Cis	74:26	54:46	46:54	81	6
14	R = <i>t</i> -Bu; R' = Me	Trans	<i>d</i>	30:70	<i>d</i>	32	6
15	R = <i>t</i> -Bu; R' = Et	Cis	73:27	60:40	51:49	<i>d</i>	10
16	R = <i>t</i> -Bu; R' = Et	Trans	68:32	38:62	<i>d</i>	<i>d</i>	10
17	R = Et; R' = Me	Cis	56:44	42:58	44:56	91	6
18	R = Et; R' = Me	Trans	41:59	38:62	32:68	56	6
19	R = Me; R' = H ^e		81:19			<i>d</i>	11

^a Unless otherwise stated, the solvent was pentane, the ozonolysis temperature -70 to -75 °C, and the solution concentration 1 M. ^b Pair A is the higher molecular weight cross ozonide, pair B the normal ozonide, and pair C the lower molecular weight cross ozonide. ^c The solution concentration was 0.3 M. ^d Not determined. ^e The solvent was isobutane and the ozonolysis temperature -95 °C.

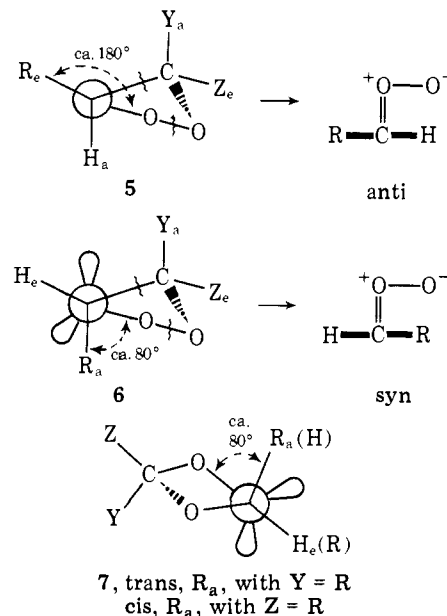


^a a, axial. ^b e, equatorial.

proposal,⁹ microwave spectral studies,^{11,21} supported by CNDO/2 calculations,²² revealed that simple final ozonides (1,2,4-trioxolanes), at least those with small substituents, have O-O half-chair, **4**, rather than C-O half-chair, **3**, conformations. For this reason the third Bauld-Bailey rule (below) has been revised accordingly. The others remain unchanged.

The three rules are (1) equatorial substituents are preferentially converted into anti, and axial substituents into syn, carbonyl oxides; (2) an equatorial substituent is incorporated into a carbonyl oxide in preference to an axial substituent; (3) (revised), aldehydes preferentially interact with anti carbonyl oxides to orient bulky substituents on the 1,2,4-trioxolane ring, **4**, into an axial-equatorial conformation (cis) and with syn carbonyl oxides to orient bulky substituents diaxially (trans). On the basis of these three rules, plus the assumption that a trans 1,2,3-trioxolane with large substituents, as shown in **2**, should prefer the diaxial conformation with its substituents anti rather than the diequatorial conformation with gauche substituents, most of the data of Table I can be rationalized for olefins with large double-bond substituents.

Because Kuczkowski et al.¹¹ have stated that the rationale concerning Bauld-Bailey rule 1 (in regard to axial substituents) and rule 2 are not clear and that there is no rationale for the revised rule 3, the theory behind the three rules must be further detailed. The underlying principle for all three rules is that of *least motion*. If one views along the carbon-oxygen bond of the incipient carbonyl oxide in the C-C half-chair conformation of the primary ozonide, it becomes evident that an equatorial substituent (e.g., in **5**) is already very close to the required 180° angle with the oxygen-oxygen bond of a developing carbonyl oxide and that the carbon-hydrogen bond on the same carbon atom is $<90^\circ$ ($\sim 80^\circ$) away from the same oxygen-oxygen bond. The exact opposite is true when the substituent is axial (e.g., in **6**) and the hydrogen on the same carbon atom is equatorial. Thus, by the least motion principle, equatorial and axial substituents should preferentially produce anti and syn carbonyl oxides, respectively (rule 1). Since, however, during the cleavage and rehybridization processes greater steric repulsions are encountered as an axial substituent

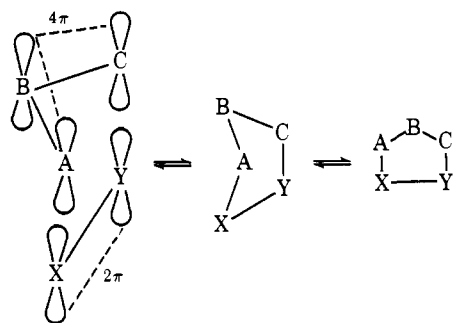


uent, relative to an axial hydrogen, moves inward toward the ring, it follows that an equatorial substituent should be able to assimilate itself into a carbonyl oxide more easily than should an axial substituent (rule 2). Thus, *trans* primary ozonides (**6**, $Y = R$) and *cis* primary ozonides (**5**, $Y = R$), with large substituents, should preferentially produce *syn* and *anti* carbonyl oxides, respectively.

The rationale for rule 3 follows similar principles. The least motion requirement is met in incorporating an *anti* carbonyl oxide substituent into an equatorial position and a *syn* carbonyl oxide substituent into an axial position since, in the O-O half-chair (**7**, with the Newman projection being for the carbonyl oxide C-O bond), an equatorial substituent is already nearly at a 180° angle and an axial substituent about an 80° angle relative to the O-O bond of the former carbonyl oxide moiety. The aldehyde also has a choice. If the carbonyl oxide substituent begins to incorporate itself into the ring axially, the aldehyde substituent also prefers to orient itself in such a manner as to become axial. This minimizes not only substituent-substituent, **4**, but also substituent-adjacent-oxygen lone-pair interactions (e.g., in **7** with Newman projection involving the carbon of the former aldehyde moiety and the terminal carbonyl oxide oxygen). Thus, *syn* carbonyl oxides are produced from *trans* olefins and result in *trans* final ozonides, **4** (a,a), or **7**, predominantly. If the carbonyl oxide substituent begins to assume an equatorial position, the aldehyde orients its substituent axially to provide the least possible substituent-adjacent-oxygen lone-pair interactions, e.g., **7**. Thus, *anti* carbonyl oxides are produced from *cis* olefins and yield *cis* final ozonides, **4** (a,e) or **7**, predominantly.

The Kuczkowski scheme¹¹ also assumes all three processes in ozonide formation to be concerted 1,3-dipolar cycloadditions or cycloreversions and emphasizes the supra-supra mode of addition or reversion, involving orbital alignment and exaggerated envelope transition states, as illustrated in Scheme I.

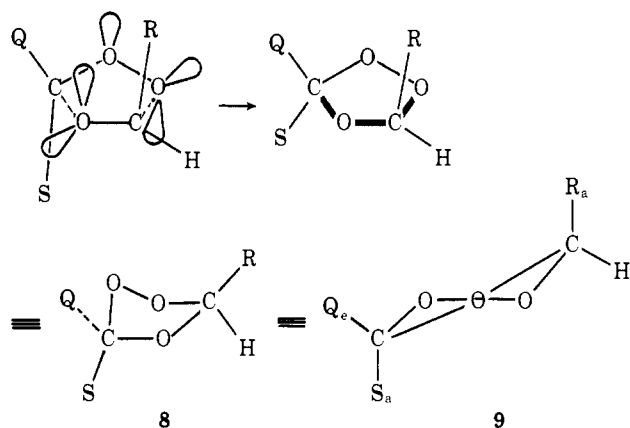
Scheme I. Supra-Supra Addition or Cycloreversion of 4π and 2π Systems¹¹



Kuczkowski et al.¹¹ treat the recombination of carbonyl and carbonyl oxide moieties first, because the rationale is much simpler than that for decomposition of the primary ozonide. The aldehyde always orients itself as shown in Scheme II, to avoid interaction with the lone pairs of the terminal carbonyl oxide oxygen. Thus, *anti* and *syn* carbonyl oxides afford *cis* and *trans* final ozonides, respectively.

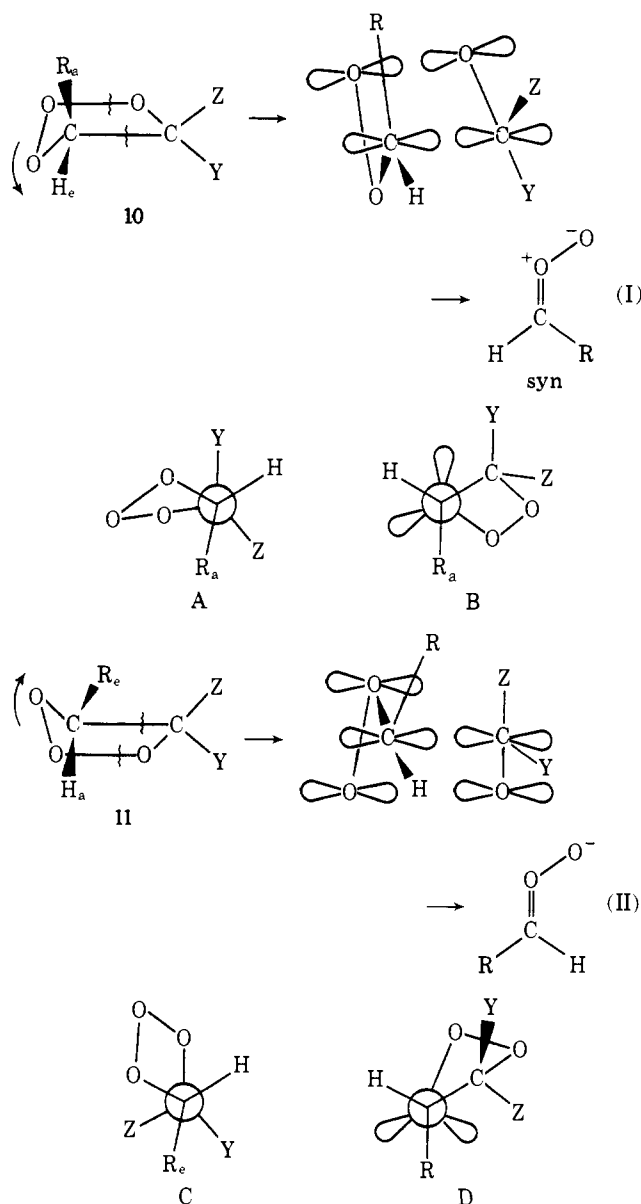
The cycloreversion of the primary ozonide to *syn* and *anti* carbonyl oxides, outlined in Scheme III, is more complicated and predictions hinge upon "preferred" conformational relationships in the transition state between (1) the substituents themselves, (2) across ring bonds, and (3) substituents and ring-carbon-oxygen bonds.¹¹ For a *trans* olefin with bulky substituents, route I, as illustrated by A in Scheme III, is chosen since it is assumed to be preferable to orient the alkyl groups *anti* to each other rather than to place the incipient carbonyl oxide R group *anti* to the ring bond but *gauche* to the other alkyl group, Y, as in C. Kuczkowski et al.¹¹ also assume

Scheme II. View from Above as Aldehyde Approaches Carbonyl Oxide in Recombination to Final Ozonide^a



^a Q = alkyl and S = H = *anti* gives *cis* final ozonide. Q = H and S = alkyl = *syn* gives *trans* final ozonide.

Scheme III. Oxygen Envelope Primary Ozonide Projections^a



^a Carbon with R group is becoming the carbonyl oxide. A and C are C-C projections and B and D are C-O projections. For 1-alkenes $Z = Y = H$; for *trans*-alkenes $Z = H$, $Y = R$; for *cis*-alkenes $Z = R$, $Y = H$.

Table II. Predictions of Predominant Final Ozonide Stereochemistry By Simple Bauld–Bailey⁹ and Kuczkowski¹¹ Schemes

Olefin confgn	Primary ozonide conform ^a		Final ozonide				
	B–B ^b (C–C half-chair)	K ^{b,c} (O envelope)	Zwitterion congn		Conformn, B–B (O–O half-chair)	Congn	
			B–B	K		B–B	K
1-Alkene	eq ^d	eq	Anti	Anti	eq, ax ^e	Cis ^e	Cis ^e
Trans ^f	ax, ax	ax	Syn	Syn	ax, ax	Trans	Trans
Cis ^{f,g}	eq, ax	eq	Anti	Anti	eq, ax	Cis	Cis
Cis ^h		ax		Syn			Trans

^a The primary ozonide configuration in both cases is the same as that of the olefin. ^b B–B, Bauld–Bailey; K, Kuczkowski; ax, axial, and eq, equatorial, substituent(s). ^c eq or ax below refers to R group of incipient carbonyl oxide. ^d Based on conformational analyses of Fliszar and coworkers.²³ ^e Obtained as a cross ozonide. ^f These predictions are only for olefins bearing large double-bond substituents. Although the Kuczkowski scheme also attempts to rationalize results with olefins bearing small substituents, the rationale is forced and unsatisfactory. ^g For symmetrical olefins with bulky groups or for larger groups of unsymmetrical olefins incorporating into the carbonyl oxide. For the latter the Bauld–Bailey scheme is based on conformational analyses of Fliszar et al.²³ ^h Kuczkowski scheme for incorporating the smaller substituent of an unsymmetrical olefin into the carbonyl oxide.

this to be the route for trans olefins with small substituents, but this appears to be based more on an effort to fit experimental facts than upon a clear rationale.

For cis symmetrical olefins with large substituents, the Kuczkowski scheme chooses route II over route I (Scheme III), on the basis that route II has one less gauche and one more anti interaction than does route I (cf. A and B with C and D), although the substituents are gauche to each other in both pathways. However, to our minds, this advantage is counterbalanced by the severe gauche substituent–oxygen lone-pair interaction in pathway II (cf. B and D). Kuczkowski et al.¹¹ admit difficulty with cis symmetrical olefins with small double-bond substituents. For cis unsymmetrical olefins Kuczkowski et al.¹¹ choose route II (Scheme III) for incorporation of the larger substituent into the carbonyl oxide and route I for assimilation of the small substituent into the carbonyl oxide, since in each case the larger substituent is oriented anti to the ring bonds (e.g., A and C). For the same reason pathway II is chosen for 1-alkenes.

Comparison. Both the Bauld–Bailey⁹ and the Kuczkowski¹¹ predictions are included in Table II. It is noteworthy that all phases of the predictions made for bulky olefins by the Kuczkowski and Bauld–Bailey schemes are the same. This results from the fact that the Kuczkowski scheme adapts the principles laid down by the Bauld–Bailey mechanism⁹ to different conformations of the primary and final ozonides (or, rather, to different transition state conformations thereof).

An obvious difference between the Bauld–Bailey and the Kuczkowski schemes, however, is that the Bauld–Bailey mechanism describes the conformations of the reacting primary ozonide and the produced final ozonide, but neglects to describe adequately the transition states involved, whereas the Kuczkowski scheme does exactly the opposite. Thus, it appears that the Bauld–Bailey approach is thermodynamic whereas that of Kuczkowski is kinetic. On this basis, Kuczkowski et al.¹¹ level several criticisms at the Bauld–Bailey mechanism. First, although extended Hückel LCAO–MO calculations by Fliszar^{23a} and Rouse²⁴ confirmed the C–C half-chair, **1**, as the predominant primary ozonide conformation, CNDO/2 calculations by Rouse^{24,25} have indicated that there is no predominant conformation for the 1,2,3-trioxolane ring and that several conformations lie very close together in energy. Similarly, ab initio SCF calculations by Hiberty²⁶ have indicated that the C–C half-chair, **1**, and an O envelope (**10** or **11**, Scheme III) conformation for ethylene primary ozonide are very close together in energy, with the latter, perhaps, being slightly more stable. Second, the 1967–1968 Bauld–Bailey scheme⁹ did not emphasize the necessary supra–supra orbital alignment of moieties in 1,3-dipolar cycloadditions and reversions as done by Kuczkowski et al.¹¹ Third, because of the seemingly thermodynamic emphasis given in the Bauld–Bailey

scheme, the transition state for the 1,3-dipolar cycloaddition to the final ozonide appears to resemble the product rather than the carbonyl oxide and aldehyde moieties, which is contrary to the Hammond principle²⁷ regarding an (apparently) highly exothermic reaction. These and other criticisms will be discussed in turn.

First, in spite of the distrust of Rouse²⁵ for the extended Hückel method, it is probably more accurate than CNDO/2 for predicting 1,2,3-trioxolane conformations, since it better accounts for lone pair–lone pair interactions.²⁸ Furthermore, Rouse's²⁵ calculations are based on assumed geometric parameters, only the twist angles being varied. The calculations of Hiberty²⁶ neither support nor impugn the C–C half-chair as the predominant primary ozonide conformation. In addition, they were performed on an unsubstituted 1,2,3-trioxolane and may not be relevant to the systems of interest. Regardless of this, however, the Bauld–Bailey scheme does not necessarily require the most stable primary ozonide conformer, but rather the one which most easily decomposes to a syn or an anti carbonyl oxide. This could be one of several in equilibrium with each other. The decomposition of a primary ozonide is known to be a highly exothermic reaction²⁹ and the transition state must, therefore, strongly resemble the primary ozonide. It should also have well-defined axial and equatorial substituents to account for the stereoselective decomposition. We believe that our model fits these requirements better than does the Kuczkowski model and that our rationale better accounts for the experimental facts. The decomposition of the C–C half-chair, **2**, to the carbonyl oxide and aldehyde moieties just as surely involves the supra–supra orbital alignment as does the decomposition of the envelope conformation, **10** or **11**. Furthermore, since in the decomposition of a 1,2,3-trioxolane the weaker O–O bond should lead the way, the perfectly symmetrical, exaggerated envelope transition state of Kuczkowski et al.¹¹ is unlikely. Thus, we will stay with the C–C conformation until experiment rather than calculation requires a change. If this should happen, as stated earlier, the concepts of the Bauld–Bailey mechanism can be applied to other models.

Unfortunately, the transition state in the original Bauld–Bailey proposal⁹ for 1,3-dipolar cycloaddition of the carbonyl oxide and carbonyl moieties also was inadequately described. However, it most certainly must have the supra–supra alignment and resemble the reactants, in agreement with the Hammond²⁷ principle. It is interesting, however, to follow through with this to the exaggerated envelope, **8**, stage of the reaction (Scheme II), where it can be seen, through use of molecular models, that little difference exists between conformation **8** and the O–O half-chair conformation, **9**, used by the Bauld–Bailey scheme for the final ozonide. Thus, the two approaches essentially converge in regard to final ozonide

Table III. Cis-Trans Ozonide Ratios from Ozonolyses of Various Olefins Under Various Conditions

Expt	R and R' in RCH=CHR'	Alkene confign	No complexing agent ^a			Complexing agent, ^{a,b} -155 °C (slow)
			-78 °C (slow)	-155 °C (fast)	-155 °C (slow)	
1	R = R' = <i>t</i> -Bu	Cis	70:30	69:31	70:30	71:29-89:11
2	R = R' = <i>t</i> -Bu	Trans	15:85	6:94	19:81	18:82-20:80
3	R = R' = <i>i</i> -Pr	Cis	54:45	65:35	69:31	75:25-77:23
4	R = R' = <i>i</i> -Pr	Trans	50:50	47:53	60:40	61:39-65:35
5	R = R' = Et	Cis	50:50	50:50	54:46	56:44-60:40
6	R = R' = Et	Trans	51:49	41:59	45:55	44:56-48:52
7	R = R' = CH ₃	Cis	38:62	37:63	43:57	45:55
8	R = R' = CH ₃	Trans	37:63	40:60	41:59	
9	R = CH ₃ ; R' = <i>i</i> -Pr	Cis NMW ^c	46:54	48:52	70:30	67:33-69:31
10	R = CH ₃ ; R' = <i>i</i> -Pr	Cis HMW ^c	77:23	68:32	85:15	85:15-87:13
11	R = CH ₃ ; R' = <i>i</i> -Pr	Trans NMW ^c	44:56	45:55	41:59	40:60-45:55
12	R = CH ₃ ; R' = <i>i</i> -Pr	Trans HMW ^c	24:76	24:76	21:79	22:78-26:74

^a Solvent is isopentane at the ozonolysis temperature indicated below. Fast and slow refer to the rate of warm-up. ^b The range shown is with various complexing agents. Except with *cis*-1,2-di-*tert*-butylethylene the differences were small. ^c NMW, normal ozonide; HMW, high molecular weight cross ozonide produced from the olefin.

formation. Since the transition state can resemble the reactants but yet have characteristics of the products (particularly since we do not know the extent of the exothermicity of the cycloaddition), we prefer our least motion and subsequent aldehyde orientation rationale to that of Kuczkowski et al.¹¹ for the stereoselectivity of the cycloaddition.

Certainly, the criticism of Kuczkowski et al.¹¹ that the bulk of the aldehyde plays no role in the Bauld-Bailey scheme is unjustified. This is untrue using either the old or the revised rule 3. Even though the aldehyde substituent orients itself the same way (axially in revised rule 3) with either syn or anti carbonyl oxides, it does so through choice. For example, should it place its substituent equatorially, along with an equatorial carbonyl oxide substituent, the substituent-adjacent-oxygen lone-pair interactions would be doubled, with no appreciable gain from a decrease in substituent-substituent interaction. The Kuczkowski scheme,¹¹ of course, also orients the aldehyde substituent in exactly the same direction for either syn or anti carbonyl oxides, for similar reasons (Scheme II). Thus, in both schemes the steric roles of the aldehyde and carbonyl oxide moieties are equal in determining final ozonide stereochemistry, in line with the experimental findings of Murray and Williams.³⁰

As mentioned earlier, the Kuczkowski scheme is nebulous and/or forced in regard to cis symmetrical olefins with either large or small double-bond substituents and with trans olefins having small substituents. In spite of this, Kuczkowski et al.¹¹ state "a weakness of the Bauld-Bailey proposal lies in its inability to correctly predict the stereochemical course of ozonolysis for small olefins". Actually, we never made the attempt, because we felt that no simple set of rules could explain the complicated stereochemistry of ozonide formation with both bulky and nonbulky olefins.

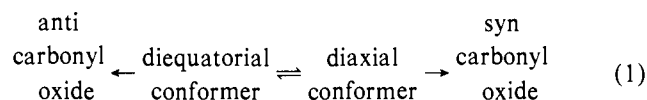
When one considers some of the new data described in the preceding paper,¹⁷ pertinent portions of which are included in Table III, it becomes evident that, likewise, no one set of rules will explain all data obtained from ozonolyses of bulky olefins. This particularly applies to very low vs. medium low temperatures, fast vs. slow warm-up, and the presence or absence of a complexing agent. For example, at -155 °C with a slow warm-up, *trans*-1,2-diisopropylethylene affords more cis than trans final ozonide, which is contrary to predictions made by either the original Bauld-Bailey or the Kuczkowski schemes (Table II).

The Kuczkowski scheme, which is based upon one specific, preferred conformation for each transition state involved in ozonide formation, is less capable of adjusting to these new data than is the Bauld-Bailey concept, which involves two or more primary ozonide conformations in equilibrium with each

other, each with its own transition state. It should be emphasized, however, just as it was with the original proposal,⁹ that the principles set forth below can be made to apply to some other conformation or set of conformations as well as the ones discussed herewith, provided there are clear axial-equatorial relationships in regard to the incipient carbonyl oxide substituent.

A More Flexible Carbonyl Oxide Mechanism. The major new principles involved have already been mentioned: (1) least motion and (2) the primary ozonide conformation decomposing to carbonyl oxide and carbonyl moieties is not necessarily the thermodynamically most stable or predominant one, but rather the one in an equilibrium mixture of conformers which is kinetically more facile in its decomposition.³¹ In addition, the final cis-trans ozonide ratio obtained from a given olefin under a given set of conditions reflects competition among a number of factors: (1) decomposition of the thermodynamically predominant primary ozonide conformer; (2) decomposition of the kinetically favored primary ozonide conformer; (3) competitions in regard to Bauld-Bailey rule 2 (and possibly 3) with olefins having small double-bond substituents; (4) equilibration of syn and anti carbonyl oxide stereoisomers before recombination with the carbonyl moiety.

These competitions will be illustrated with a number of examples, beginning with *trans*-1,2-diisopropylethylene. When a fast warm-up is used with either a -78 °C (Table I, presumably) or a -155 °C ozonolysis mixture, the trans ozonide is predominant in the final ozonide mixture, in agreement with the original Bauld-Bailey and Kuczkowski schemes. With a slow warm-up, however, the -78 and -155 °C ozonolyses afford 50:50 and 60:40 cis-trans ozonide ratios, respectively (Table III). As discussed earlier, the C-C half-chair conformer with diaxial substituents should be more stable than that with diequatorial substituents (see 2), not only because the substituents are anti rather than gauche, but also because there is less substituent-adjacent-oxygen lone-pair interaction (i.e., 6). However, the activation energy for decomposition of the diequatorial conformer should be less than that for the diaxial conformer because of the least motion principle discussed earlier (cf. axial and equatorial substituents in 5 and 6). The situation can be described by eq 1). During a slow warm-up,



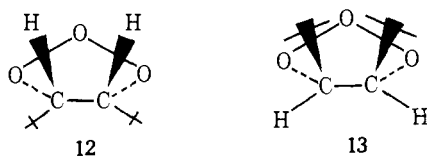
the diequatorial conformer decomposes more rapidly than does the diaxial conformer and there is time for the equilibrium

between conformers to continually shift in favor of the more rapidly cleaving diequatorial conformer. During a fast warm-up, however, the decomposition of both conformers is so rapid that no appreciable equilibrium shift occurs.

Table III shows that the effect just discussed is of little importance in the case of *trans*-1,2-di-*tert*-butylethylene. This must be due to the fact that the diaxial conformer is so much more stable than the diequatorial conformer that the equilibrium between the two would be insignificant. Thus, decomposition of the thermodynamically predominant conformer is by far the major reaction. The slight increase in the *cis*-*trans* ozonide ratio in going from fast to slow warm-up (6:94 → 19:81) or from the -78 to the -155 °C ozonolysis (15:85 → 19:81), both with a slow warm-up, could indicate a slight equilibrium between diaxial and diequatorial conformers, resulting in the higher *cis*-*trans* ratios, but it more probably reflects some degree of isomerization of *syn* to *anti* carbonyl oxide before recombination under the slower conditions.¹⁷

The results with the corresponding *cis*-diisopropyl- and di-*tert*-butylethylenes are also interesting. The *cis*-*trans* ozonide ratio from *cis*-1,2-diisopropylethylene is greater than unity under all conditions (Table III). The fact that it is greater at -155 °C with a slow warm-up than at -155 ° with a fast warm-up or at -78 °C could reflect a greater tendency for the equatorial substituent to produce the carbonyl oxide under the conditions of less thermal energy availability and, therefore, greater selectivity. It also could be due, to a greater or lesser extent, to isomerization of *anti* to *syn* zwitterion under the more energetic conditions, as discussed in the accompanying paper.¹⁷

The only surprising aspect of the *cis*-1,2-di-*tert*-butylethylene results is that the *cis*-*trans* ozonide ratio in the -155 °C reaction with slow warm-up is not appreciably higher than that for *cis*-diisopropylethylene. However, although the primary ozonide of *cis*-diisopropylethylene has been observed,¹⁷ that of *cis*-di-*tert*-butylethylene has not, and calculations of Fliszar^{23a} indicate that it exists only as a transition state which, presumably, immediately falls apart into the carbonyl and carbonyl oxide moieties. Two transition states are possible for the 1,3-dipolar cycloaddition of ozone to *cis*-1,2-di-*tert*-butylethylene, an *exo*, **12**, and an *endo*, **13**, type. One would

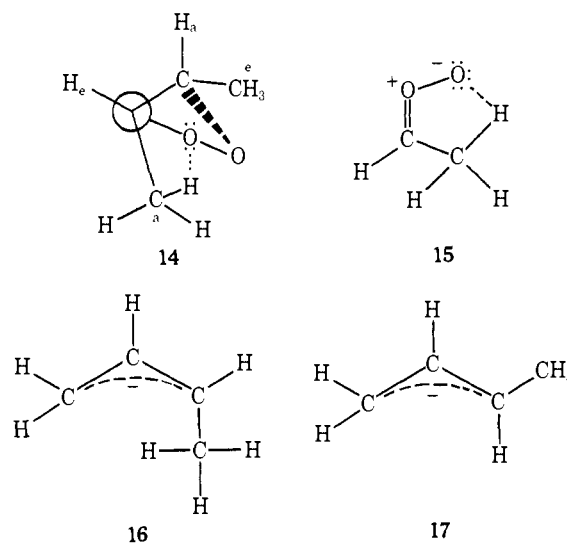


expect the *exo* to be formed predominantly, but probably not exclusively, since there would be considerable substituent-adjacent-oxygen lone-pair interaction. By the least motion principle the *exo* envelope, **12**, and the *endo* envelope, **13**, should decompose predominantly to *anti* and *syn* carbonyl oxides, respectively, and a predominance of *cis* final ozonide would, therefore, be expected. The fact that the same *cis*-*trans* ratio was obtained at -78 and at -155 °C by both warm-up procedures implies that immediate decomposition of the primary ozonide occurs, as described. It also indicates that equilibration of the *tert*-butyl carbonyl oxides lies much more toward the *anti* isomer than in the case of the isopropyl carbonyl oxides, where hydrogen-bonding stabilization of the *syn* stereoisomer is possible.¹⁷

The 3-hexenes and 2-butenes should not be expected to follow as well the rules discussed above for olefins bearing bulky double bond substituents, since competitions at all points in the reaction coordinate are possible. This is especially apparent with the *cis*- and *trans*-2-butenes, both of which give *cis*-*trans* ozonide ratios less than unity under all reaction conditions, although the ratio increases slightly as the reaction

temperature decreases, in changing from a fast to a slow warm-up, and in ozonizing in the presence of a complexing agent at -155 °C (cf. Tables I and III).

The surprising results with *cis*-2-butene are in agreement with the, at first sight, equally surprising calculations and experiments of Fliszar et al.^{23a,c} which indicate that an axial methyl group incorporates itself into a carbonyl oxide more readily than does an equatorial methyl group. Upon reflection, however, it should not be unexpected that with a group as small as methyl other factors should outweigh the least motion effect. It was suggested in the accompanying paper¹⁷ that certain *syn* carbonyl oxides are stabilized through hydrogen bonding. This should be especially important with the *syn* methyl carbonyl oxide, **15**, the α -hydrogen atoms of which are not only greater in number but are more acidic than α -hydrogen atoms of other alkyl groups. Thus, the axial substituent might be expected to be incorporated into the carbonyl oxide in preference to the equatorial substituent, as indicated in transition state **14**, and the *syn* carbonyl oxide would, therefore, be favored over the *anti* isomer. By analogy, there is evidence that the *cis*-methylallyl anion, **16**, is more stable than the *trans* isomer, **17**.³²



In the case of *trans*-2-butene, the calculations of Renard and Fliszar^{23a} indicate that the axial-axial and the equatorial-equatorial half-chair conformations are equally stable. Again, one might expect the driving force to the stabilized *syn* carbonyl oxide, **15**, to outweigh any least motion effect favoring decomposition of the diequatorial conformer.

On the other hand, the fact that the 2-butene cross ozonide obtained from ozonolysis of propene is largely *cis*¹¹ (Table I) is also to be expected, since Renard and Fliszar's^{23a} calculations show that the methyl group of the propene primary ozonide occupies an equatorial position. It, therefore, affords an *anti* carbonyl oxide and a *cis* cross ozonide, in agreement with the Bauld-Bailey scheme (rule 2, also Table II).

The results with *cis*- and *trans*-3-hexene fall in between those from the 2-butenes and the 1,2-diisopropylethylenes, as might be expected on the basis of relative alkyl substituent bulk and degree of stabilization of the *syn* carbonyl oxides through hydrogen bonding. With both the *cis* and the *trans* isomers there is a slight increase in *cis* ozonide content observed in the -155 °C ozonolysis with slow warm-up compared to the -155 °C ozonolysis with fast warm-up or to the -78 °C ozonolysis (Table III). This is indicative of minor effects of the same type observed with the diisopropylethylenes.

Results with unsymmetrical olefins are more difficult to rationalize, especially if one group is methyl as with the 4-methyl-2-pentenes. The most interesting and important observation was the large increase in *cis*-*trans* normal ozonide ratio for the *cis* olefin at -155 °C with slow warm-up (70:30)

in comparison with fast warm-up (48:52) or to ozonolysis at $-78\text{ }^{\circ}\text{C}$ (46:54). The ratio for the high molecular weight cross ozonide also increased correspondingly, although it was greater than unity for all three ozonolysis conditions (Table III). Fliszar et al.²³ have reported that the most stable conformation for the primary ozonide is the C-C half-chair bearing the large substituent axially; they also found that the methyl group preferentially produced the carbonyl oxide to the extent of 57%. However, this conformation is only slightly more stable than the one with an axial methyl group. We suggest that the equatorial methyl, axial isopropyl conformation is only slightly favored in the $-78\text{ }^{\circ}\text{C}$ ozonolysis and the $-155\text{ }^{\circ}\text{C}$ ozonolysis with fast warm-up and that the cross ozonides, produced in minor amounts, come largely from the other conformer. This would account for the approximately 50:50 ratio for the normal ozonide, and greater than unity and less than unity ratios for the larger cross ozonide (Table III) and smaller cross ozonide (Table I), respectively. Under the slow warm-up conditions, the less thermodynamically stable, but kinetically more reactive, conformer with equatorial isopropyl and axial methyl groups must have reacted predominantly, and the isopropyl group must have been preferentially incorporated into the carbonyl oxide. Thus, the same kind of phenomenon is evident here as found for *trans*-1,2-diisopropylethylene. It is also quite likely that, in the $-78\text{ }^{\circ}\text{C}$ reaction, equilibration of syn and anti isopropyl carbonyl oxides played a role.

The results with *trans*-4-methyl-2-pentene are, perhaps, less difficult to interpret. According to Fliszar et al.,²³ the C-C half-chair with diaxial substituents is favored for the primary ozonide and the methyl group preferentially incorporates into the carbonyl oxide to the extent of 71%. The forces which stabilize a developing syn methyl carbonyl oxide, **15**, must already be active (e.g., **14**) and thus stabilize, also, the diaxial conformer to such an extent that equilibrium with the diequatorial conformer is negligible. Thus, all three ozonides have low cis contents, regardless of the reaction conditions, just as with *trans*-2-butene.

The above discussion emphasizes the point made earlier. It is unrealistic to expect one set of *rules* to explain the stereochemistry of ozonide formation from all olefins. However, we believe that the logical application of a set of principles and guidelines such as set forth in the present and accompanying papers,¹⁷ in regard to competitions occurring during ozonide formation, provides the flexibility necessary to rationalize most, if not all, of the presently available data concerning the stereochemistry of ozonide formation and to make predictions regarding examples not yet studied. For example, the fact that *trans*-1,2-diisopropylethylene gives a *cis*-*trans* ozonide ratio >1 under slow warm-up conditions and that *cis*-2-butene affords *cis*-*trans* ozonide ratios <1 are not exceptions to or contradictions of rules, but are logical consequences of the competitions involved.

Although we believe the principles set forth here provide the foundation upon which the entire stereochemistry of ozonide formation can be rationalized, it is to be expected that additional principles will be necessary as more facts become known. There are, also, other aspects of the ozonolysis reaction which are not yet understood as well as the stereochemistry of ozonide formation. We believe, however, that developing this understanding also is a matter of ferreting out the complex set of

competitions involved and learning how these are affected by numerous factors, such as structure of the olefin, the type of solvent, conditions of temperature, reactant concentration, etc. Although we believe that the reactions just discussed are predominantly concerted, it is quite possible that with other solvents and other conditions nonconcerted cycloadditions and cleavages are involved. This certainly is true in gas phase reactions.⁵

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