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The Reaction of Singlet Oxygen with Olefins: The Question of Mechanism

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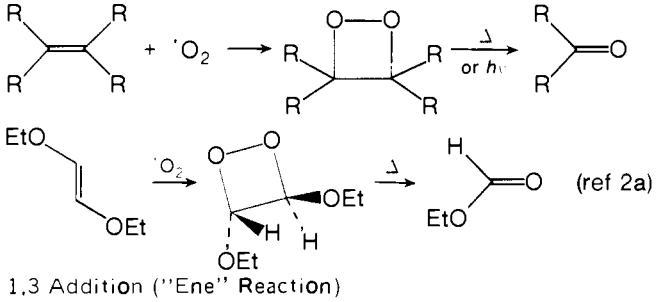
I. Introduction

The reactions of singlet molecular oxygen ($^1O_2$)[1] with olefins may be categorized into three classes outlined in Chart I. The first of these involves a [2 + 2] cycloaddition to electron-rich[1] or sterically hindered[3-6a] olefins; to strained acetylenes;[6b] to ketenes,[7-9] allenes,[10] and sulfines;[11a] to oximes;[11b] to 1-methylene-2,5-cyclohexadienes[12] and the analogous 4*H*-pyran and thiopyran-4-thiones;[13] and most recently to phosphorus ylides.[14-15] The resulting dioxetane is sometimes of moderate stability but readily cleaves thermally or photolytically into two carbonyl-containing fragments.

The second type is the photooxygenation of olefins that contain at least one allylic hydrogen to yield allylic hydroperoxides in which the double bond has shifted to a position adjacent to the original double bond. This reaction bears a formal resemblance to the Alder ene reaction.[16] Silyloxyolefins also undergo an ene type of reaction with $^1O_2$ producing silylperoxy ketones.[17-21] In this transformation the trimethylsilyl group takes the place of an allylic hydrogen and the oxygen replaces the allylic carbon.

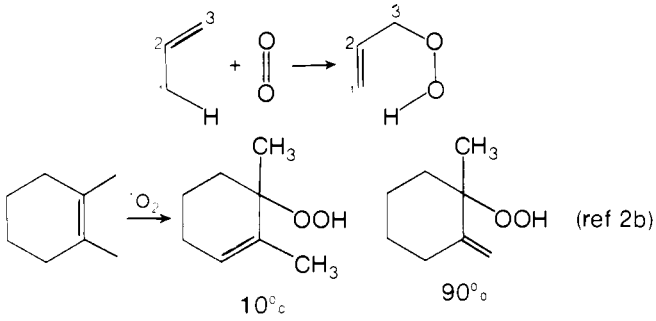
CHART I

1,2 Addition (Dioxetane Formation)



(ref 2a)

1,3 Addition ("Ene" Reaction)



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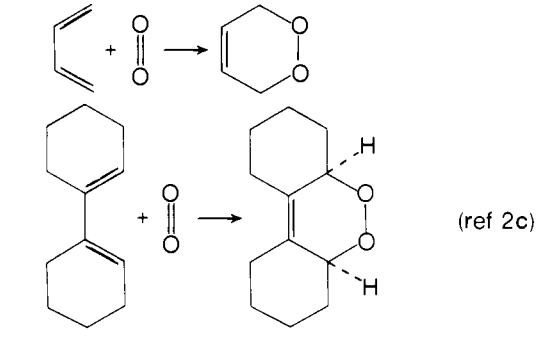
1,4 Addition (Endoperoxide Formation)



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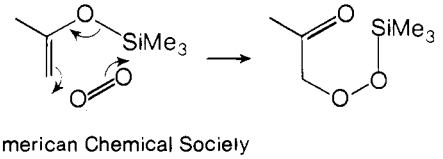

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The third mode involves the addition of singlet oxygen[22] to diene systems to produce endoperoxides. The reaction is analogous to a photo-induced Diels–Alder reaction in which the oxygen is the dienophile. The cisoid 1,3-diene system commonly resides in a nonaromatic system (e.g., substituted 1,3-butadienes) or in a polyaromatic system (e.g., anthracene, rubrene, etc.). Recent work[29-38] has, however, shown that vinyl aromatic systems undergo this reaction as well.

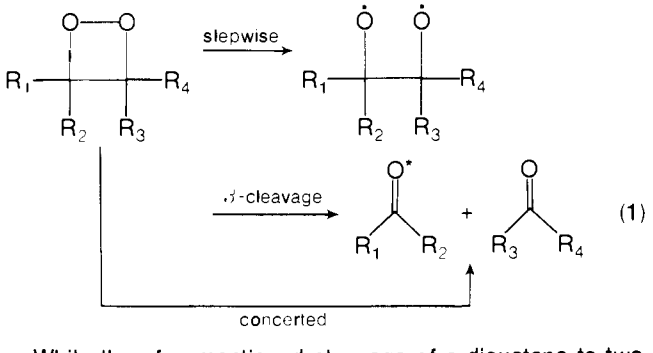
While it is indeed accurate to say that 1,2-cycloaddition of $^1O_2$ to olefins yields dioxetanes, 1,3-addition an allylic hydroperoxide, and 1,4-cycloaddition an endoperoxide, the converse is not always true. For example, the isolation of dioxetanes or the corresponding carbonyl fragments in the product mixture is not a sure sign that a 1,2-addition has occurred as the primary process. Because product analysis is the most common method for determining the mode of reaction, the unpublicized secondary reactions of the singlet oxygen products have brought about a great deal of confusion in the literature regarding the assignment of the mode and direction of $^1O_2$ attack. This in turn has led even the most careful researchers to erroneous conclusions regarding the mechanistic details of $^1O_2$ reactions.

This review, therefore, will be divided into two parts. In the first we will discuss at length the secondary reactions and interconversions of the primary singlet oxygen products. We will suggest as well some possible tests by which ambiguities regarding the exact mode of reaction can be eliminated. In the second part we will discuss critically the most recent data (from ca. 1971) concerning the mechanistic details of the various modes.

II. Dioxetanes[40] and Their Reactions

A. Cleavage

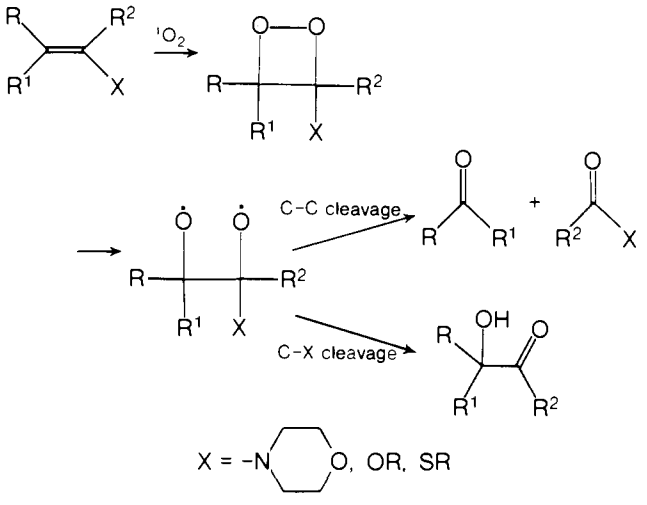
In general, dioxetanes cleave thermally[41,47] or photochemically[30,42] producing carbonyl fragments[42,43] and chemiluminescence.[43,44] Two mechanistic schemes have been suggested for this decomposition. The first, originally considered by McCapra[45] and Kearns[46] postulates simultaneous cleavage of both the oxygen–oxygen and the carbon–carbon bonds in a concerted manner to directly generate electronically excited product. Turro[363] expanded this approach by suggesting that a spin multiplicity change occurred coincidentally with bond cleavage. The second general mechanistic scheme was advanced by Richardson[47] who suggested a stepwise mechanism in which a 1,4-biradical is formed by cleavage of the oxygen–oxygen bond. This is then followed by a double β-cleavage to produce two carbonyl fragments. Recent experimental evidence has indicated that a stepwise mechanism is indeed in effect[43,44,48,49,353] (see eq 1).



(1)

While the aforementioned cleavage of a dioxetane to two carbonyl fragments predominates for alkyl- and aryl-substituted dioxetanes,[41] those substituted with sulfur, nitrogen, or oxygen groups may show a different mode of fragmentation. In particular fission of the C–S, C–N, or C–O bond subsequent to O–O bond homolysis may also occur. This mode leads to the expulsion of the heteroatomic substituent and the formation of a hydroxy

SCHEME I



ketone. Much of the research in this area has been performed by Ando and co-workers,[49-54] and the mechanism suggested by these authors is outlined in Scheme I.

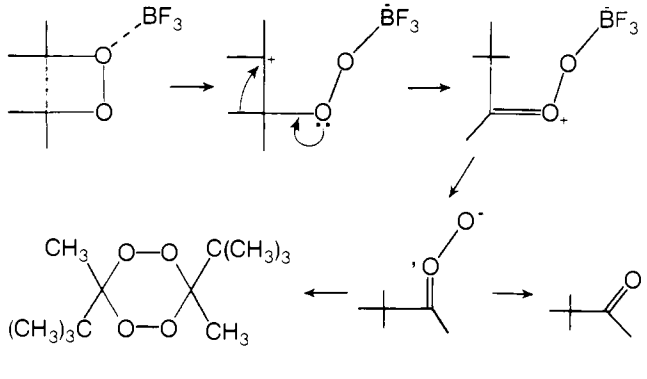
It should be noted that the rate of decomposition of dioxetanes is catalyzed by traces of metals,[55-58] silica gel,[364] and electron donors[349] such as enol ethers,[59] amines,[59] and phosphines.[41] Kopecky[41] has found that dioxetanes are quite stable to strong protic acid, and the rate of decomposition of tetramethyldioxetane (TMD) to acetone at 50 °C in benzene containing 1 M trifluoroacetic acid was only twice that in acid-free CCl_4. The stability of dioxetanes in base varies from dioxetane to dioxetane, but in most cases the products are those resulting exclusively from cleavage.

B. Rearrangements and Nucleophilic Displacements

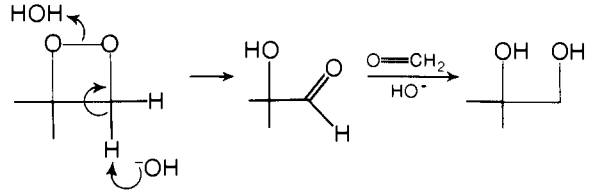
Alkyl and aryl dioxetanes do not undergo thermal processes other than cleavage,[41] and are generally inert to nucleophilic attack at carbon. TMD, for example, is quite insensitive to acidic, basic, or neutral methanol at 25 °C or below.[41] The only decomposition products observed were those resulting from O–O and C–C bond cleavage. Neither allylic hydroperoxides nor solvent addition products could be isolated. TMD, however, is rearranged to pinacolone and the latter's cyclic peroxide by the action of a strong Lewis acid such as boron trifluoride.[60] A reasonable first step involves the initial coordination of BF_3 with one of the TMD oxygens followed by rearrangement of the complex to pinacolone oxide (Scheme II).

Trimethyldioxetane has been reported[41] to react with alkali to give a variety of products among which acetaldehyde, acetone, and diol predominate. Mumford[365] notes that the mechanism of the diol-forming reaction involves attack at oxygen and not at carbon, though no evidence is presented. In the related case of 3,3-dimethyl-1,2-dioxetane (DMD) studied by Richardson

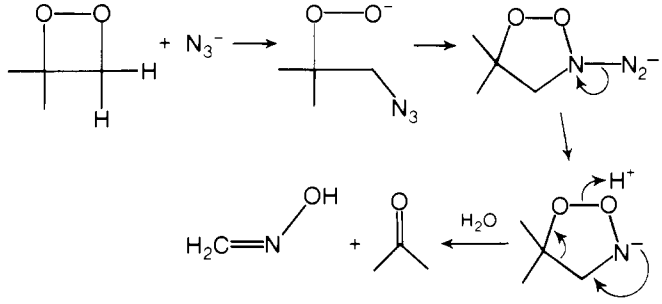
SCHEME II



SCHEME III



SCHEME IV



and Hodge,[61] a combination of kinetic and product data lead these authors to suggest that basic decomposition produces α-hydroxyisobutyraldehyde as the initial product. A subsequent Cannizzaro reaction with formaldehyde leads to diol (Scheme III). This course of events does not explain, however, diol formation in the case of trimethyldioxetane. The role of trace metals should not be overlooked.

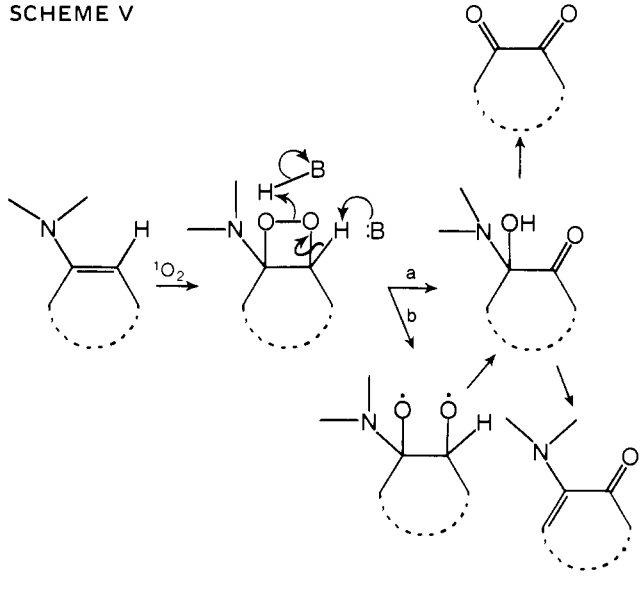
Richardson and Hodge[366] also report that azide reacts with the unhindered dioxetane DMD to give acetone, formaldoxime, and N_2, but again the mechanistic details are not clear. The proposed mechanism is outlined in Scheme IV.

In contradistinction to alkyl and aryl dioxetanes, a large variety of reactions have been observed for dioxetanes substituted with heteroatomic groups and in particular oxygen-, nitrogen-, and sulfur-based substrates; these are reviewed below.

1. Rearrangement of Dioxetanes to α-Hydroxy Ketones

Wasserman and Terao[62] have pointed out that while the photooxidation of the enamines of acyclic systems produces carbonyl fragments, the photooxidation of the enamines of a series of cyclic ketones yields α-hydroxy ketones as the primary products. This reaction, they suggest, is in effect the well-known Kornblum–DeLaMare reaction[63,64] (Scheme V, path a) in which a peroxide with an α hydrogen is cleaved to a ketone and an alcohol. A similar mechanism has been invoked by Lightner[65,66] in the photooxidation of pyroles and by Abello et al.[67] in the photooxidation of 17β-acetoxy-4-azaandrost-5-en-3-one.

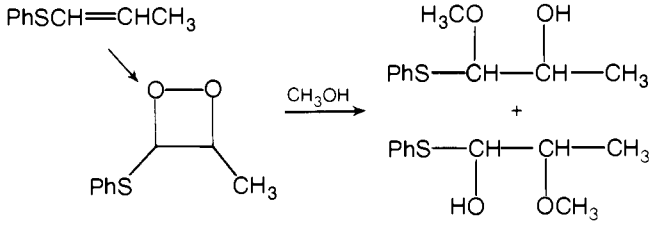
SCHEME V



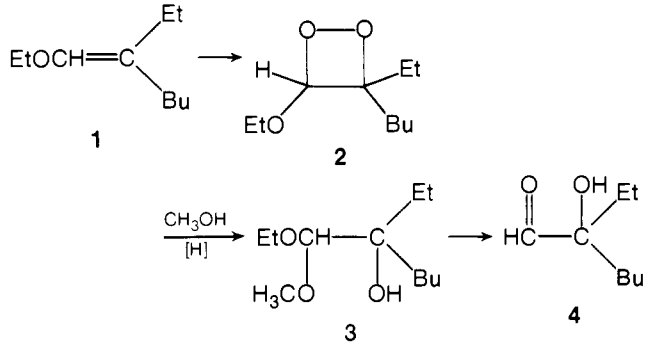
We have noted above (section II.A) the work of Ando et al.[49–54] who suggest that α-hydroxy ketones are formed from dioxetanes by a free-radical process. For the case of Wasserman and Terao, Ando would probably propose[367] an initial O–O cleavage followed by internal hydrogen transfer (path b). The two mechanistic pathways are obviously not mutually exclusive. However, should they coexist, the Wasserman mechanism ought to be favored under basic conditions where the Kornblum–DeLaMare reaction is known to be catalyzed, while the Ando mechanism is likely to prevail under conditions favoring O–O bond homolysis (e.g., trace metals, electron-donor olefins, etc., see end of section II.A).

2. Nucleophilic Addition

Ando[50] has reported that in the photooxidation of 1-phenylthiopropene in methanol, a 12% yield of solvent addition product was isolated.[68] In an analogous fashion, the photooxidation of

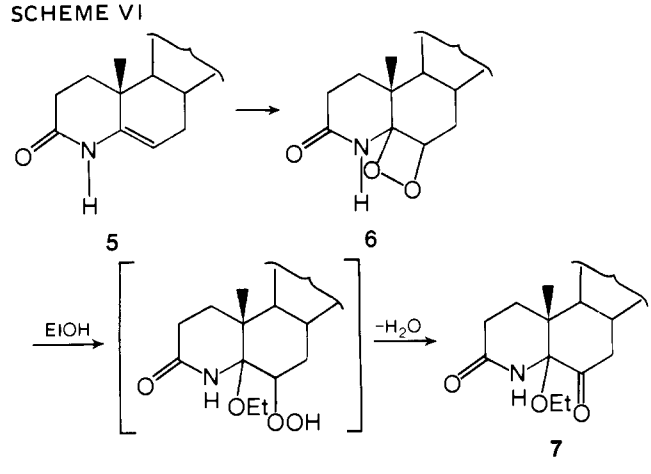


1-ethoxy-2-ethyl-1-hexene (compound **1**) in methanol leads to a 31% yield of hydroxyaldehyde **4** which is formed presumably via the corresponding dioxetane **2** and hydroxyacetal **3**.[51] Similar solvent addition products were observed in the photooxidation of 1-ethoxycyclohexene, 1-ethylthio-2-ethyl-1-hexene, and 1-ethylthiocyclohexene.

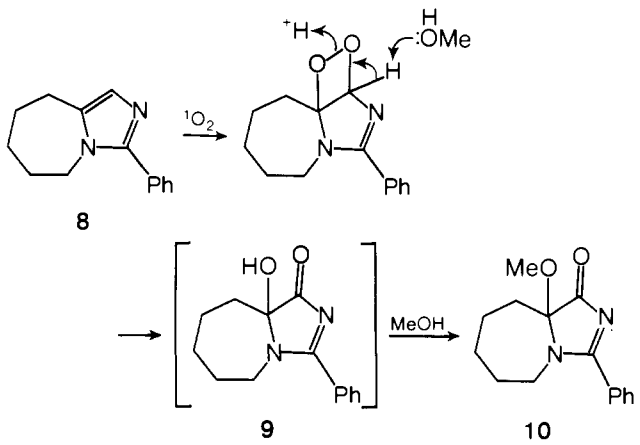


Abello et al.[67] claim to see this transformation when the photooxidation of 17β-acetoxy-4-azaandrost-5-en-3-one (**5**) is carried out in an ethanol–chloroform solvent mixture. The initially formed dioxetane (**6**) is converted to an α-ethoxy ketone (**7**) and the authors suggest that it proceeds via the solvolysis mecha-

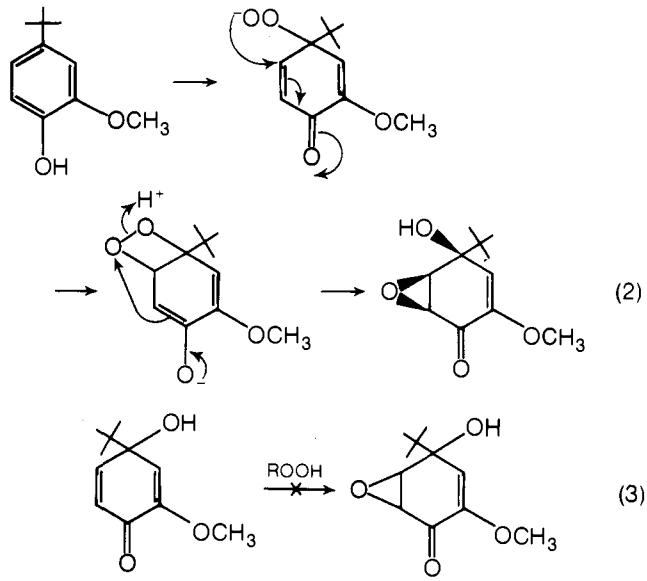
SCHEME VI



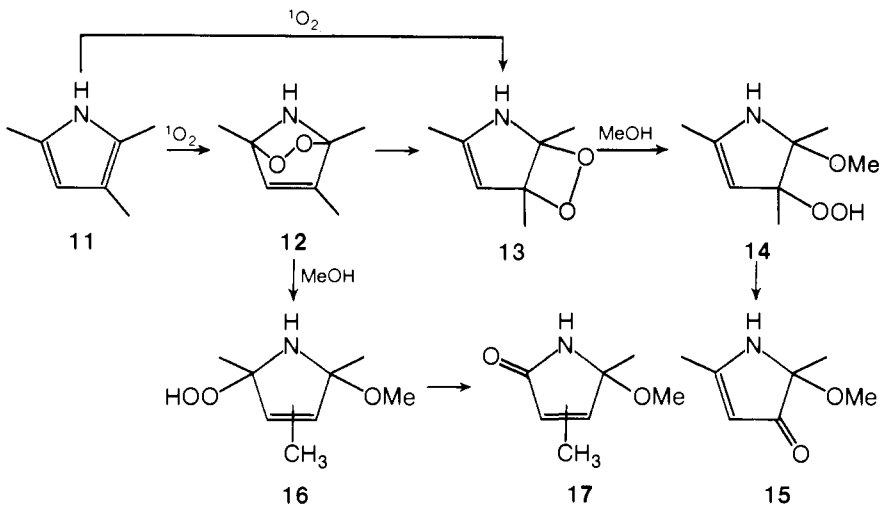
nism in Scheme VI. However, Wasserman and Wolfe[69] in the related photooxygenation of imidazole **8** suggest that the α-alkoxy ketone **10** might simply be the solvolysis product of the corresponding α-hydroxy ketone **9** produced as described in section II.B1. An identical course of events may be occurring in Abello's case as well. Since neither group brings forth proof to their position,[367] the question of mechanism perforce remains open. Further research is clearly called for.



Lightner[70] reports that dioxetane **13,** presumably formed in the photooxidation of 2,3,5-trimethylpyrrole (**11**), undergoes



Another transformation in this class involves the rearrangement of a 3-aldehydo-1,2-dioxetane to a 1-formyloxy-1,2-epoxide. This course of events has been invoked by Carmier and Deglise[368] to rationalize the formation of such products in a low-temperature gas-phase photooxidation of acrolein and crotonaldehyde. Though the mechanism proposed below is



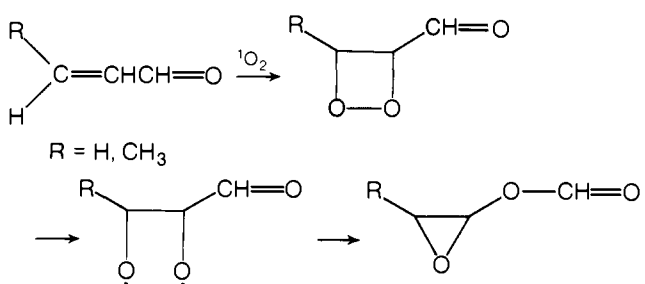
solvolysis in methanol to form 2-methoxy-2,6-dimethyl-4-pyrrolin-3-one (**15**). However, it is equally likely that methoxy hydroperoxide **14,** which is the acknowledged precursor to **15,** is merely the product of a 1,3-allylic hydroperoxide shift (vide infra section III.B) in methoxy hydroperoxide **16.** The latter is formed by the solvolysis of endoperoxide **12.** Here, too, the issue of mechanism remains moot.

3. *Rearrangements of 3,4-Unsaturated-1,2-Dioxetanes*

Two types of rearrangements have been suggested. The first entails the rearrangement of an enol dioxetane to an epoxy alcohol. There is no solid evidence for this type of rearrangement, though it is repeatedly invoked[71-74,326,327,354] to explain the formation of epoxy quinols in the base-catalyzed autoxidation of hindered phenols. A typical mechanistic scheme is outlined in eq 2.

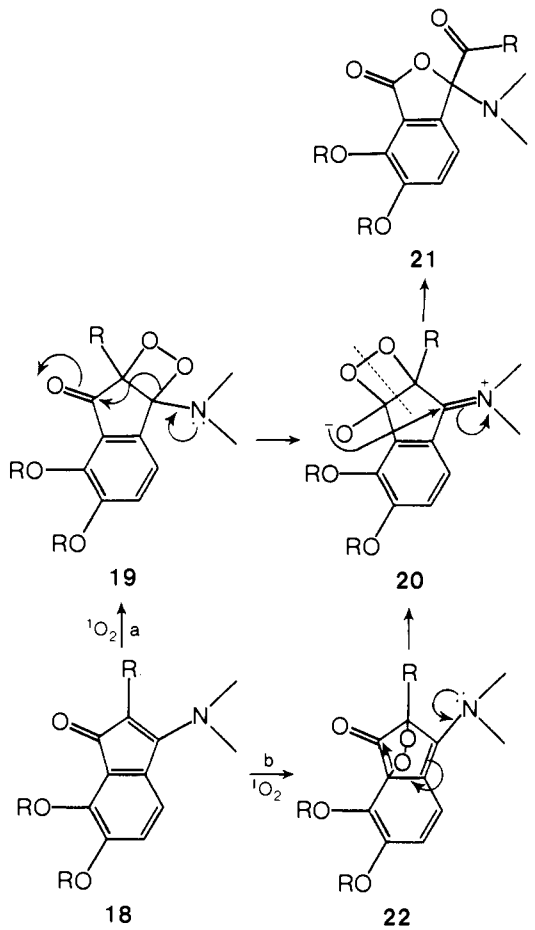
Equation 2, it should be noted, simply represents an intramolecular base-catalyzed epoxidation of an enone by a hydroperoxide.[76,77] An intermolecular process[75] has been ruled out by the observation that no epoxy quinols are formed from the reaction of *p*-quinols with hydroperoxides (eq 3).[326]

consistent with the low-temperature infrared spectral data, no firm experimental evidence is presented which supports it.



4. *A 1,3-Shift*

Orito et al.[78] have photooxygenated enamino ketone **18** and obtained lacto ketone **21** and suggest that the reaction proceeds via the transformation of dioxetane **19** into dioxetane **20** (path a). Here again, however, it is more likely that endoperoxide **22** (path b) is the primary product which rearranges to dioxetane **20,** thus allowing for rearomatization. Both the formation of endoperoxides, despite the loss of aromaticity,[1] and the sub-

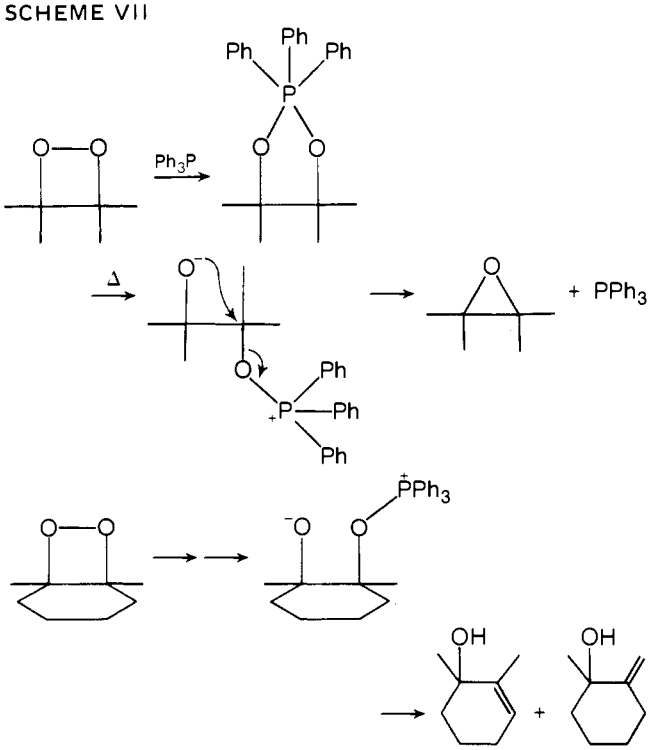


sequent rearrangement of an endoperoxide to a dioxetane (see section IV.A) have a good deal of precedent.

C. Reduction

Dioxetanes have been reduced to diols most cleanly by the action of $LiAlH_4$[15,41,79,82] and in lower yields by iodide ion in acetic acid,[41] by bromide ion,[61] and by high concentrations of basic formaldehyde (a known hydride source).[61] Most recently Takeshita and co-workers[324,325] have reported that dioxetanes are convertible into cis 1,2-glycols by visible-light irradiations with relatively large amounts of xanthene dyes, such as Rose Bengal, in protic solutions. Trivalent phosphorus compounds such as phosphines[20,41,84,85,369] and phosphites[86,88,353] react readily with dioxetanes to yield pentacovalent phosphoranes which collapse upon heating, presumably via a zwitterionic intermediate, to reduction products and phosphorus oxides (Scheme VII). The nature of the final products seems to depend on the structure of the starting dioxetane. For open-chain dioxetanes, epoxides are the major product since free rotation allows the two oxygen functions of the zwitterion to align trans to each other, thus permitting backside intramolecular displacement of the phosphorus oxide. For cyclic systems where free rotation is precluded, elimination occurs instead to give allylic alcohols. In a similar fashion bisulfite ion,[41] sulfoxylates,[87] and sulfides[87,89] are all reported to react with acyclic dioxetanes to yield O–O bond insertion products which collapse to give epoxides.

SCHEME VII

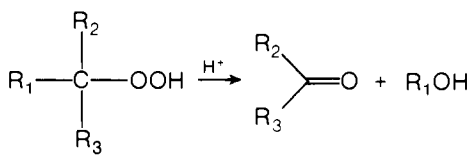


III. Reactions of Allylic Hydroperoxides

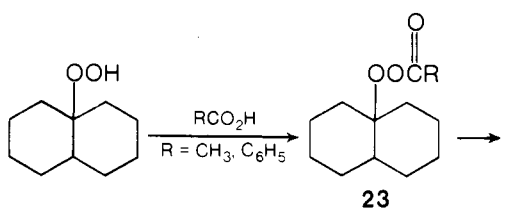
Three common classes of transformations occur with allylic hydroperoxides: (A) heterolysis of the O–O bond leading to skeletal changes in the carbon framework which are initiated by migration of groups to positive oxygen (in particular, we are concerned with the formation of two carbonyl fragments ("Hock-cleavage")); (B) 1,3-allylic isomerization; and (C) homolysis of the O–O bond leading to carbonyl (dehydration), alcoholic (reduction), fragmentation (β-scission), or oxirane (radical cyclization) products.

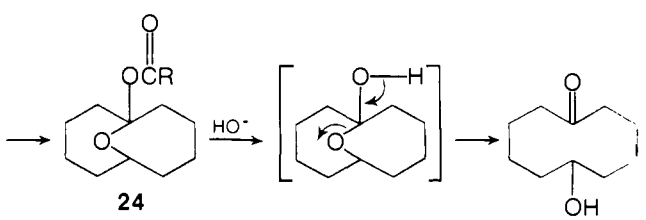
A. Heterolysis of the Oxygen–Oxygen Bond

The acid-catalyzed cleavage of hydroperoxides to alcoholic and ketonic fragments has been well studied,[90-92] and the industrial preparation of phenol and acetone from cumene hydroperoxide is a case in point ($R_1 = C_6H_5$; $R_2 = R_3 = CH_3$).

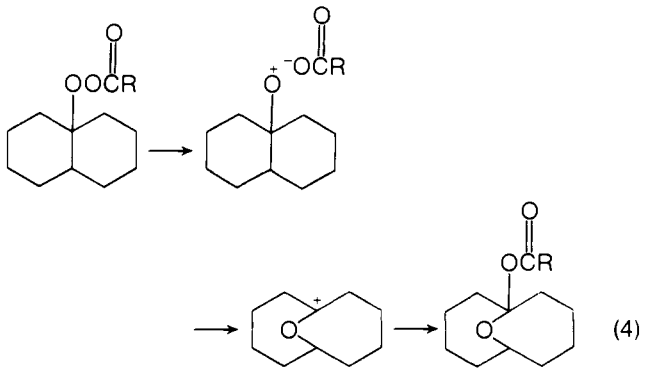


The first real clues to the mechanism came in 1944 when Criegee noted[93] that peroxy esters (**23**) rearrange to hemiacetalic esters (**24**). Based on this and similar observations, he



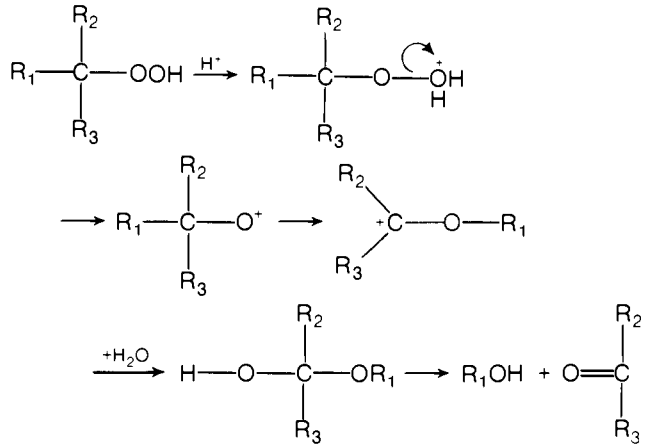


suggested[94] a mechanism in which, subsequent to heterolysis of the peroxy linkage, the developing charge on oxygen induces the ensuing skeletal changes (eq 4). In the following years the mechanism was scrutinized, tested, and generalized[95-97] and the accepted mechanism[90] for the rearrangement of allylic hydroperoxides is outlined in Scheme VIII.



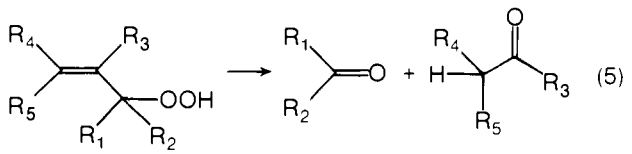
(4)

SCHEME VIII



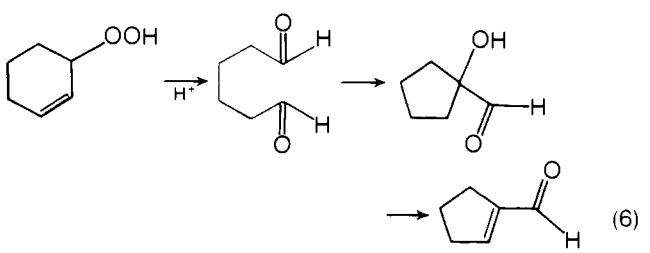
Hiatt[90] has surveyed the various studies in which relative migratory aptitudes have been determined and has drawn up the following qualitative ordering of these aptitudes: cyclobutyl > aryl > vinyl > hydrogen > cyclopentyl ≃ cyclohexyl ≫ alkyl.

In the particular case of allylic hydroperoxides, the migrating group, R, is generally[98] a vinyl group and the resulting fragments are both ketonic (eq 5). Because of this fundamental difference



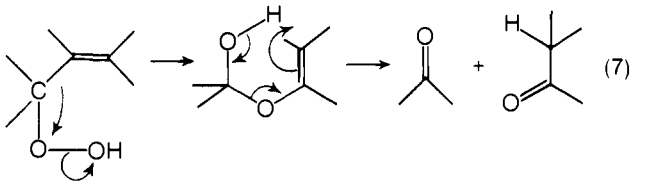
(5)

in the make-up of the products, this class of reactions has for a long time been dealt with separately. The transformation of allylic hydroperoxides to two carbonyl fragments has been dubbed Hock-cleavage after Hock, who first reported[100-102] in 1936 that cyclohexene hydroperoxide,[103] when allowed to stand with sulfuric acid at 35–40 °C, gave cyclopentenecarboxaldehyde in about 20% yield (eq 6). The formation of the latter was explained as the result of an internal aldol condensation of the initially formed hexane-1,6-dial, followed by dehydration. Subsequent to Hock's discovery, similar rearrangements were observed in many other systems (refs 39, 96, 97, 104–112, 350–352). While these cleavages are generally acid catalyzed, several have been reported to occur thermally as well, in the absence of any added acid (refs 96, 108, 110–113, 350–352).



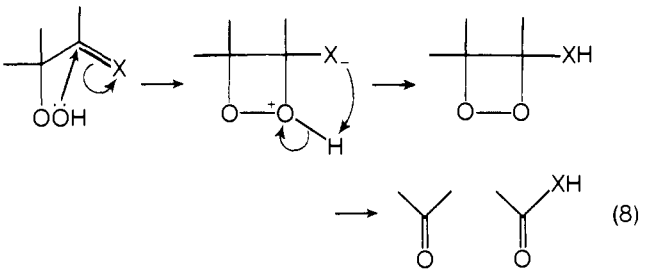
(6)

Although the Criegee mechanism is clearly applicable to the case of allylic hydroperoxides (eq 7), it is of interest to examine an alternate possibility. In 1942, Farmer and Sundralingam[104]



(7)

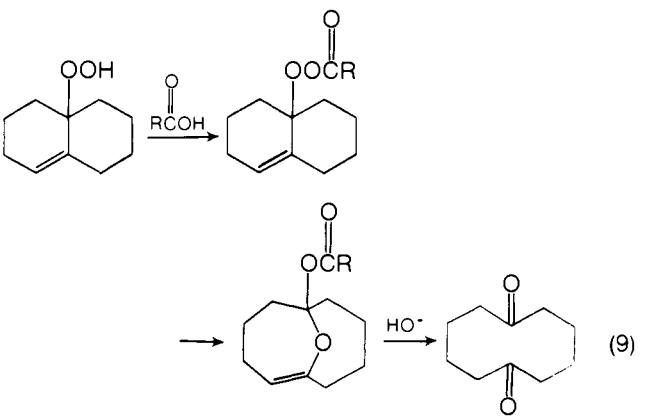
suggested a mechanism for Hock-cleavage which proceeds via a dioxetane intermediate (eq 8, X = CR_2). A similar process has been suggested for the thermal cleavage of α-keto[114-116] (X = O), α-imino[117,118] (X = N–R), and α-cyano[119] (X = –N) hydroperoxides, as well as for the hydrogen peroxide cleavage of α-diketones and α-keto acids[120] (X = O).



(8)

While this mechanism has yet to be excluded for this process, there are several indications that it does not play a role:

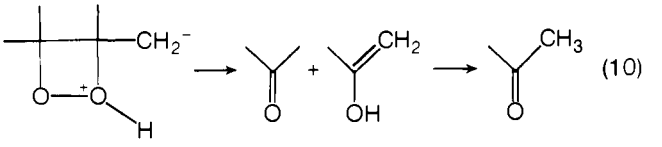
(a) Schenck and Schulte-Elte[106] repeated Criegee's 9-decalyl perester rearrangement[93,94] using the corresponding unsaturated analog, and similar products were indeed obtained (eq 9). Thus,



(9)

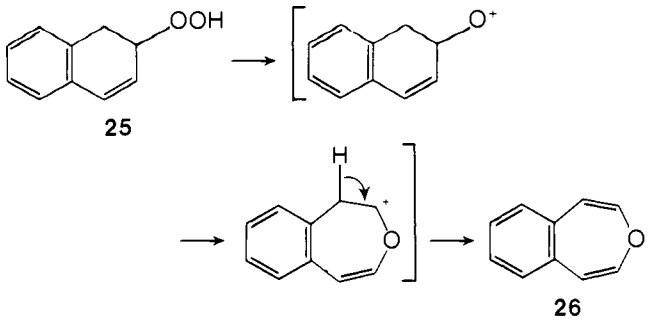
it is probable that both the saturated and unsaturated hydroperoxides cleave and rearrange by related mechanisms. It can be argued, however, that in the case of peroxy esters, formation of a dioxetane intermediate is pretty much precluded. Furthermore, while the Criegee mechanism may be operative in acid-catalyzed rearrangements, thermal Hock-cleavage may yet proceed via a dioxetane.

(b) At least in one case[98] where Hock-cleavage occurs, the addition of Ph_2S,[89] a dioxetane trap, to the reaction mixture in no way affected the product distribution. We note, however, that the cleavage may proceed according to the Farmer and Sundralingam mechanism directly from the zwitterion, in which case no true dioxetane would be present.



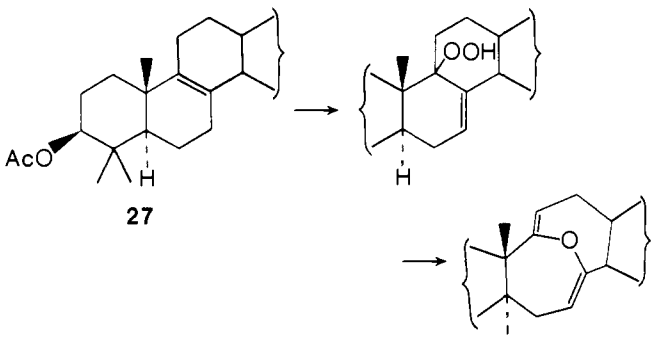
(10)

(c) Jeffrey and Jerina[121] reported that 1,2-dihydronaphthalene 2-hydroperoxide (**25**) rearranges thermally to 3-benzoxepin (**26**).



25 26

Similarly, in the photooxidation of 3β-acetoxylanost-8-ene[122] (**27**), a divinyl ether (**28**) was isolated, presumably also a rearrangement elimination product of the corresponding allylic hydroperoxide. Both these rearrangements are readily understood in terms of the Criegee mechanism. It should be noted, however, that, while both these rearrangements occur thermally, under acid conditions, which normally catalyzes Hock-cleavage, hydroperoxide **25** gives only naphthalene. Hence, it may be argued that these rearrangements proceed via an initial homolytic decomposition of the hydroperoxide.[121]



27 28

The question of mechanism aside, it should be clear that care must be taken to distinguish between dicarbonyl compounds or carbonyl fragments resulting from the decomposition of a dioxetane and those stemming from Hock-cleavage of the corresponding allylic hydroperoxides formed in an "ene" reaction. Below are listed several techniques by which this may be accomplished.

1. The reaction can be run in the presence of Ph_2S,[39] which while inert to $^1O_2$,[89] endoperoxides, and hydroperoxides,[123] reacts rapidly with dioxetanes.[89]

2. Since most hydroperoxides are thermally stable at −78 °C, a low-temperature photolysis followed by reduction by Ph_3P[124-127] at −78 °C may allow characterization of the hydroperoxide as its alcohol before it has a chance to cleave. Alternatively, labile hydroperoxides can be reduced in situ with excess phosphite.[110,126] This latter technique, however, bears the following caveat. Phosphites themselves undergo photoinitated oxidation[128,129] and are also reported to react with $^1O_2$ quite rapidly.[130] Triphenyl phosphite reacts sluggishly with triplet[128] and singlet[131] oxygen and hence would seem to be the reagent of choice. As noted above (section II.C), dioxetanes also react with trivalent phosphorus compounds such as phosphines[84] and phosphites.[88] In this reaction, a pentacovalent phosphorane is produced which collapses to an epoxide in the case of open-chain dioxetanes and to an allylic hydroperoxide in the case of cyclic systems. Hence, careful product analysis with and without added phosphine may aid in elucidating the mechanism.

3. Since hydrides reduce hydroperoxides to alcohols and dioxetanes to glycols, low-temperature photooxidation and reduction of the product mixture with $LiAlH_4$ or $NaBH_4$ may readily allow one to distinguish between Hock-cleavage and dioxetane decomposition.[328]

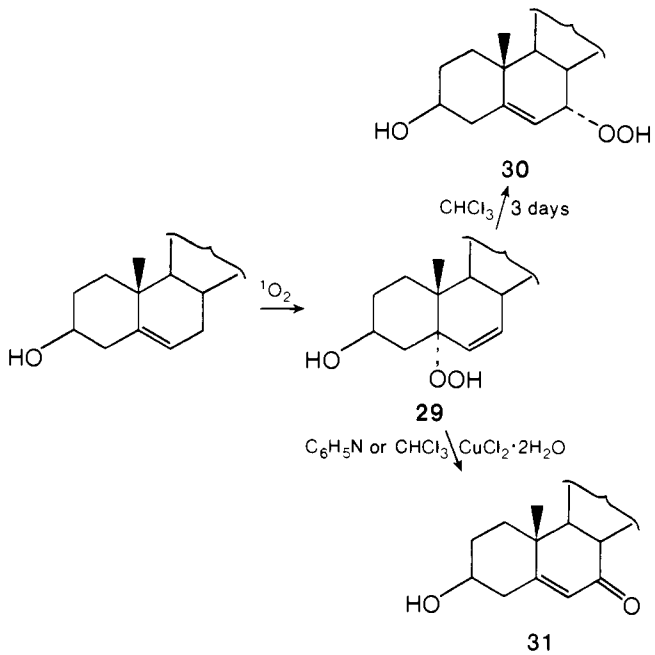
4. Low-temperature photolysis may also allow for isolation of the dioxetanes.[30,42,132,133] Cutoff filters may be necessary, however, to prevent photolysis of the dioxetanes by UV light.[30,42]

5. Dioxetanes may be reduced in the course of the photooxidation to cis 1,2-glycols by carrying the reaction out in protic solvent and using large amounts of xanthene dyes, such as Rose Bengal.[324,325]

6. Finally, if the reaction is run in methanol-*d* (CH_3OD), Hock-cleavage, irrespective of the mechanism, should result in deuterium incorporation α to one of the carbonyl groups.[134] The absence of such incorporation, as determined by NMR or MS, ought to indicate the intermediacy of a dioxetane. Considering, however, that hydrogens α to carbonyl groups are readily exchangeable, one has to be careful to prevent loss of the deuterium label because of a poor choice of workup conditions or isolation techniques.[135]

B. 1,3-Allylic Isomerization

In the late 1950s, Schenck[105,136] reported that tertiary hydroperoxide 3β-hydroxy-5α-hydroperoxycholest-6-ene (**29**) slowly rearranged to its allylic isomer, **30**, a secondary hydroperoxide, with complete retention of the α configuration. When



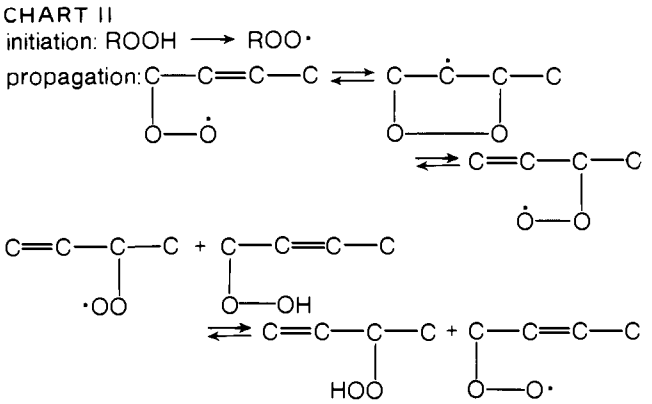
30 29 31

copper salts were used to catalyze the reaction, this 1,3-isomerization was accompanied by dehydration (see section III.C). Several subsequent reports[137-143] indicate that this tertiary to secondary allylic hydroperoxide transformation is quite general for cyclic systems and has been shown to be intramolecular and occur stereospecifically cis.[136,137]

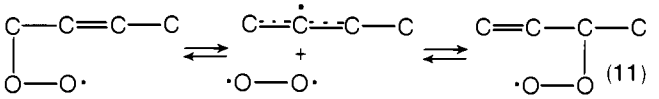
Brill[144,145] has studied this transformation in some detail using acyclic systems. He concludes that this rearrangement is a free-radical intramolecular process and occurs via a five-membered cyclic intermediate[137] (Chart II). The rearrangement is catalyzed by UV light, inhibited by 2,6-di(*tert*-butyl)-4-methylphenol, and occurs most rapidly in dilute solutions of hydroperoxide in nonpolar aprotic solvents. Finally, while tertiary and secondary acyclic allylic hydroperoxides seem to be of equal stability,[144] a primary hydroperoxide represents the least stable allylic structure.[145]

Chan et al.[323] have recently reexamined the 1,5 hydroperoxy

CHART II



shift in the thermal isomerization of methyl linoleate hydroperoxides. Using an ^{18}O-enriched hydroperoxide, these researchers showed that pentadienyl hydroperoxides undergo a rearrangement in which the oxygen atoms of the hydroperoxy group exchanged with atmospheric oxygen. This suggests that the 1,5 rearrangement and perhaps its 1,3 analog do not proceed via the cyclic peroxide intermediate suggested by Brill. Rather, these transformations involve breakage of the carbon–oxygen bond of the COO group followed by recombination (eq 11).


(11)

Because of the growing number of reports of allylic isomerization, caution must be observed in interpreting the hydroperoxide products determined by the prevalent technique of reducing oxidation mixtures and identifying the alcohols formed. In particular, although the $^1O_2$ ene reaction involves migration of the double bond while free-radical autoxidation very often does not,[146] it should be clear that a determination of the mechanism of the reaction cannot be based simply on the nature of the allylic hydroperoxide isolated.

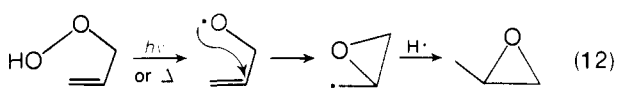
C. Homolysis of the Oxygen–Oxygen Bond

Because of the relative weakness of the peroxide bond, its homolysis to alkoxy radicals at room temperature or above (e.g., VPC injector port) is a prevalent phenomenon.[147] In many cases this reaction is to be considered a metal-catalyzed process, particularly since rarely are precautions taken to eliminate the presence of 10^{-8} mol of metal ions which suffice to catalyze the homolytic decomposition of hydroperoxides.[148,149]

Subsequent to homolysis, two general pathways are available to the alkoxy radical (refs 70, 108, 112, 139, 145, 147, 150–154): (1) hydrogen abstraction to produce alcohols; (2) β-cleavage to produce carbonyls. In the case of primary and secondary hydroperoxides this latter path usually involves loss of a hydrogen atom and in sum total represents dehydration of the hydroperoxide. For tertiary hydroperoxides carbon–carbon bond cleavage is required, while for α-hydroperoxy ethers[112] or esters[139] carbon–oxygen bond scission occurs.

One interesting case is the photooxidation of 1-methoxycyclohexene[112,153] which produces two hydroperoxides (**33** and **34**) and a dioxetane (**35**) as primary products. 3-Hydroperoxy-2-methoxycyclohexene (**33**) is thermolyzed in the VPC injector port to the corresponding allylic ketone **36** and alcohol **37.** 3-Hydroperoxy-3-methoxycyclohexene (**34**) is thermolyzed to cyclohexenone (**38**) and Hock-cleavage product, dione **39.** The latter is, of course, also the dioxetane cleavage product.

There is, however, a third pathway for the allylic alkoxy radical and that is to cyclize, ultimately forming an epoxide (eq 12). The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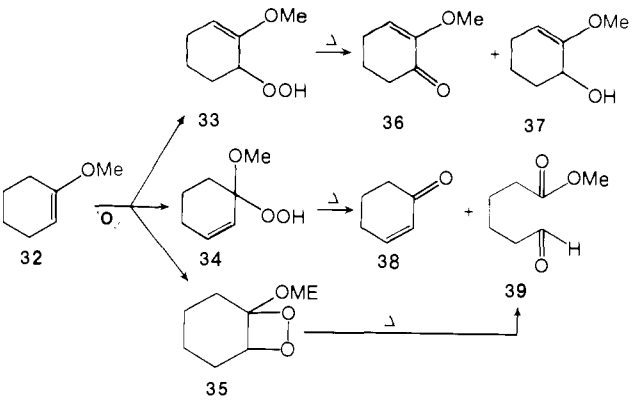
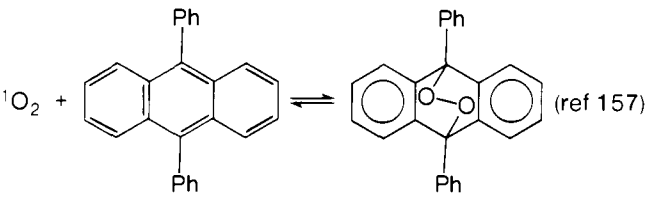


possibility of such a reaction was suggested by Gollnick[336] but has recently been documented by Jefford and Rimbault[337] in their study of the photooxidation of methylidenenorborn-5-ene.[344] While it has been unequivocally shown[287,296,338] that epoxides may result in photooxidations by free-radical processes without the intervention of allylic hydroperoxides, this third pathway should be kept in mind when considering reaction mechanisms.

IV. Reactions of Endoperoxides

A. Thermal Rearrangements

It has been common knowledge for a while now that, although endoperoxides are in general substantially more stable than dioxetanes, they too are thermally and photochemically labile. The thermolysis of an endoperoxide, which results either in its retroreversion to $^1O_2$ and an aromatic hydrocarbon or in the formation of bisepoxides and/or epoxyaldehydes, has been well reviewed[1,155,156] (eq 13).



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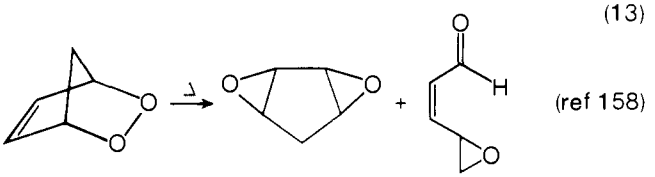
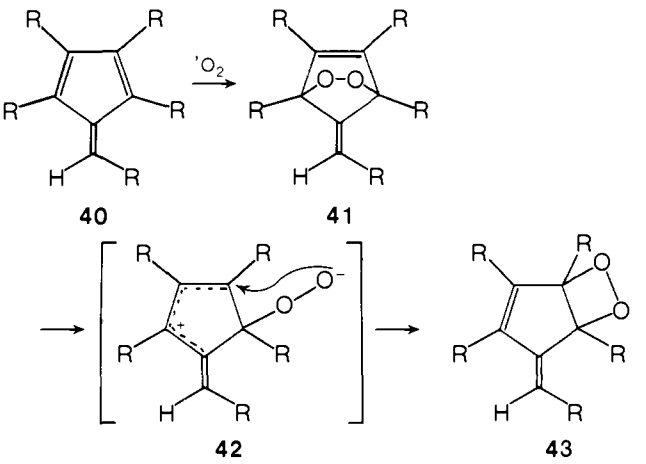
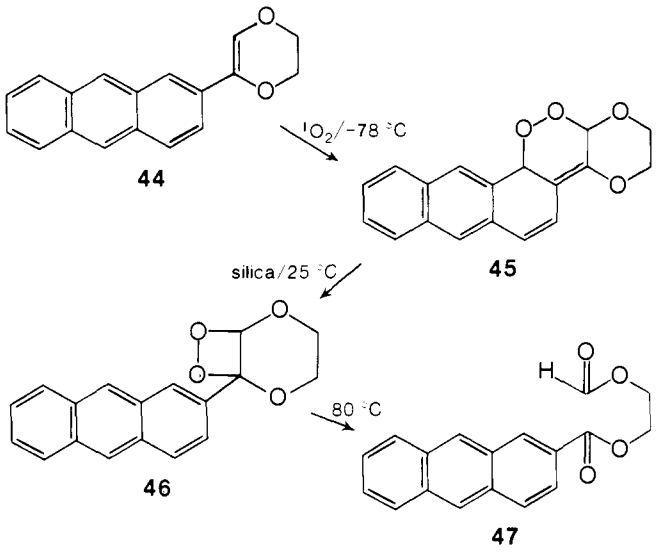


One reaction which, until recently, has not been sufficiently publicized, is the rearrangement of endoperoxides to dioxetanes.[66,67,70,159–175,182] For example, Le Roux and Goasdoue[172]



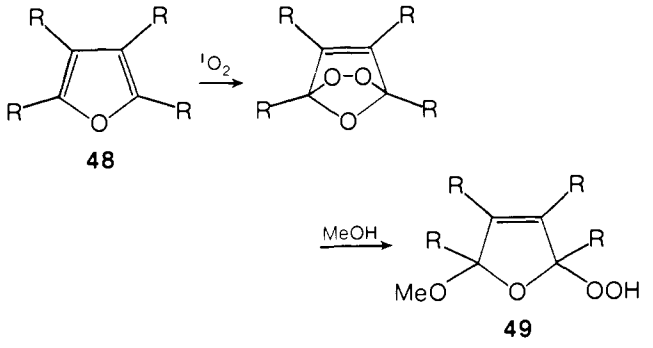
have recently prepared 1,2-dioxetanes (**43**) from the acid-catalyzed rearrangement of polyarylfulvene endoperoxides (**41**) and suggest that the rearrangement proceeds via a zwitterion (**42**). Schaap et al.[175a] have succeeded in isolating dioxetane **46** from the silica gel catalyzed rearrangement of the endoperoxide (**45**) formed in the photooxidation of 2-(2′-anthryl)-1,4-dioxene (**44**). It should be clear, therefore, that the formation of carbonyl fragments in the photooxidation of a diene is not necessarily an indication of the formation of a dioxetane as a primary product.



44 45 46 47

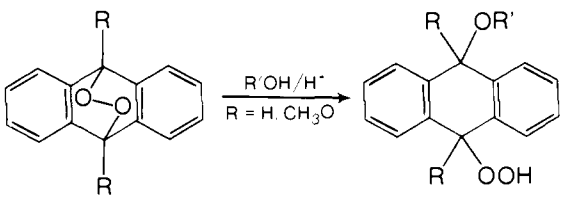
B. Reactions with Nucleophiles and Bases

Of importance in our future discussion is the solvolysis of endoperoxides which commonly leads to hydroperoxides. For example, the photooxidation of furans (**48**) in methanol results in the formation of 2-methoxy-5-hydroperoxyfurans (**49**).[176]



48 49

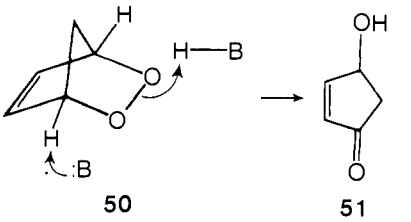
Similarly, the endoperoxides of 9,10-disubstituted anthracenes undergo hydrolysis or methanolysis upon addition of dilute acid[177] (eq 14).



(14)

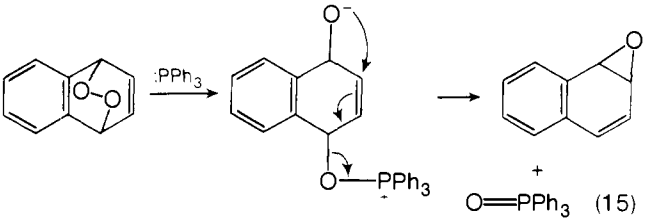
In the presence of weak bases (e.g., dilute aqueous hydroxide, pyridine, etc.), peroxides (including hydroperoxides) having α hydrogens can undergo the Kornblum–DeLaMare reaction[63,64,156] which involves an intramolecular carbanion displacement. The conversion[158] of the endoperoxide derived from cyclopentadiene (**50**) to 1-hydroxycyclopent-2-en-4-one (**51**) is typical.

Trivalent phosphorus compounds in general, and in particular



50 51

Ph_3P, reduce 1,4-endoperoxides to the corresponding 3,4-unsaturated-1,2-epoxide.[178-181] The reaction sequence is exemplified by the reduction of naphthalene endoperoxide[181] (eq 15). Endoperoxides also react with lithium aluminum hydride to give the corresponding 2-ene-1,4-diols and are reduced to 1,4-diols by hydrogen and platinum.[183]

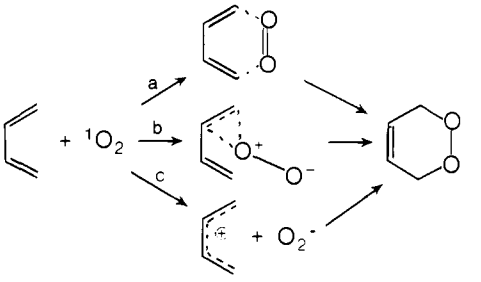


(15)

V. Mechanism of the Singlet Oxygen Diels–Alder Reaction

It is generally maintained[1,26,184] that the [2 + 4] addition of singlet oxygen to 1,3-dienes to form endoperoxides is concerted and proceeds through a six-membered ring transition state (Scheme IX, path a), analogous to the Diels–Alder reaction ($2_s + 4_s$).[185] Recently, however, there have been two dissenting

SCHEME IX



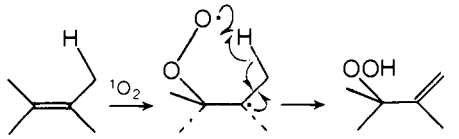
views expressed. The first is that of Dewar and Thiel.[186] Based on MINDO/3 calculations these authors suggest that the initial rate-determining step is the formation of a perepoxide which subsequently rearranges to an endoperoxide (Scheme IX path b). The transition state ($E_a \cong 11$ kcal) is reactant like with little charge separation. This suggestion of a two-step process finds support[187] in the formation of endoperoxides in the cases of 1,1,4,4-tetraphenyl-[188] and tetramethylbutadienes[189,355] (see section VII.A.2) despite the steric hindrance to coplanarity which is a prerequisite to a concerted Diels–Alder process.[190]

It has also been suggested by Ogryzlo[243] that a charge-transfer complex may be involved. There is some correlation between the ionization energies of the dienes and their reactivities. Other than these two suggestions the consensus is that the process is concerted. There is much disagreement, however, regarding the mechanistic details of the other two modes of $^1O_2$ attack, and it is to them that we turn our attention.

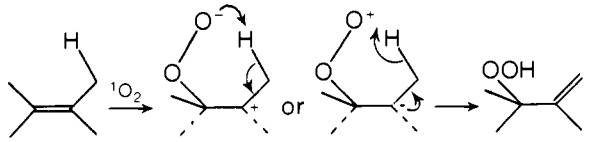
VI. Mechanism of the Ene Reaction[191]

Several different mechanisms and intermediates have been proposed for the formation of the allylic hydroperoxides and they are outlined in Chart III. Of the five proposed, three have traditionally been removed from consideration.

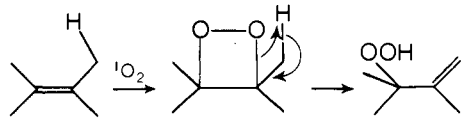
CHART III
Radical intermediate



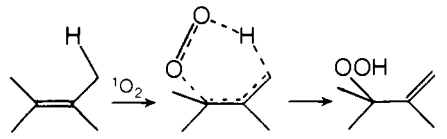
Ionic intermediate



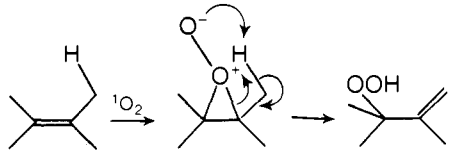
Dioxetane intermediate



"Ene" mechanism



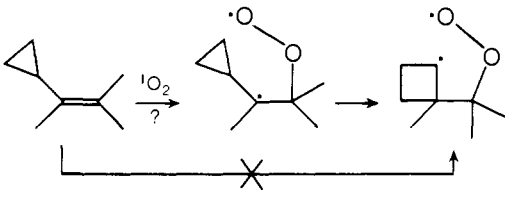
Peroxirane intermediate



A. Radical Intermediates

Radical intermediates may be ruled out because of the following observations: radical traps do not quench singlet oxygen reactions;[192,193a] there is a lack of substituent effects in the photooxidation of substituted styrenes;[194] there is no loss of optical activity or isomerization during photooxidations despite a good driving force (e.g., stabilization possibilities);[193] and finally, there is no correlation between relative rates of photooxygenation and rates of reaction with radicals.[195,196]

Recently the possible intermediacy of biradical intermediates has been resurrected by the ab initio calculations of Harding and Goddard.[370] While their suggestion may be consonant with the data they cite, they neglect the vast abundance of evidence which gainsay this possibility. Furthermore, as Rousseau et al.[331]



(16)

note, in the case of the photooxidation of vinylcyclopropanes a biradical intermediate would lead to a species particularly suited for ring opening (eq 16). Yet no such reaction has been observed for acyclic cyclopropylethylenes.[111,332,375] Moreover, it has been pointed out[331] that the GVB–CI ab initio calculations of Goddard and Harding overestimate biradical structures.

B. Ionic Intermediates

Ionic intermediates have been generally discounted since one would expect to find significant solvent effects on the rates of reaction. Experimentally, the solvent effects are small,[197] and the variations do not correlate at all with the polarity of the solvent. Furthermore, as cited above, the absence of Markownikoff-type or substituent[111,194,375] directing effects suggests that the product-determining transition state possesses neither localized charge nor localized radical character.

C. Dioxetane Intermediates

Dioxetane intermediates, though undoubtedly formed in certain photooxidations, cannot be invoked as intermediates for the "ene" reaction. Several stable dioxetanes have been synthesized from olefins containing allylic hydrogens,[41] and they decompose thermally or photolytically to give carbonyl compounds, not allylic hydroperoxides (see section II.A).

The two possibilities remaining, and the cause of a much heated debate, are the concerted "ene" and the two-step peroxirane or perepoxide mechanisms. The concerted ene is attractive since it nicely accounts for the fact that only those allylic hydrogens which are cis-oriented with respect to the oxygen attack are used in the reaction. This mechanism is consistent with the lack of solvent[197] and Markownikoff-type and substituent directing effects.[111,194] It readily accounts for the absence of radical intermediates and retention of optical activity, and is consistent with a correlation of increased reactivity with increased electron density of the double bond.

The proponents of the perepoxide mechanism, however, argue that a peroxirane is required both by theoretical calculations and certain experimental observations. Let us, then, turn to a critical discussion of the arguments for and against each of these two mechanisms.

D. Perepoxide Mechanism

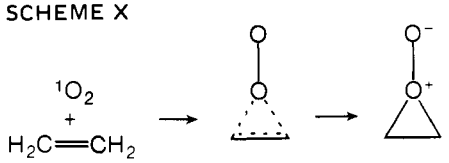
This mechanism is based on the following observations.[198]

(1) MINDO/3 Calculations. Perepoxide proponents adduce theoretical calculations both to buttress their position and to aid them in describing the elusive perepoxide more accurately. MINDO/3 studies[205,206] have been carried out by Dewar et al. and their conclusions are as follows.

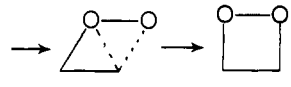
(a) The addition of $^1O_2$ to ethylene proceeds via a polar peroxirane[207] which rearranges through an unsymmetrical rate-determining transition state, **53**, to a 1,2-dioxetane (Scheme X). Both transition states leading from starting material to peroxirane, **52**, and from the latter to dioxetane, **53**, occur early. However, the rearrangement of peroxiranes to dioxetanes demands substantial activation, and, in the specific case of ethylene, MINDO/3 predicts that the reversion of the peroxirane to olefin and oxygen is easier than the corresponding rearrangement to the dioxetane.[209] This overall analysis should apply not only to ethylene but equally well to any olefin without allylic hydrogens or where ene reaction is precluded by Bredt's rule.

(b) Where allylic hydrogens are available, only allylic hydroperoxides are formed via a cis perepoxide, as exemplified by **54** for the case of propene (Scheme XI). While both cis and trans peroxirane might theoretically proceed to dioxetane, this process requires approximately 35 kcal/mol in activation energy. In contradistinction, interconversion of the trans to cis perepoxide and then on to ene product requires substantially less energy, approximately 23 kcal/mol. Hence only allylic hydro-

SCHEME X

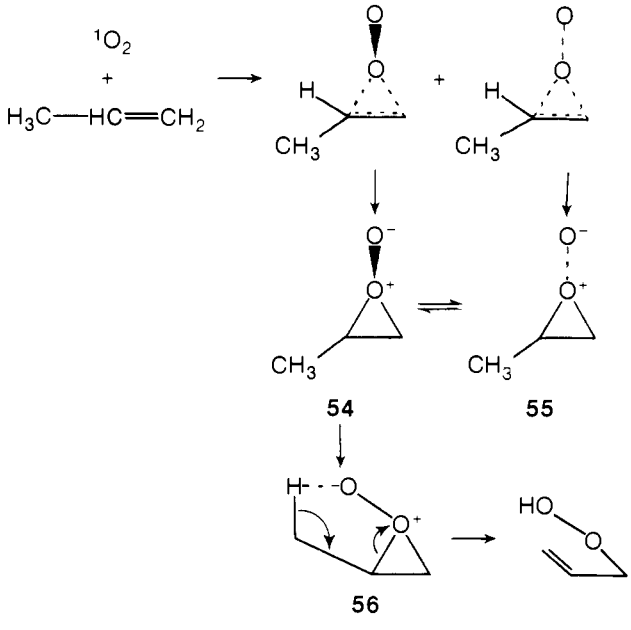


52

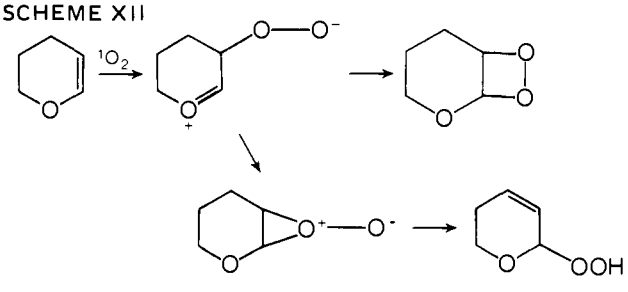


53

SCHEME XI



SCHEME XII



peroxides are expected. The rate-determining transition state is that leading to the polar perepoxide (E_a = 11.5 kcal/mol), but since it occurs early it is weakly polar and reactant like in structure. The transition state leading from perepoxide to product also occurs early and, hence, the breaking C–H bond is still rather strong and the forming O–H still rather weak. The geometry of the second transition state, **56,** has the same chair-type geometry expected for the concerted ene, differing only in that the C–O bond is already fully formed and the presence of an additional C–O interaction.

(c) In the case of enol ethers and enamines (i.e., double bonds with $-E$ substituents), the first and rate-determining step leads to a zwitterion which can proceed to ene product via a perepoxide or rearrange directly to a dioxetane (Scheme XII). Again, all transition states occur early and that leading to the zwitterion is relatively nonpolar.

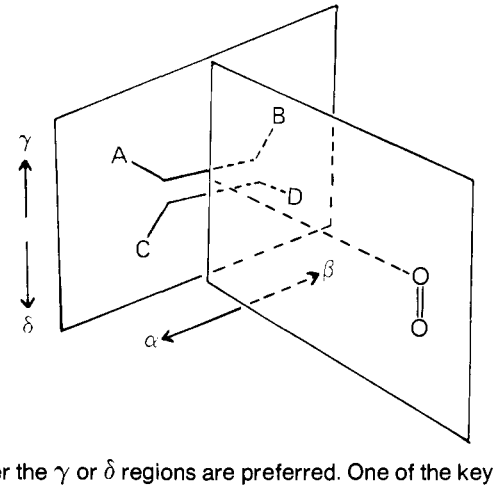
Some general observations are worth emphasizing. (a) All the reactions appear to be nonconcerted involving peroxiranes or zwitterions as intermediates which occupy shallow minima on the potential surface. (b) The rate-determining step in the ene reaction is the initial attack on the double bond. This is consistent with the aforementioned correlation of rate with electron density and with the small kinetic isotope effects observed (vide infra). (c) Peroxiranes rearrange to ene products extremely easily with rearrangement to dioxetanes requiring far more activation. Such, however, is not the case with zwitterions which can form dioxetanes and/or peroxiranes (and hence ene product if allylic hydrogens are available) with equal ease. (d) Since the rearrangements of the perepoxide to ene product and of the zwitterion to dioxetanes require very little activation, the lifetime of these species should be short and they, as a result, should be detectable and/or trapped only with the greatest difficulty.

Let us close this presentation of Dewar's work by noting that the MINDO/3 calculation of an 11.5 kcal/mol energy of activation leading to a perepoxide is for the specific case of the monosubstituted olefin propene. For double bonds substantially more substituted the E_a should drop significantly. Koch[211] has determined that the E_a for $^1O_2$ reactions in solution are usually less than 4 kcal/mol and are as low as 0.5 kcal/mol in the case of the tetrasubstituted olefin tetramethylethylene (TME). On the other hand, the E_a for the interconversion of cis and trans perepoxides, calculated to involve approximately 23 kcal should remain rather constant from propene to TME. Dewar considers this interconversion barrier to be relatively small with cis and trans equilibrating rapidly. If we assume that the relative thermodynamic stabilities of starting material and perepoxides in the more substituted cases do not change drastically from that of propene ($\Delta H = -16$ kcal/mol), then it is conceivable that perepoxide formation is itself a reversible process in the more substituted cases. This possibility, most recently argued by Conia,[212] has been considered unlikely by several other authors.[41,213]

These MINDO/3 calculations by Dewar have come under serious attack by Harding and Goddard[214,370] who, based on ab initio calculations, conclude that it is highly unlikely that peroxiranes play any role in the mechanism of $^1O_2$ reactions. They attribute the error in the MINDO/3 studies to its general overestimation of the stability of compounds involving small rings or adjacent heteroatoms. In particular, they find that MINDO/3 puts dioxetanes and peroxiranes, 29 and 33 kcal too stable with respect to products and reactants. It should be emphasized that Dewar et al. are aware of this tendency toward overestimation; however, they maintain that the magnitude of the error is in the region of 14 kcal which they feel would not invalidate their conclusions.

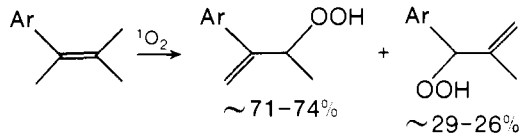
(2) Orbital Interaction Studies. Theoretical calculations based on studies of the HOMO–LUMO interactions possible have been carried out by Fukui[215–217] and seem to give a "compromise" picture. While the addition of $^1O_2$ to olefins indeed seems to proceed via a perepoxide-like structure, it is not clear that it is more than a transition state. If any energy minimum exists, it is very shallow and it is probable that the perepoxide cannot be isolated. In such a sense, then, the perepoxide structure cannot be a genuine intermediate and is termed by these authors as a "quasi-intermediate".

Fukui has further theorized[217] that the orientation of $^1O_2$ attack on an olefin is determined by the factors that control the orientation of the initially attacking oxygen atom and the tailing one in a perepoxide structure. The orientation of the attacking oxygen determines whether region α or β is preferred (see diagram below) while the orientation of the tail oxygen determines



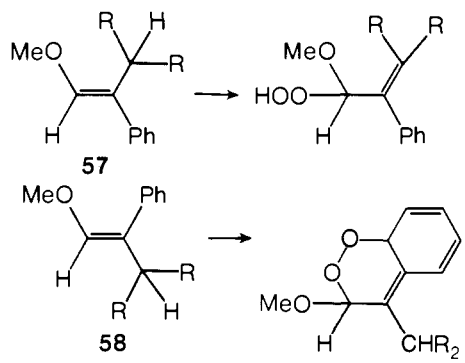
whether the γ or δ regions are preferred. One of the key factors in the orientation of the initially attacking oxygen is the polarity of the carbon–carbon unsaturated bond. Electron-donating substituents increase electron density on the olefinic carbon β to it. If, for example, A is the $-E$ substituent, the head oxygen

would be directed toward the β region. Hence, in the ene reaction, the hydrogen abstraction of the tail oxygen atom occurs at the substituents in the α region, i.e., A and/or C. If A and C are unreactive, a [2 + 2] cycloaddition will occur. Thus, in 1-phenyl-2-methyl-*cis*-2-butene [A = Ph; B, C, and D = Me], the allylic hydrogen on the methyl group geminal to the phenyl group is preferentially abstracted by the tailing oxygen. Since A is inert attack occurs at C.



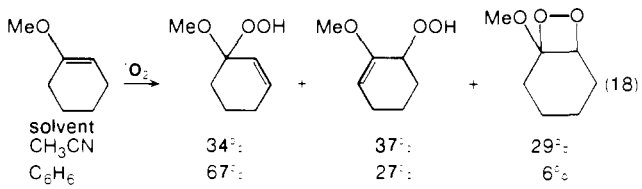
(17)

On the other hand, the factor that determines the orientation of the tailing oxygen, i.e., whether the γ or δ regions are preferred for reaction, is the nonbonded attraction of the substituents and the oxygen. For example, if substituent A bears lone pairs of electrons, we would expect preferential attack on the substituents in the γ region. Thus, in the photooxidation of *cis*- and *trans*-2-phenyl-1-methoxy-1-propene (**57** and **58,** respectively, R = H),[333] the substituent cis to the methoxy group is attacked.



Similar stereocontrol was observed by Conia[331,332] for *cis*- and *trans*-1-cyclopropyl-1-phenyl-2-methoxyethylene (**57** and **58,** R_2 = $-CH_2CH_2-$) and for *cis*- and *trans*-2-cyclopropyl-1-methoxypropene and the analogous ethylene.[376]

Fukui's predictions, however, are not consistent with the recent work of Bartlett and Frimer[112] on the photooxidation of 1-methoxycyclohexene (eq 18). In this case, Fukui's rules would

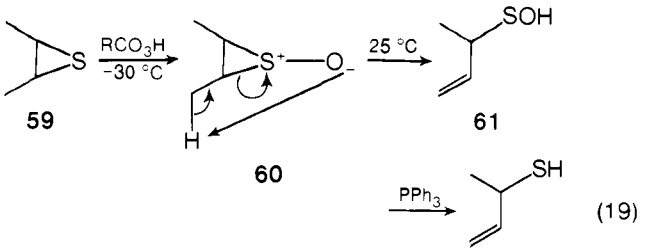


(18)

predict preferential hydrogen abstraction from the methylene group geminal to the methoxy substituent. The experimental results indicate that this is just not the case. These authors[112b] suggest that preferences in this case may be understood in terms of the most stable conformation. As has been noted quite often, $^1O_2$ tends to attack an olefin in its most stable conformation.[2b,183]

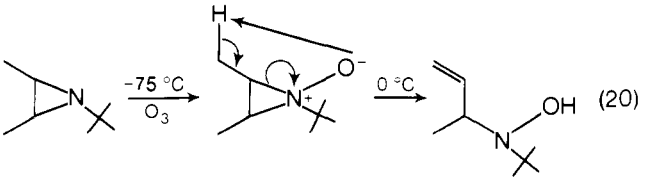
A similar preference for hydrogen abstraction trans to the *-E* substituent and in contradiction to Fukui's prediction has been observed by Ando et al. in the case of ethoxycyclohexene[51] and by Pusset[218] for 3-acetoxy- and 3-benzoyloxy-2-cholestene.

(3) Analogous Heteroatomic Systems. Several reports in analogous systems strengthen the suggestion that a perepoxide intermediate can indeed be expected to rearrange to allylic hydroperoxides or, if allylic hydrogens are unavailable, to dioxetanes. The episulfoxide **60** has been prepared[219] at −30 °C by peracid oxidation of the corresponding episulfide **59.** It rearranges at room temperature to allylic sulfenic acid **61** which



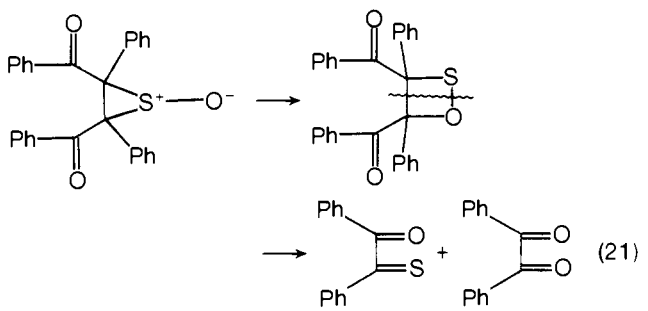
(19)

is the sulfur counterpart of a singlet oxygen ene product. Similarly, alkyl-substituted aziridine *N*-oxides rearrange upon warming to room temperature to give allylhydroxylamines (eq



(20)

20).[220] In the absence of allylic hydrogens, other reactions are observed. For example, Dittmer[221] reports that episulfoxides of dibenzoylstilbene can be thermalized to monothiobenzil and benzil presumably via a 1,2-oxathietane (eq 21).



(21)

(4) There are several experimental indications that the allylic hydrogen is not involved in the transition state. Firstly, kinetic isotope effects appear to be small (less than 1.4).[193,222-227] Secondly, it is clear from several systems that steric hindrance to C–O bond formation in the photosensitized oxygenation reaction is more important than hindrance to C–H bond cleavage.[225-230] Finally, it must be explained, according to the cyclic "ene" mechanism, why thermodynamic stability of the final double bond has little effect on the reaction,[111] why conformational ring inversion (which sometimes must accompany a double bond shift) does not block oxygenation, and why the susceptibility of C–H to abstraction is not inherently related to whether it is primary, secondary, or tertiary.[222]

To this concerted "ene" mechanism proponents[222,230-232] respond that all the results can be explained if we assume a product-forming transition state in which oxygen, while partially bonded to olefinic carbon and to allylic C–H, has neither much perturbed the olefin geometry, nor extensively weakened the C–H bond.[233,234]

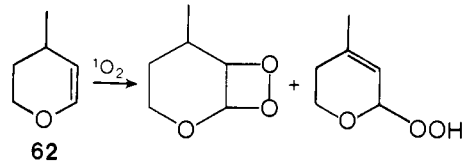
To the suggestion[235,236] that the low isotope effects might not be primary isotope effects but rather simply the result of cumulative secondary isotope effects in multideuterated systems, Nickon answered that for a transition state that resembles reactant (i.e., no hybridization change at CD_3) there should be virtually no secondary (i.e., α) isotope effect.[237] Furthermore, the slightly smaller steric size and slightly larger electron-donating effect[238] of CD_3 vs. CH_3 could favor attack at an olefinic carbon carrying CD_3 and thus produce inverse secondary effects. If secondary effects are operating they are making the numbers slightly smaller than they would otherwise be.[224,237]

Kopecky[226] has suggested several other explanations for the low isotope effect despite a concerted process. Firstly, the reaction has a very small E_a[211] so that a large isotope effect is not

expected. Furthermore, in the transition state for the concerted reaction, it is unlikely that the oxygen, hydrogen, and carbon atoms involved in the hydrogen transfer are colinear. In such a situation the isotope effect should be smaller than for a process in which all these atoms are colinear.[239,240,371] Finally, it is theoretically possible to have small and even inverse isotope effects for reactions in which hydrogen is transferred from carbon to oxygen.[241,242]

(5) Both Koch[211] and Ogryzlo[243] have studied the temperature dependence of $^1O_2$ reactions with olefins, the former in methanol and the latter in the gas phase. Koch reports that activation energies in solution are very small, ranging from 0.5 kcal for the tetrasubstituted olefin tetramethylethylene (TME) to 5.4 kcal for the disubstituted olefin cyclohexene. Ogryzlo states that in the gas phase the activation energies are a bit higher, ranging from 3.2 kcal for TME to greater than 8.3 kcal for cyclohexene. Such differences in the activation energies of the two phases in the case of nonpolar reactants is evidence for a polar transition state.[243] This could be nicely accommodated by a perepoxide mechanism. In truth, however, there is no reason to believe that the concerted ene transition state would not be somewhat polar, particularly in view of the electrophilic nature of $^1O_2$. Hence, a concerted mechanism with a polar transition state would also explain the data.

(6) Frimer et al.[112b,227] have carried out an in-depth study of the photooxidation of 4-methyl-2,3-dihydro-γ-pyran (**62**), in which both ene reaction and [2 + 2] cycloaddition compete, and its 4,4-dimethyl analog (**63**) in which dioxetane is the sole product. The kinetic isotope effects measured for position 5 of



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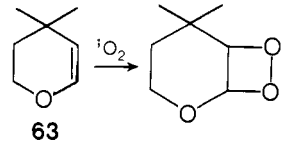


63

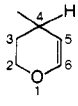
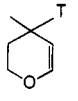
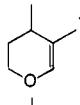
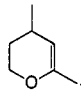
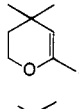
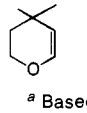
62 and **63** are particularly enlightening (see Table I). Firstly, they indicate that substantial rehybridization from sp^2 to sp^3 has occurred in the transition state. This puts into question the suggestion expressed by both perepoxide[234] and concerted ene proponents[220,230-232] that the transition state occurs early and is reactant like. More importantly, however, the data demonstrate that in both the ene reaction and dioxetane formation, position 5 undergoes rehybridization and is very much involved in the transition state. The simplest concerted ene mechanism seems, therefore, to be clearly ruled out in the photooxidation of these enol ethers.

On the other hand, the kinetic isotope effects for the α position 6 of compounds **62** and **63** indicate that in the transition state no rehybridization occurs at position 6 in acetonitrile and little if any in benzene. With respect to compound **62**, it is ene product that predominates in benzene, and, consequently, isotope effects at position 6, as well as those already mentioned for position 5, speak against the concerted mechanism—at least for these enol ethers. The values do not rule out the possibility of a zwitterion or perepoxide as intermediates on the way to product formation but suggest that the rate-determining transition state occurs substantially later than has been previously suggested.

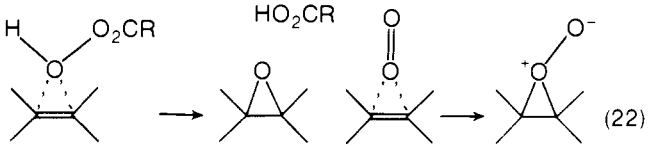
(7) There is excellent correlation between rates of peracid oxidation of olefins and their singlet oxygen reaction rates, and this would be anticipated in terms of the similarities of two mechanism as shown in eq 22.[244,245,358]

Concerted ene proponents might note that though substituent effects on the rate of reaction in the general ene have not been

TABLE I. Isotope Effects on the Photooxidation of 4-Methyl-2,3-dihydro-γ-pyran (62)

compound	quantity	CH_3CN/MB	benzene/TPP
	product compn	75.77% dioxetane[a] 24.23% hydroperoxide	24.26% 75.74%
	product compn	84.83% dioxetane[a] 15.17% hydroperoxide	25.82% 74.18%
	$\left[\frac{k_H}{k_D}\right]_{product}$[b]	1.787 ± 0.050 (2.310)[c]	1.087 ± 0.055 (1.128)[c]
	$\left[\frac{k_H}{k_T}\right]_{kinetic}$	1.211 ± 0.017 (1.142)[d]	1.335 ± 0.023 (1.222)[d]
	$\left[\frac{k_H}{k_T}\right]_{kinetic}$	0.866 ± 0.003 (0.905)[d]	0.908 ± 0.006 (0.935)[d]
	$\left[\frac{k_H}{k_T}\right]_{kinetic}$	1.067 ± 0.010 (1.046)[d]	0.980 ± 0.010 (0.986)[d]
	$\left[\frac{k_H}{k_T}\right]_{kinetic}$	0.897 ± 0.006 (0.927)[d]	0.897 ± 0.002 (0.927)[d]
	$\left[\frac{k_H}{k_T}\right]_{kinetic}$	1.001 ± 0.015 (1.001)[d]	0.994 ± 0.007 (0.996)[d]
	product compn	100% dioxetane	100% dioxetane

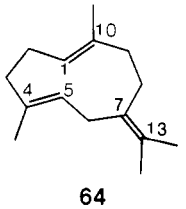
[a] Based on VPC peak area ratios using flame ionization detector. [b] $[k_H/k_D]_{product}$ = (hydroperoxide/dioxetane)$_H$/(hydroperoxide/dioxetane)$_D$. [c] Corresponding calculated k_H/k_T values. [d] Corresponding calculated k_H/k_D values.



(22)

investigated thoroughly, relative rates obtained from competition experiments indicate that feeding electrons into the double bond increases rates here as well.[16,246] In addition Foote and Denny[194] have also noted that for substituted trimethylstyrenes both the photooxidation and epoxidation reactions are mildly electrophilic ($\rho = -0.92$ and -0.87, respectively). Nevertheless, "the correlation of the photooxidation rates with σ indicates that no great resonance electron demand is made on the substituents at the transition state; this behavior contrasts with that of perbenzoic acid, where the best fit is obtained with a parameter containing 37% σ^+".

More importantly, it is now clear that Kopecky's correlation between photooxidation and peracid epoxidation rates is far from universal.[247,248] Germacratriene (**64**), for example, has been shown[247] to react with peracetic acid to yield the 1,10-, 4,5-, and 7,13-monoepoxides in the ratio 30:70:2. If the singlet oxygen



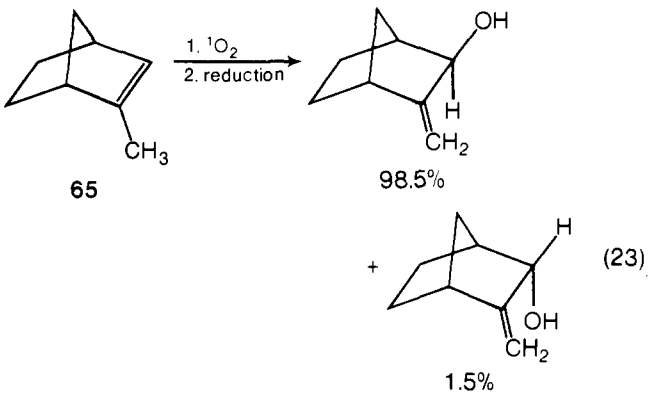
64

TABLE II. Analysis of Major Photooxygenation Product 67

solvent	D/H ratio	S/R ratio	rel amounts of R_H	R_D	S_D	S_H
acetone	1.0	1.0	1	0	1	0
methanol	2.0	1.0	2	1	3	0

reaction involved the rate-determining formation of a perepoxide intermediate, similar relative reactivity of the double bonds of **64** might be expected. In addition, possible internal nucleophilic attack on the perepoxide by the other endocyclic double bond could occur, leading to cyclization. The qualitative picture which emerges from the experimental data is that in contrast to epoxidation, the exocyclic isopropylidene 7,13 double bond of germacrene is ca. 9 times more reactive to singlet oxygen than the endocyclic double bonds. No cyclization was observed.

In addition Jefford and co-workers[231] studied the singlet oxygen reaction of 2-methylnorborn-2-ene (**65**) and obtained upon reduction the products shown in eq 23 (exo:endo ratio of 66:1). They note that although it is the relative steric environment



(23)

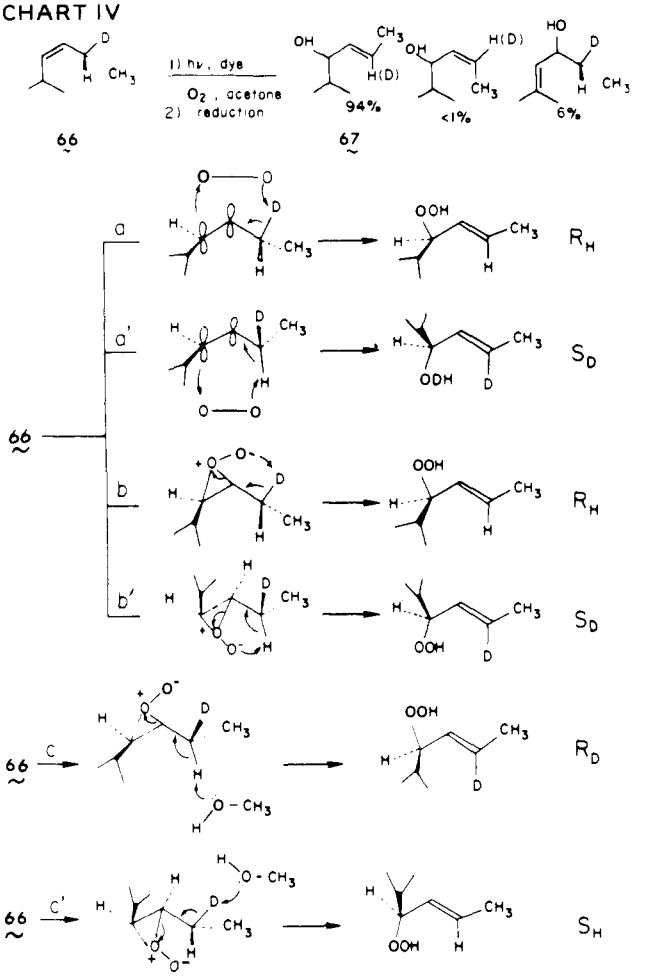
about the double bond which steers the incoming oxygen, nevertheless, the steric exigencies are less severe than those experienced for typical one-step cyclic additions such as hydroboration or epoxidation[248] where the exo:endo ratio is 200:1. They accordingly conclude that the singlet oxygen ene reaction passes through a "loose" cyclic transition state in which steric factors present in the reactant are determinative. It should be pointed out, however, that the difference between 66:1 and 200:1 is rather small. It is, therefore, questionable whether such a small difference can properly serve as the base for a mechanistic argument. Furthermore, singlet oxygen is an excited molecule and hence, deactivation or excess energy considerations may come into play.[362]

(8) Stephenson has reported[213,342] that when olefin **66** is photooxidized in acetone, allylic hydroperoxides R_H and S_D are isolated with both a D/H and S/R ratio of approximately 1. These results are explicable both by the perepoxide (paths b and b′) and ene (paths a and a′) mechanisms as shown in Chart IV.

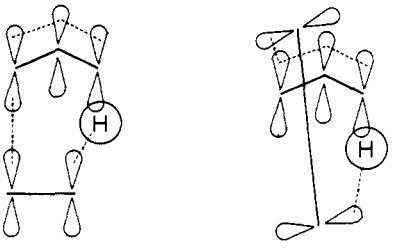
When, however, **66** is photooxidized in methanol, the D/H and S/R ratios no longer match (see Table II), primarily due to the appearance of product R_D at the expense of R_H. This uncoupling of the enantiomeric and isotopic ratios is difficult to attribute to the conventional concerted ene mechanism but may be consistent with the perepoxide mechanism if we assume solvent-assisted β-elimination via proton abstraction by methanol (path c), competing favorably with intramolecular deuteron abstraction by perepoxide. No S_H is formed according to this scheme since solvent-assisted β-elimination would require deuteron abstraction by CH_3OH (path c′) to compete with the intramolecular proton abstraction.

In a footnote to their paper[249] the authors comment: ". . . the result in acetone can be explained by a concerted ene transformation with a small isotope effect, and . . . the result in

CHART IV



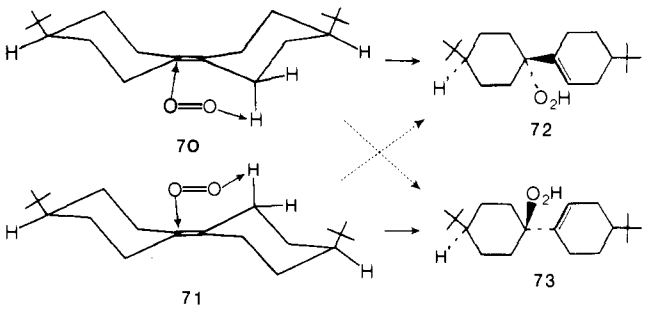
methanol can be accommodated to a *mixture* of concerted mechanisms". They would seem to be raising the fascinating possibility that the concerted ene reaction proceeds not only by a cis-addition ($_\sigma2_s + _\pi2_s + _\pi2_s$) mechanism (**68**) but perhaps by a trans process ($_\sigma2_a + _\pi2_s + _\pi2_a$) (**69**) as well. Such a crosswise



68 69

approach of $^1O_2$ to the double bond has been suggested by Bartlett[16,29,40,250,251] for the dioxetane-forming reaction (vide infra, section VII) for which he proposes a $_\pi2_s + _\pi2_a$ process. While a mixture of concerted mechanisms is indeed possible, it is not clear why one should obtain them both only in methanol and not in acetone as well. Nevertheless, such a suggestion is interesting and deserves further deliberation.

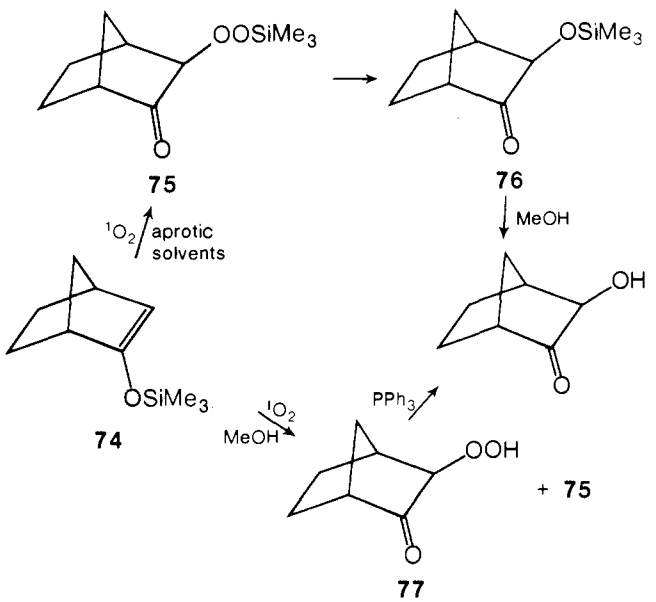
(9) A related stereochemical study has been carried out by Kellog and Kaiser.[83] This group studied the photooxidation of cyclohexylidenecyclohexane which comes in two fixed conformers **70** and **71.** Only the equatorial face of **70** is available for a concerted all-suprafacial ene reaction and, hence, **70** would be expected to yield **73** exclusively. In contradistinction, the alkene faces of **71** are equivalent but with regard to any one face only that alkylidene carbon which is furthest from the axial allylic hydrogen is able to bond in an all-suprafacial concerted ene



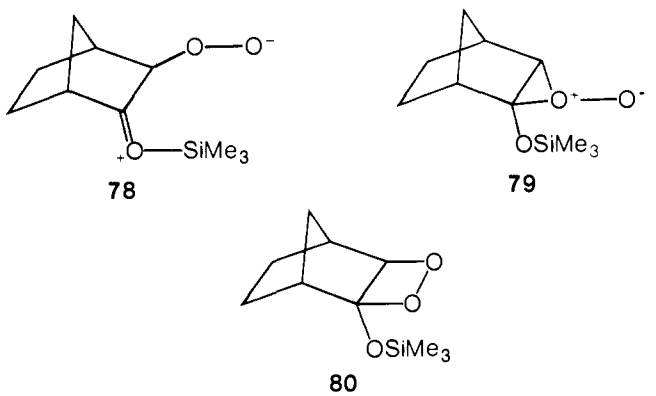
process. Nevertheless, both **72** and **73** are obtained from either **70** or **71.**

These results are explicable if we assume the initial formation of an intermediate, perhaps a peroxirane, which lives long enough to react from an attainable but energetically unfavorable flexible form in which a quasi-axial hydrogen is presented. The results, however, may also suggest an antarafacial component to the ene reaction, as has been argued in the previous section.

(10) Jefford and Rimbault[20] report that 2-trimethylsilyloxynorbornene (**74**), unlike norbornene, reacts rapidly with $^1O_2$ in aprotic solvents (CCl_4, $CHCl_3$, CH_3CN) to produce silylperoxy ketone **75** in a 95% yield. Nevertheless, $^1O_2$ in methanol produces a 15% yield of hydroperoxy ketone **77** in addition to **75.**



Since **75** is completely stable under the reaction conditions, it cannot be the source of **77.** The authors suggest the initial formation of a zwitterion **78** or perepoxide **79** as the key intermediate. While migration of the trimethylsilyl group leading to **75** is the sole reaction in aprotic solvent, in methanol proton abstraction from the solvent can compete producing **77.** These

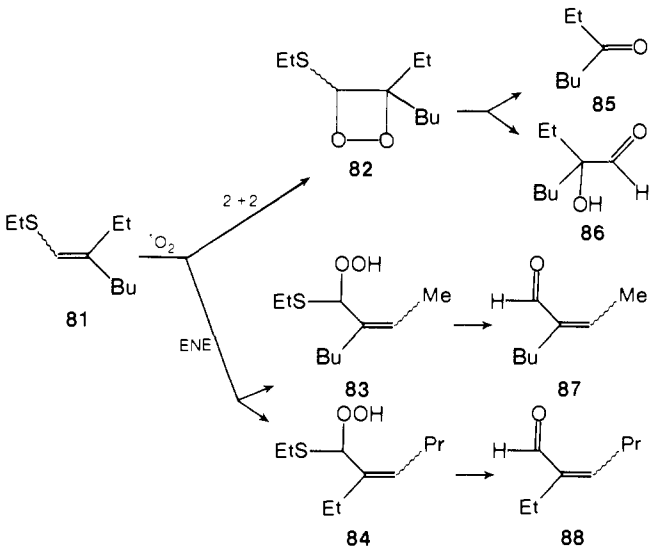


authors thus conclude that an intermediate is clearly involved in the photooxidation of, at least, enol ethers.

Jefford and Rimbault mention that they have ruled out the possibility of methanol addition to a dioxetane (**80**) on the grounds that such solvolyses are not observed. As we have discussed earlier (section II.B), while this generalization is true for tetraalkyldioxetanes, it is by no means true for all dioxetanes. Indeed we have cited several examples including two enol ethers studied by Ando.[51] Hence here too it is perhaps possible that dioxetane solvolysis is at play. Actually, however, it is unlikely that dioxetanes are involved for two reasons. Firstly, it would be difficult to explain why dioxetane formation would be preferred specifically in methanol. In the case of other enol ethers[112,227] polar solvents in general were found to favor [2 + 2] addition, but this does not seem to be true here. More importantly, in the other cases of silylether photooxidation reported,[17-21] only ene reaction occurs and there is no reason to assume that this case would differ.

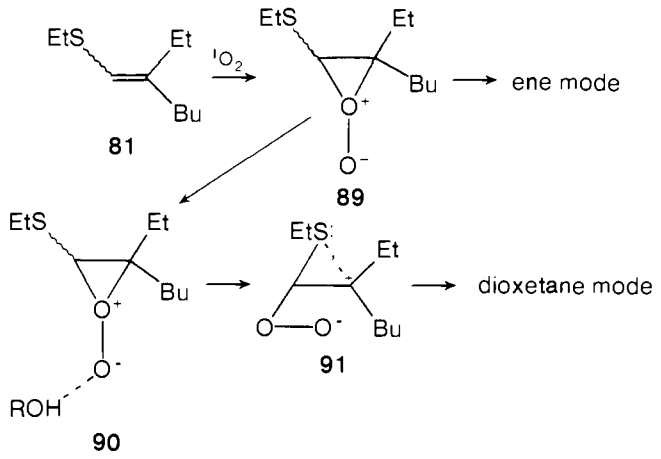
It would seem that the true answer lies elsewhere. Jefford and Rimbault note that **75,** is stable under the reaction conditions (−20 °C) and is not converted to **77** except at higher temperatures. It is often forgotten that singlet oxygen is an excited molecule and hence excess energy considerations come into play once product is formed. It is indeed plausable that it is this excess energy which enables some of **75** to undergo the higher energy transformation.

(11) Ando et al.,[51] have researched the photooxidation of 1-ethylthio-2-ethylhexene-1 and report that although both ene and dioxetane product are formed in aprotic solvent (in a ratio of 17/83 for CH_3CN and 36/64 for CCl_4), alcoholic solvents (CH_3OH, C_2H_5OH, i-C_3H_7OH) give dioxetane product exclusively.



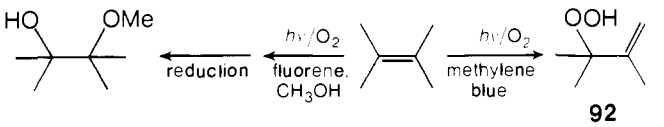
These authors suggest that the results are best explained by the intermediacy of a perepoxide (**89**) which decomposes by hydrogen abstraction to ene product or via a zwitterion to dioxetane product. Protic solvents may decrease the negative charge density of the tail oxygen by hydrogen bonding thus promoting nucleophilic attack by neighboring sulfur (**90**). This in turn stabilizes the polar zwitterion (**91**) leading to dioxetane.

This evidence, however, is circumstantial and by no means rules out a concerted mechanism. For example, it is not clear how a change from aprotic to protic solvent affects Hock-cleavage (see section III.A) of the initially formed allylic α-ethyl thiohydroperoxides. Indeed, as mentioned in section III.C above, Bartlett and Frimer[112] have studied the analogous photooxidation of 1-methoxycyclohexene in which one of the "ene" products, an α-methoxy hydroperoxide, yields substantial amounts of Hock-cleavage product upon thermolysis. Furthermore, protic solvents with their abstractable hydrogens may allow the α-ethyl



thiohydroperoxides to proceed to **86** rather than to **87** and **88.** These points clearly deserve further investigation.

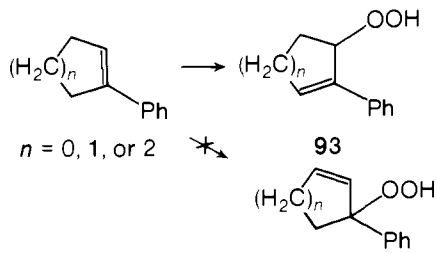
(12) Nickon and co-workers[183] have found that, whereas methylene blue sensitized photooxygenation of 2,3-dimethyl-2-butene in methanol gave only allylic hydroperoxide, **92,** other sensitizers (e.g., fluorene, benzophenone, benzil) produced a methanol adduct in various proportions. They note that if this



92

adduct were derived simply by competitive nucleophilic attack of methanol on a perepoxide or other intermediate, it would be surprising if the sensitizer could influence the extent of interception. They posit, therefore, that extraneous side reactions, perhaps involving radicals or epoxide intermediates[296] may be competing. It has also been suggested that superoxide radical anion O_2^- might well be implicated in this reaction. However, Frimer and Rosenthal[14b,372] have demonstrated that O_2^- does not react with simple olefins.

(13) The photooxidation of phenylcycloalkenes has been studied by Jefford and Rimbault[33] who report that only allylic hydroperoxides in which the double bond is conjugated with the phenyl ring are formed. They suggest that the dominant Mar-

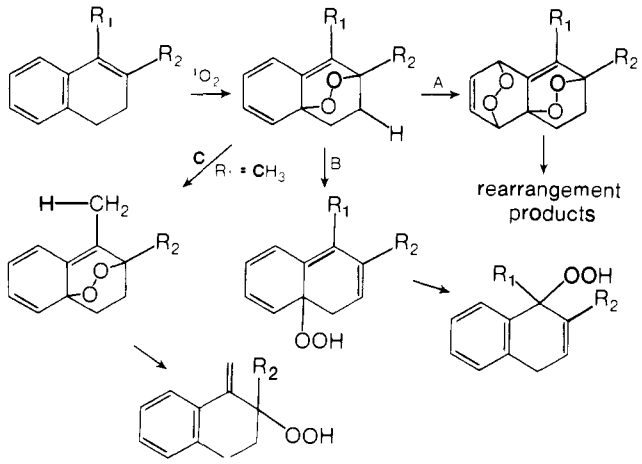


kownikoff effect requires a perepoxide intermediate. Exclusively conjugated products have been observed by Foote and Burns[32] in the photooxidation of 1,2-dihydronaphthalenes and predominantly conjugated products have been obtained by Foote and Denny[194] in the case of α,β,β-trimethylstyrenes. Regarding both these cases, however, Foote[32] argues that this tendency probably reflects product-like character in the transition state. As noted above, both concerted ene and many perepoxide proponents have argued in favor of an early reactant-like transition state.

It is plausible, however, that two other factors may be involved:

(A) *The steric effect of the phenyl group forces the oxygen to attack from the less hindered side,* i.e., at the olefinic carbon β to the phenyl group. Foote[194] rejected this explanation for the case of α,β,β-trimethylstyrene citing 2,3,4-trimethyl-2-pentene

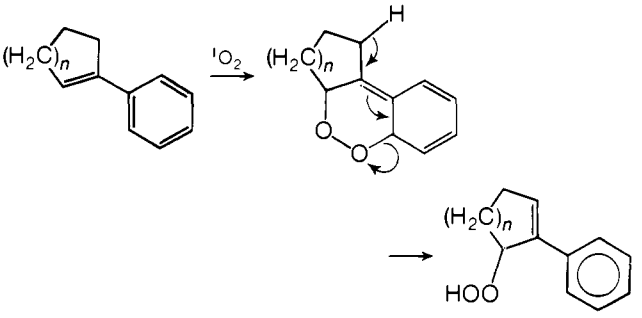
SCHEME XIII



as precedent. Here attack by the oxygen at the olefinic carbon α to the isopropyl group is preferred by a 2:1 ratio over β attack. Assuming that isopropyl is a good model for phenyl, this would indicate that steric bulk is not a controlling factor in these types of compounds. We note, however, that product distributions are heavily controlled by the most stable conformation[2b,183] of the starting material not merely steric size. Hence, the isopropyl group with its sp^3 hybridization and tertiary hydrogen may not be a good model for the planar benzene ring.

(B) *The allylic hydroperoxide is a rearrangement product of the initially formed endoperoxide.* Such a course of events would explain the effect of substituents on the product distribution reported by Foote for the photooxidation of dihydronaphthalenes[32] (see Scheme XIII). In those cases, where R_1 = phenyl the initially formed monoendoperoxide should be stabilized, thus allowing for a second Diels–Alder reaction (path A) to take place. Where R_2 = phenyl, loss of a hydrogen (path B) producing extended conjugation should compete favorably. This is followed by a 1,3-allylic hydroperoxide shift which allows for rearomatization. Where R_1 = CH_3, path c leads to the exocyclic allylic hydroperoxide product.

A similar course of events would explain the formation of exclusively conjugated ene product in the case of 2-phenylcycloalkenes. [We will return to this paper and the question of endoperoxide formation in the next section (VII.A.8)].



E. Concerted Ene Mechanism

Proponents note that there are several pieces of experimental evidence that must be explained if we are to accept the perepoxide mechanism:[191]

(1) The perepoxide mechanism might have been expected to be affected by solvent polarity, at least to some degree, since some charge separation would be involved.[194] In defense of the perepoxide it has been noted[206-208] that this argument is based on the assumption that the transition state for this reaction is highly polar. Theoretical calculations[206-208] indicate that this is not the case. On the contrary, the transition state occurs early and is reactant like in structure and polarity, with the oxygen

atoms of the peroxirane bearing relatively little charge (~0.36 electron). Solvent effects cannot be used, therefore, to rule out this mode of reactivity.

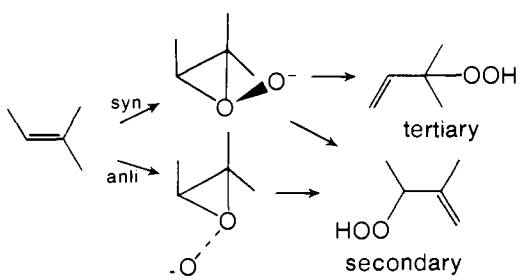
Furthermore, in comparing the Arrhenius parameters of the gas and condensed phases, Ogryzlo[243] has concluded that the effect of solvent is to reduce both the E_a (which raises the rate constant, k) and the preexponential factor (which lowers k). Consequently, when the E_a becomes very small, as it does when these $^1O_2$ reactions are carried out in a solvent, the effect of any further change in the E_a, such as might result from a change in the solvent polarity, is decreased relative to a compensating change in the preexponential factor.

Finally, we note that missing solvent effects (a requirement for one-step calculations) have been reported for several dipolar cycloaddition reactions.[252,253]

(2) The direction of opening of a perepoxide would be expected to be affected by substituents, since the C–O bond would be weakened by electron donation.[194] Perepoxide defenders[206] retort that the MINDO/3 calculated transition state for the ene rearrangement of methylperoxirane strongly resembles the peroxirane itself in structure with the breaking C–H and C–O bonds still quite strong and the nascent O–H bond still very weak. Since the transition state for the ene rearrangement is so similar to the reactant in structure, substituents should have little effect on its energy and hence on the relative rates of different modes of rearrangements. Similar remarks apply to the known specificity[1] of the ene reaction. As noted above, the calculated transition state leading from peroxirane to allylic hydroperoxide differs from that expected for a concerted reaction only in that the C–O bond is already fully formed and by the presence of an additional C–O interaction. Otherwise the former has the same chair-like geometry that would be expected for the pericyclic transition state.

Although this explanation may account for the lack of Markownikoff directing effects on the perepoxide opening, it does not correspond to results observed by Ogryzlo[243] for gas-phase photooxidations. While 2-methyl-2-butene gives tertiary and secondary hydroperoxides in nearly equal amounts when photooxidized in methanol, in the gas phase a 71 to 29% result is obtained. The cleavage here is anti-Markownikoff and indicates that oxygen has a slight preference for bonding to the more electronegative center. This would suggest that a concerted ene mechanism is involved in which the product is determined by the direction of initial oxygen attack. Nevertheless, Fukui's suggestion[215-217] of a perepoxide-like *transition state* on the way to ene product, in contradistinction to a distinct intermediate, may also be consistent with the above result.

(3) On stereochemical grounds the possibility of a perepoxide intermediate can be doubted for the following reason. In the photooxidation of trimethylethylene, two perepoxides are possible: a syn and an anti form (with respect to the monomethylated carbon) as shown in eq 24. While the syn perepoxide could give



(24)

either the tertiary or secondary hydroperoxide, the anti form can only give the latter. Statistically, therefore, only one-fourth of the olefin undergoing reaction would give the tertiary hydroperoxide. One might, however, still argue that pure statistics allows for a 50:50 mixture of secondary and tertiary hydroperoxide if the latter forms whenever it can. Nevertheless, cleavage of the syn endoperoxide might be expected to proceed such as to give a tertiary carbonium ion and, hence, secondary hydroperoxide. Furthermore, in the singlet oxygen reaction of trimethylethylene, the predominating perepoxide should be in the anti form for steric reasons. In actuality, however, the secondary and tertiary hydroperoxides are formed in about equal yields.

This argument assumes, however, that the different peroxirane intermediates of the same acceptor are not interconvertible. MINDO/3 calculations[206] suggest that both cis and trans perepoxides have access to the preferred transition state which, as noted previously, is very similar to that expected for the concerted reaction.

(4) If indeed the perepoxide is an intermediate and not merely a transition state, then it would be expected to show a reactivity similar to that of the corresponding epoxides and this is simply not the case. For example, norbornene epoxides and exo onium type intermediates of norbornene are notorious for the facility of their skeletal rearrangement. Consequently, the consistent observation of hydroperoxides of unrearranged structure renders the intermediacy of the perepoxide unlikely.[232,254] Similarly, epoxy ethers react quite rapidly with all nucleophiles to give the corresponding addition product.[255] Nevertheless, the photooxidation of dihydropyran in methanol yielded no solvent addition product.[227,112b] On the other hand, these latter results may merely be an indication of the rapidity with which the perepoxide rearranges intramolecularly such that no intermolecular process can compete.

(5) Recently, Carmier and Deglise[256] followed the photooxidation of tetramethylethylene in the gas phase (at −190 and +20 °C) and liquid phase (20 °C) by infrared spectroscopy. The only new bands that developed were due to allylic hydroperoxide. Even at −190 °C, no evidence whatsoever for an intermediate could be observed. The authors thus conclude that, ". . . le seul mécanisme possible de formation de l'hydroperoxyde allylique est un mécanisme d'addition concertée de l'oxygene singulet sur l'olefine, *sans intermediaire* . . .". This conclusion, however, does not take into consideration the possibility that the perepoxide is present in a low steady-state concentration. Indeed, theoretical calculations[206,215,216] indicate that the lifetimes of any intermediates involved (zwitterions and/or peroxiranes) should be very short and these species should therefore be hard to detect.

(6) Kopecky[225,226,257,258] has studied the dehydrobromination reaction of several β-bromo hydroperoxides formed from tetrasubstituted ethylenes. The evidence indicates that an intermediate is formed in the course of the reaction in which the carbon attached to the –OOH and the carbon originally bearing the bromine become equivalent with respect to the oxygen atoms of the hydroperoxy group. The intermediate is not the dioxetane, however, and is presumed to be the perepoxide. Since different kinetic isotope effects and product yields were observed for the formation of the allylic hydroperoxides, via the β-halo hydroperoxide and via direct photooxygenation, the evidence would seem to indicate that the perepoxide is not an intermediate in the singlet oxygen reactions.

The above results are contradicted by the work of Baldwin and Lever[259] who studied the dehydrobromination of β-bromo hydroperoxides **94** and **95** formed from isopropylidenecyclohex-

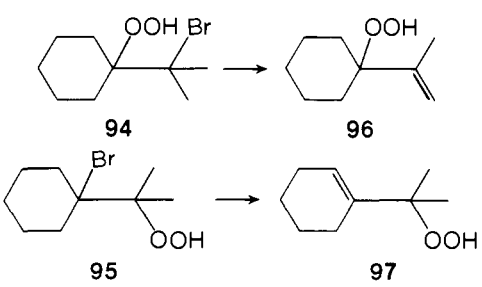
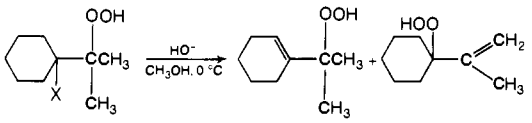
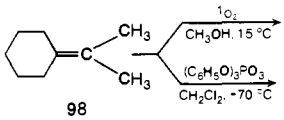
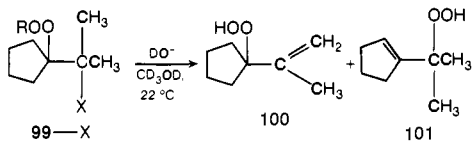


TABLE III

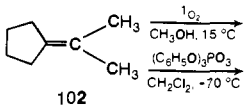


95—X 97 96

X	product distribution, %		total yield, %
Cl	93	7	98
Br	94	6	99
I	94	6	100
 98	10	90	
	0	100	99



99—X 100 101

X	R[a]	product distribution, %		total yield, %
Cl	PNB	23	77	99
Br	H	29	71	101
Br	PNB	26	74	95
I	H	29	71	
I	PNB	30	70	99
 102		42	58	84
		39	61	80

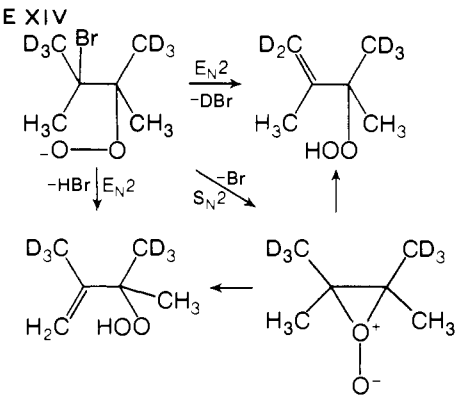
[a] PNB = *p*-nitrobenzoyl.

ane. Upon base treatment, **94** yielded **96,** and **95** yielded **97** exclusively, thus excluding the possibility of a common intermediate.

Kopecky[257] has independently studied the isopropylidene–cyclohexane and –cyclopentane systems and the data are presented in Table III. In the former system, Kopecky's research on analytically pure hydroperoxide **95** revealed a small amount of rearrangement that seems to have been undetected by Baldwin and Lever. Furthermore, the results for the cyclopentane system indicate that there has been substantial hydroperoxide migration probably via a perepoxide as originally suggested by Kopecky.[225,226] Since the product distribution for photooxygenation is substantially different from that observed in the dehydrobromination studies, it is likely that the perepoxide is not involved in the $^1O_2$ ene reaction of tetrasubstituted olefins.

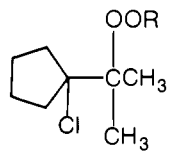
Dewar and Thiel[206] have suggested that this argument holds only if the dehydrobromination takes place entirely by a single mechanism and this they argue has not been established unambiguously. There is indeed a very reasonable alternative route

SCHEME XIV



from the bromo hydroperoxide to the allylic hydroperoxide which does not involve a peroxirane and that is an intramolecular E_N2 elimination (see Scheme XIV). If we assume its involvement, then the discrepancies can be resolved and the peroxirane may yet play a central role in both dehydrobromination and photooxidation.

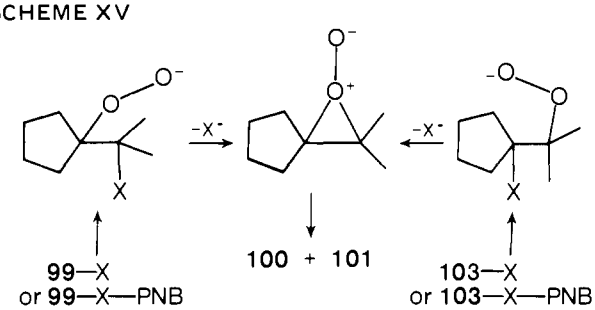
Kopecky,[257] however, has recently demonstrated that an E_N2 mechanism is not involved by the following pieces of experimental data. (1) The relative insensitivity of the product ratios to the nature of the leaving halide is evidence that both rearranged and unrearranged product are produced by *only one pathway involving a halogen-free intermediate.* (2) A 78:22 ratio of **101:100,** essentially the same as was obtained from **99**-Cl-PNB, resulted when a mixture of ~80% **99**-Cl and ~20% **103**-Cl was heated with base. Also, a 79:21 ratio of **101:100** was obtained from a mixture of 75% **99**-Cl-PNB and 25% **103**-Cl-PNB. The fact that these ratios are essentially the same as that obtained from pure **99**-Cl-PNB means that **103**-Cl and **103**-Cl-PNB are also converted exclusively to the perepoxide. Little if



103—Cl, R = H
103—Cl—PNB, R = PNB

any elimination can be occurring by a route that does not involve the perepoxide. A general scheme is given in Scheme XV.

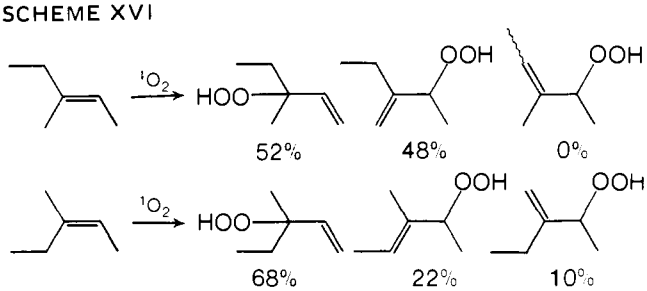
SCHEME XV



99—X or 99—X—PNB 100 + 101 103—X or 103—X—PNB

Let us close this discussion on the question of mechanism in the singlet oxygen "ene"reaction with one piece of evidence which does not seem to be in consonance with any of the current proposals.[376] Two groups[356,357] have recently observed site specificity in the $^1O_2$ ene reaction of trisubstituted olefins. Specifically, they found a strong preference for regiospecificity favoring hydrogen abstraction on that side of the olefin with two substituents. In other words, the overall reactivity of a given C–H bond is greater on the more crowded side of the trisubstituted ethylene. This is exemplified by the product distribution in the cases of (*E*)- and (*Z*)-3-methyl-2-pentene shown in Scheme XVI. Such results cannot be accommodated by a simple six-center concerted ene mechanism since steric considerations would appear to favor oxygen attack from the less hindered side.

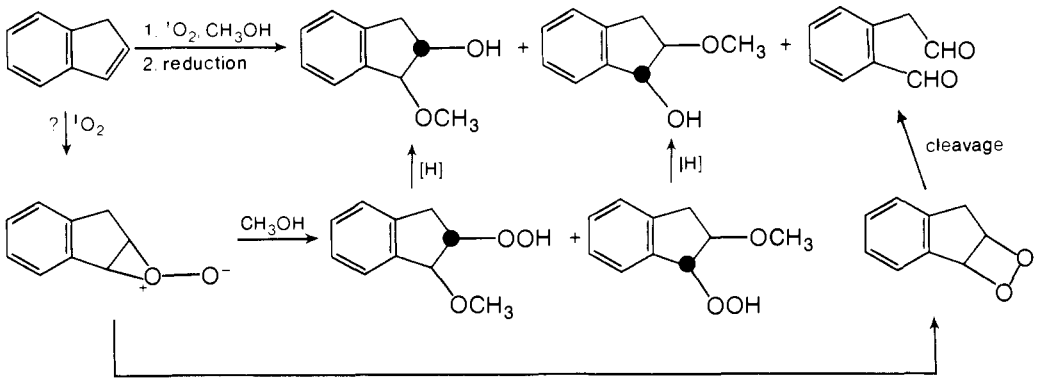
SCHEME XVI



52% 48% 0%

68% 22% 10%

SCHEME XVII



Likewise, it is not clear why a perepoxide should favor orientations leading to the observed products. Here we have a further example of the difficulties researchers in this field are having in obtaining a clear mechanistic picture.

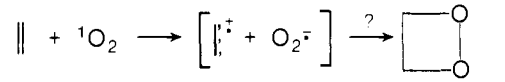
VII. Mechanism of Dioxetane Formation

The third mode of reaction exhibited by singlet oxygen is a 1,2-cycloaddition to olefins to form dioxetanes. State correlation diagrams[46,208,260-262] and orbital phase continuity diagrams[263] suggest, however, that a $[_\pi2_s + _\pi2_s]$ approach[185] is forbidden here, as it is with ethylene. Several alternate mechanisms may be considered.

(1) The 1,2-cycloaddition might proceed via a 1,4 diradical. Such a stepwise biradical addition of singlet oxygen, however, would be expected to lead to loss of configuration,[264] which is not the case. Bartlett and Schaap[2] have shown that the addition of singlet oxygen to both cis and trans isomers of diethoxyethylene is stereospecific 1,2-cis and gives the corresponding dioxetanes. Furthermore, dioxetane formation is not slowed down by the addition of radical inhibitors.[268] Hence we need not consider this mechanism any further.

(2) The dioxetane formation may proceed via zwitterionic 1,4-dipolar species. It has been well documented by Bartlett,[250,251] Huisgen[265-267] and Gompper[252] that many compounds which can act as dienophiles in the Diels–Alder reaction appear to react commonly with electron-rich olefins by the dipolar mechanism. One could expect this to be the case with singlet oxygen as well.[265]

(3 and 4) The concerted $[_\pi2_s + _\pi2_s]$ reaction is allowed through a transposition of the relative energy levels of the reactants as suggested by Kearns.[46,208,260-262] Foote[268] has noted, however, that the reaction is only allowed for the $[_\pi2_s + _\pi2_s]$ process when charge transfer from the olefin π orbital to the oxygen π^* orbitals can occur. This is a reasonable possibility with vinyl ethers, enamines, and other electron-rich olefins which have particularly low π ionization potentials. Thus, the addition might in fact be occurring by way of an electron transfer[268-273] (eq 25).



(25)

(5) The cycloaddition might occur via a concerted symmetry-allowed $[_\pi2_s + _\pi2_a]$ pathway,[185] as suggested by Bartlett.[16,28,40,250,251]

(6) The cycloaddition might proceed to dioxetane via a rate-determining formation of a perepoxide, a process which is theoretically allowed.[208,215,262]

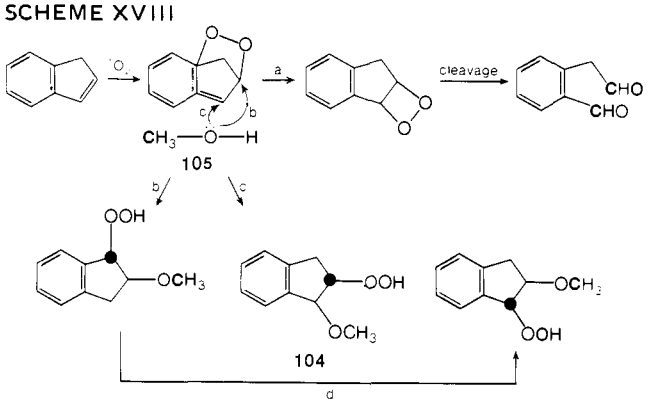
Some of the evidence regarding the mechanism of this reaction has been discussed in the previous section. In particular, the theoretical calculations of Dewar[205,206] favor a perepoxide intermediate on the way to a dioxetane in the case of normal olefins, but a zwitterion in the case of electron-rich olefins. "Spin and space symmetry conservation" criteria,[263] however, predict a $[2_s + 2_a]$ cycloaddition of $^1O_2$ to ethylene and a zwitterion in the case of aminopropylene. Let us turn now to some of the experimental data bearing on this issue. For convenience, the data will be grouped into three categories: (A) those that support a polar intermediate (perepoxide or zwitterion); (B) those that favor a concerted process (specifically $2_s + 2_a$); and (C) those that support a charge-transfer process as the initial step.

A. Evidence Supporting Polar Intermediates

(1) Photooxidation of indene[199] in methanol yielded, in addition to cleavage product, which is the sole product in inert solvent, several methanol addition products (Scheme XVII). Their origin was rationalized by assuming a perepoxide intermediate.

The system has been reinvestigated by Foote and co-workers.[29,30] Their evidence from low-temperature studies indicates that the initial intermediate formed is a 1,4-Diels–Alder adduct **105** which could then rearrange to the 2,3-dioxetane (see section

SCHEME XVIII

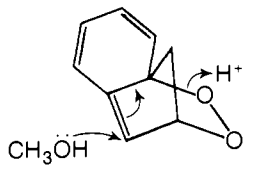


IV.A) followed by cleavage to form homophthalaldehyde (Scheme XVIII, path a). Addition products presumably result from nucleophilic attack on the 1,4-Diels–Alder adduct (paths b and c; see section IV.B) followed by a 1,3-allylic hydroperoxide shift (path d; see section III.B).[274]

Recently Jefford et al.[35] have attempted to resurrect Kearns' original proposal of a perepoxide by suggesting that nucleophilic attack upon the endoperoxide ought to proceed by an S_N2' process which should lead to a methoxyhydroperoxide of cis configuration in **104** while in fact only trans product is observed. They suggest, therefore, that indeed a perepoxide is involved which can undergo nucleophilic attack to give the desired all trans product.

It has long been assumed that S_N2' reactions proceed synfacially; i.e., the nucleophile attacks from the same side from which the leaving group leaves. There are, however, several well-documented exceptions.[360] It now appears that the stereochemistry of the S_N2' reaction may be either synfacial or

apofacial depending on the substrate and the nucleophile.[360] Considering, therefore, that endoperoxide **105** is a norbornene



105

analog,[361] the nucleophile in an S_N2' process (path c above) should approach preferentially from the exo side, resulting in apofacial stereochemistry, i.e., trans product.

(2) Photooxidation of 2,5-dimethyl-2,4-hexadiene (**106**) in neutral, basic (0.5 N NaOH) and acidic methanol gave the products shown in Scheme XIX.[189,275] Although not explicitly stated in the paper, while dioxetane cleavage products (**110** and acetone) are formed only under neutral conditions, the allylic hydroperoxide **109** is formed as a minor product under all conditions. Furthermore, its rate and amount of formation was independent of the pH of the methanol used.[277] The products from the basic and acidic methanol photooxidation, after reduction, were the same as obtained from basic and acidic cleavage of 2,5-dimethyl-2,4-hexadiene monoepoxide (**114**) and, furthermore, the products did not derive from the dioxetane (which was isolated and gave only cleavage product). Control experiments have shown that **107, 108,** and **111** are not formed from **106** in a dark reaction or from **109** or **110** under the reaction conditions; nor are **107, 108,** and **111** interconverted under the reaction conditions to an extent sufficient to account for the pH effect on product distribution. Kearns notes in passing[276] that solvent incorporation products analogous to the above were about 50% of the product mixture obtained from the photooxidation of *trans,trans*-2,4-hexadiene in neutral nucleophilic solvents. The remainder of the product was the endoperoxide which was the sole product in inert solvents.

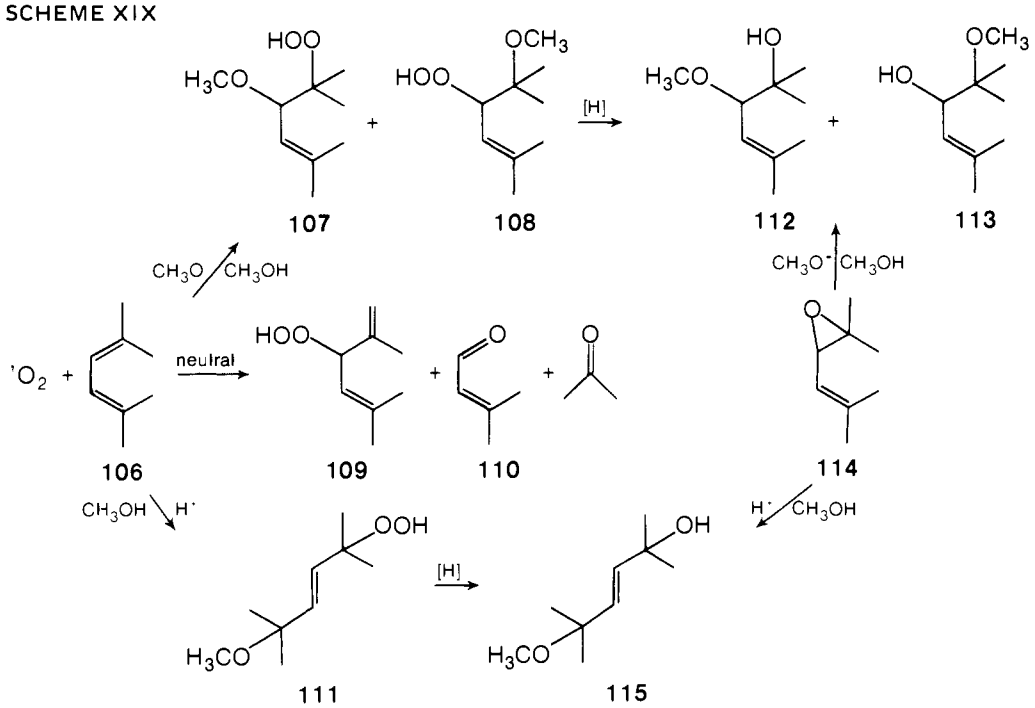
To rationalize the results, Kearns suggests the reactions in Scheme XX. The mechanism includes two concerted reactions (paths a and b) of singlet oxygen with diene to give allylic hydroperoxide and endoperoxide directly. A third, solvent-dependent reaction (path c), gives a peroxirane intermediate which can either react with solvent or rearrange to dioxetane.

Before we proceed, one important observation should be made. Kearns reports in this communication that the reactivity of **106** is greatest in methanol. This, however, is the very solvent in which the lifetime of singlet oxygen is the shortest![278] Such a situation indicates that an intermediate is formed which is in equilibrium with starting material and proceeds rapidly to product when trapped by the nucleophilic solvent. Unless we assume that perepoxide formation is reversible, the reaction for this solvent effect is by no means clear.

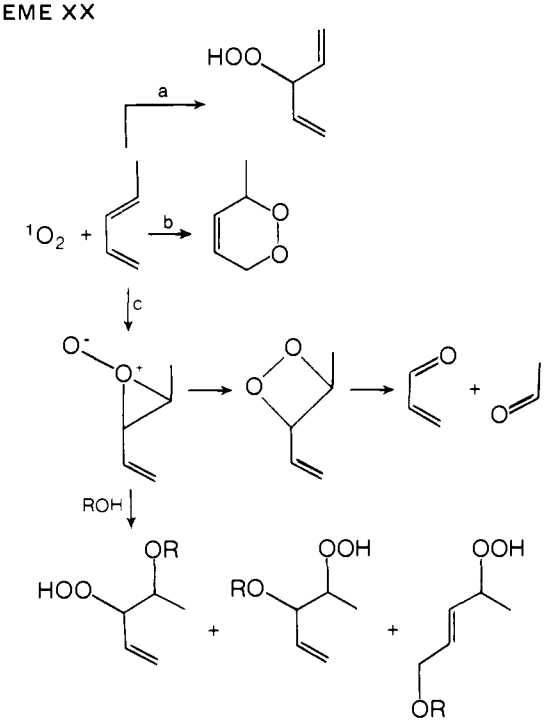
It seems to us[112b] that a more likely scheme can be drawn up to explain the observed products, which does not invoke the intermediacy of the elusive perepoxide, and does resolve the solvent effect. The mechanistic details in Scheme XXI are based on some of the same arguments presented by Foote[29] for the indene system and invokes the intermediacy of endoperoxide **117.**

Evidence for the formation of endoperoxide **117** has been reported recently by Tanielian and Chaineaux[355] who have

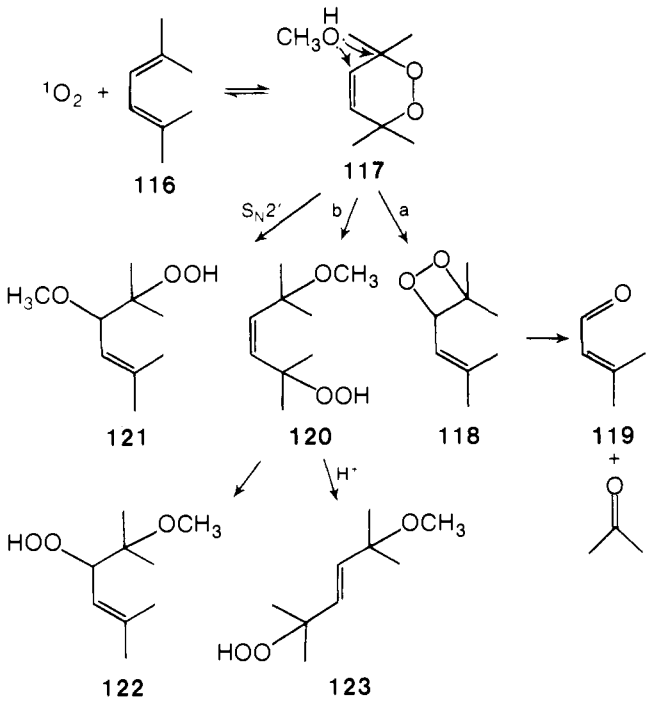
SCHEME XIX



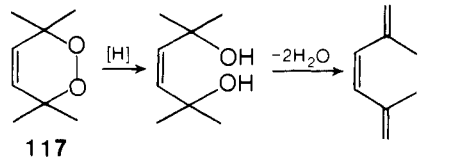
SCHEME XX



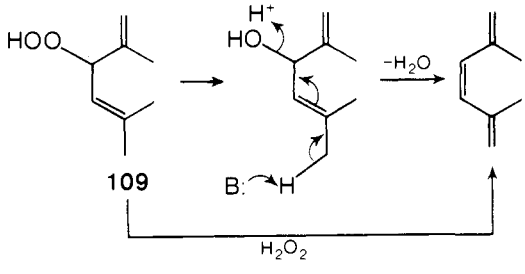
SCHEME XXI



identified 2,5-dimethyl-1,3,5-hexatriene as one of the products in the reduced reaction mixture. These authors posit that this triene must result from the double dehydration of 2,5-dimethylhex-3-ene-2,5-diol formed upon reduction of **117** (eq 26). This evidence is far from conclusive, however. It can well be argued that the reduction of **109** to the corresponding allylic alcohol and subsequent 1,4-dehydration would lead to the same triene. Alternatively, a 1,4-elimination of H_2O_2 from **109** directly may be involved (eq 27).

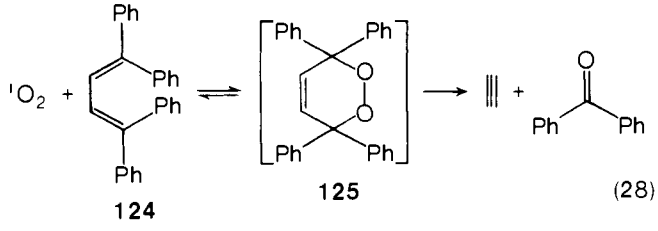


(26)



(27)

There is a related work in the literature which may be taken as precedent for the formation of such an endoperoxide, despite the extreme "reluctance" of 2,5-dimethyl-2,4-hexadiene to take an s-cisoid configuration,[190] requisite for a singlet O_2 [2 + 4] cycloaddition.[279] Rio and Berthelot[188] have reported that 1,1,4,4-tetraphenylbutadiene (**124**) reacted with singlet oxygen



(28)

to give a "photoxyde", presumably endoperoxide **125,** which decomposed to give either starting material and oxygen or acetylene and benzophenone. Reversible formation of the tetramethyl analog as well would explain the solvent effect.

Endoperoxide **117** once formed has two options. Pathway "a" involves rearrangement to give a dioxetane (see section IV.A) and subsequent cleavage products. Alternatively, the endoperoxide might be trapped by solvent to yield allylic hydroperoxide **120.** *cis*-**120** can isomerize in acid to give the more stable trans form (**123**) or undergo a 1,3-allylic hydroperoxide shift (see section II.B) to compound **122.** Finally, nucleophilic attack on the endoperoxide, most probably via an S_N2' mechanism, leads to methoxy hydroperoxide **121.**

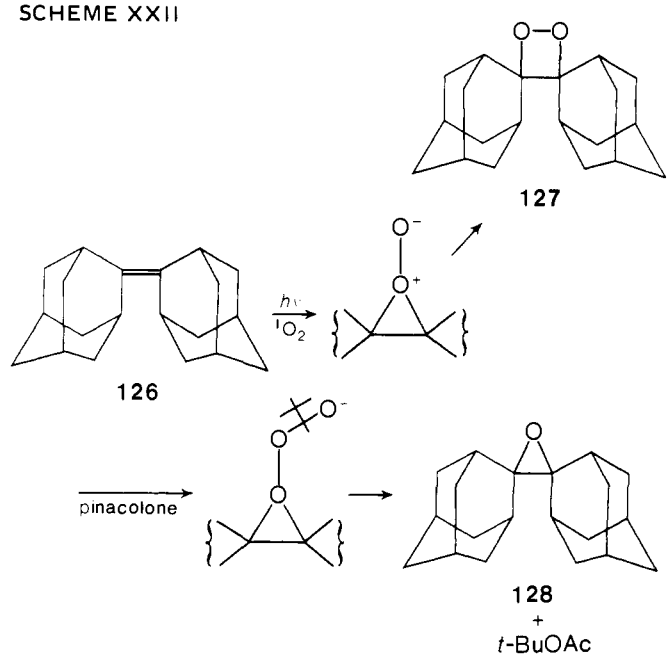
(3) Schaap[280] claims to have evidence indicating that the mode of attack by singlet oxygen is end-on to give a perepoxide which may subsequently rearrange. While photooxidation of 2,2′-biadamantylidene (**126**) in methylene chloride gives dioxetane **127** (ene product is precluded by Bredt's rule), photooxidation in pinacolone yields both dioxetane **127** and epoxide **128** with the concomitant formation of *tert*-butyl acetate (identified by VPC retention time only) (Scheme XXII). The latter was presumably formed by the deoxygenation of an intermediate perepoxide by a Baeyer–Villiger reaction with the solvent.

These results can, however, be discounted on several grounds: (1) Previous reports that pinacolone had the special property of stripping a single oxygen from ozonization intermediates[281,282] have been shown to be in error.[81,283,284] (2) In the related case of binorbornylidene,[40,285,286] all solvents tried yielded mixtures of dioxetane and epoxide, benzene yielding more epoxide than pinacolone and no solvent (including pinacolone) being detectably oxidized in the process. A series of comparable experiments showed that the same was true of biadamantylidene.[40,287]

While the pinacolone trapping experiment may well be discounted, the formation of epoxides as primary products in a variety of systems[40,280,282,288-290] would be suggestive of a role for a perepoxide. Indeed, it has been proposed by Bartlett[40] and Dewar[291] that the tailing oxygen of a perepoxide is removed by singlet oxygen itself, forming an epoxide and ozone.[182] This would be consistent with the increase in epoxide yield (with respect to dioxetane product) with decreasing olefin concentration.

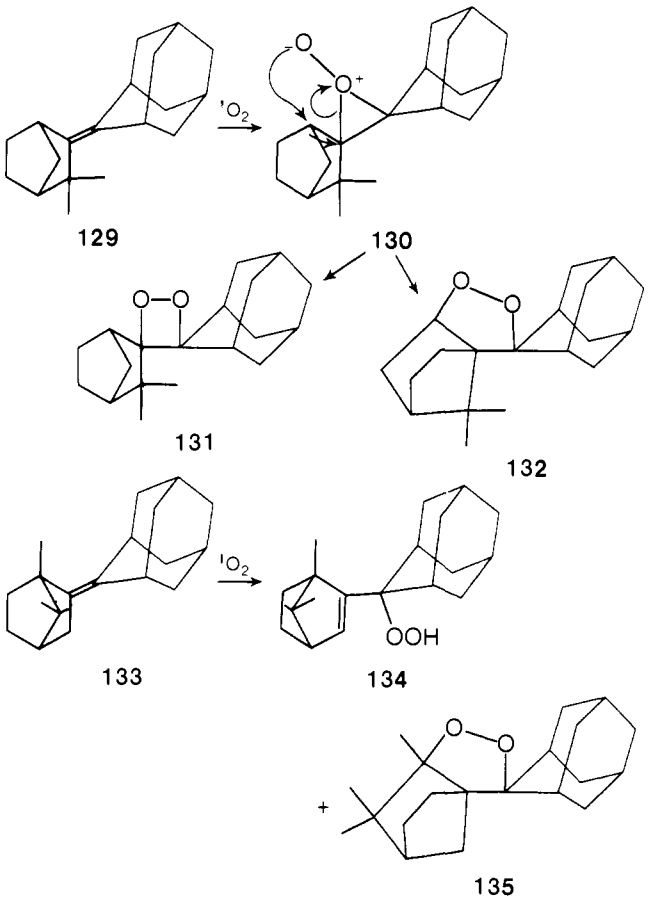
As interesting as this suggestion may be, recent evidence indicates that in actuality the epoxide is not a singlet oxygen product at all. For example, thermally generated $^1O_2$, from the

SCHEME XXII

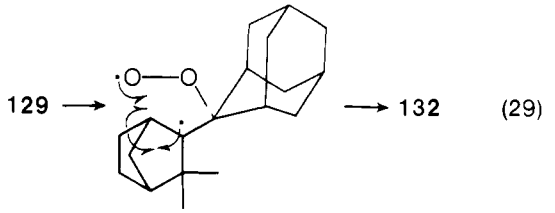


decomposition of triphenyl phosphite ozonide, reacts with biadamantylidene to produce dioxetane unaccompanied by epoxide.[292-294] Furthermore, the yield of epoxide depends on the sensitizer utilized[287,292,295] and may be dramatically reduced by the addition of free radical inhibitors such as 2,6-di(*tert*-butyl)-*p*-cresol. Bartlett and Shimizu[296] have also shown that the photooxidation of alkenes to epoxides, sensitized by biacetyl or benzil, does not involve singlet oxygen. It would thus seem that no evidence regarding perepoxide formation can be adduced from the formation of epoxides in the above systems. The story, however, is far from over.

McCapra and Beheshti[290] have recently studied the oxidation of camphenylideneadamantane (**129**) and adamantylidenecamphane (**133**). In the former case dioxetane **131** was observed, while in the latter allylic hydroperoxide **134** was obtained. In each case, however, an unexpected dioxolane (**132** and **135**) was formed. These authors suggest that the dioxolanes are rearrangement products of some highly polar intermediate, perhaps a perepoxide such as **130** in the case of **129.**



Parenthetically we would like to note that a radical process[370] of the kind in eq 29 could also conceivably explain the results. However, simple 1,2-migrations of alkyl groups in radical re-

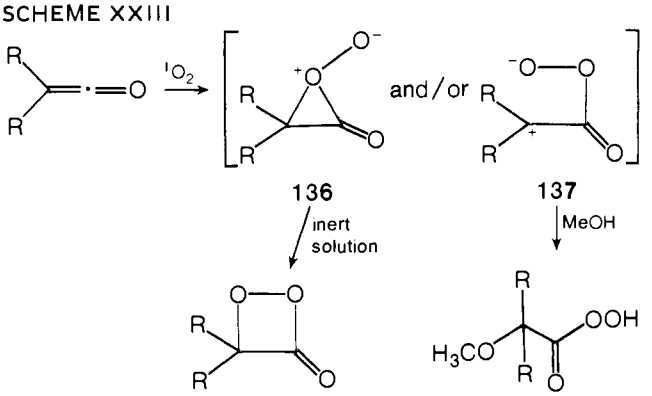


(29)

actions are not known to occur[297,298,339] even in substrates where the corresponding carbonium ion undergoes facile rearrangement. In particular, this has been shown to be the case for apobornyl[299] and the norbornyl radicals.[300]

Returning to the question at hand, McCapra and Beheshti conclude their paper by noting that in contrast to compounds **129**

SCHEME XXIII



and **133,** no rearrangements are observed in other unhindered olefins of the norbornene type; only products of the ene reaction are found. They consequently suggest that in hindered olefins rearrangement and dioxetane formation both derive from a polar intermediate whereas hydroperoxide is expected to form by a concerted mechanism.

Despite this evidence for the role of a polar intermediate, it may validly be argued that sterically hindered olefins are a unique case which demands end-on attack by singlet oxygen. The situation here resembles that of the related ozonolysis reaction of these olefins where, in addition to the normal trioxolane formation, a charged three-membered ring complex is inferred from the presence of epoxide in the products[301-304] as well as from low-temperature studies.[305] Hence, one needs to be wary about drawing general conclusions.

(4) The research groups of Turro and Adam[7] have recently reported that thermally generated $^1O_2$ (from the decomposition of $(PhO)_3PO_3$) reacts with ketones in inert solvents to yield α-peroxy lactones. However, in methanol, lactone formation is completely surpressed and α-methoxy peracids are produced instead. Since it was found that α-peroxy lactones are stable to methanol under the reaction conditions, they conclude that methanol has intercepted a precursor to the α-peroxy lactone, i.e., perepoxide **136** or zwitterion **137** (Scheme XXIII).

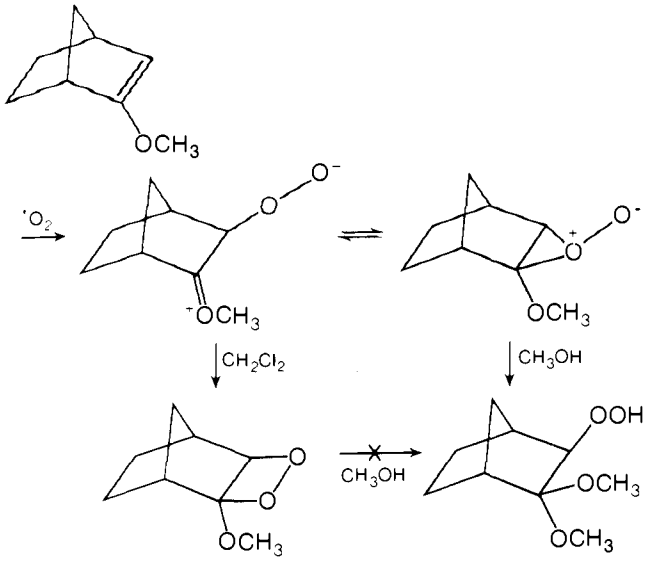
As in a previous case (section VI.D.10), the proof rests on the observation that α-peroxy lactones are stable to methanol under the reaction conditions. At higher temperatures, however, α-peroxy lactones are quite labile species.[306] Since singlet oxygen is an excited molecule, there are 22 kcal of excitation energy which come into play once product is formed. It is therefore plausible that under such conditions the hot peroxy lactone may undergo methanolysis even at −78 °C.

In response to this suggestion, Professor Adam argues that the reaction of $^1O_2$ with ketene to afford α-peroxy lactone is approximately isothermic, based on a simple thermochemical computation. Also, it would be expected that vibrational energy transfer to the medium is efficient. If not, the α-peroxy lactone would decarboxylate (a very exothermic process) rather than methanolize.[307] While Adam's argument seems reasonable, it does not rule out our suggestion completely.

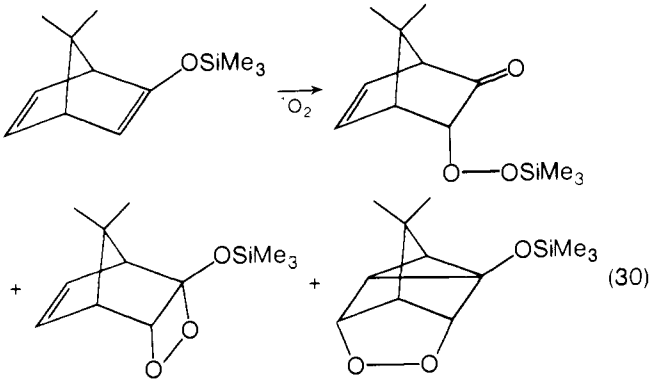
(5) Similar comments apply to the recent communication of Jefford and Rimbault.[369] The Swiss team reports that the photooxidation of 2-methoxynorborn-2-ene in inert solvents produced the corresponding dioxetane and its cleavage products. In methanol, however, an α-hydroperoxy dimethyl ketal is obtained. Since the isolated dioxetane is inert to solvolysis under the reaction conditions, the hydroperoxy ketal must result from the trapping of a polar intermediate, perhaps a zwitterion or a perepoxide.

As further proof for the formation of a dipolar species, these researchers report[330] that 7,7-dimethyl-2-trimethylsiloxy-2,5-norbornadiene reacts with $^1O_2$ in methanol to produce an endo-α-silylperoxy ketone (ene reaction), a trace of dioxetane, and, surprisingly, a nortricyclic peroxide derivative (see eq 30). Considering that cationic centers are readily captured by nor-

SCHEME XXIV



bornenyl double bonds producing nortricyclic product, the formation of such a system provides further proof for the initial formation of a dipolar species in the $^1O_2$ reaction of electron rich olefins.

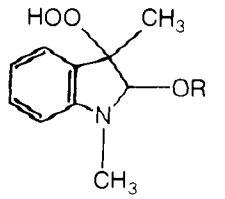


(30)

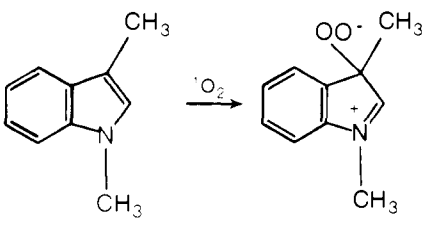
Here too we remind the reader that control experiments on ground-state dioxetanes may bear little relevance to the corresponding "hot" species such as is probably formed subsequent to the combination of $^1O_2$ with the enol ether. In the two cases cited above, the "hot" dioxetane products formed may readily undergo solvolyses or rearrangements not observed in the cool ground state.

(6) Photooxidation of 1,3-dimethylindole (**138**) at room temperature gives cleavage products (**139**) in nearly quantitative yield.[308,309] However, photooxidation in alcoholic solvent at −70 °C led to the formation of the hydroperoxyindolines **140a-c** depending on the exact alcohol used. Similarly, compounds **143a,b** react at room temperature to give cleavage products, but photooxidation at −70 °C gives **147.** The authors posit that these results clearly indicate that the initial intermediate is a peroxide capable of undergoing the addition of alcohols and secondary amines even at low temperature. The authors suggest that the results may be explained most reasonably in terms of a stepwise mechanism involving a zwitterion such as **141** and **144** which is intercepted by nucleophiles at low temperature to give hydroperoxides (**140** and **147**) or rearrange to dioxetanes at room temperature.

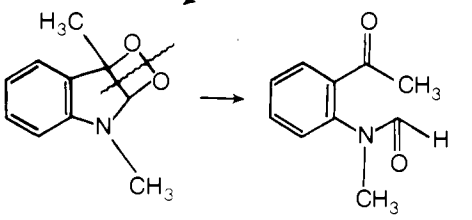
As has been done by other authors, Saito et al. in this analysis reject a concerted formation of a dioxetane, assuming that dioxetanes do not react with nucleophiles. However, as we have demonstrated in section II.B, dioxetanes substituted with heteroatoms do indeed undergo nucleophilic attack by alcohols. The temperature effect is readily understood in terms of the stability of the dioxetane to cleavage. We have noted in section



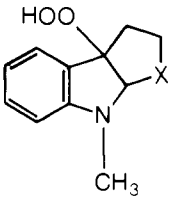
140a, R = Me
b, R = Et
c, R = CD_3



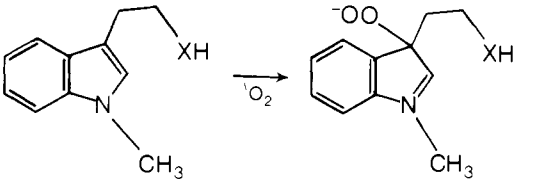
138 **141**



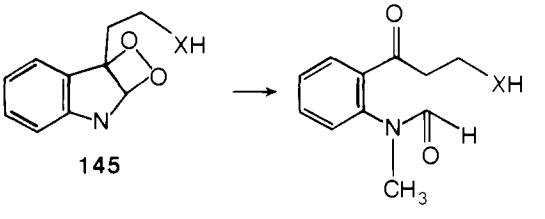
142 **139**



147



143a, X = O
b, X = NCO_2Me **144**



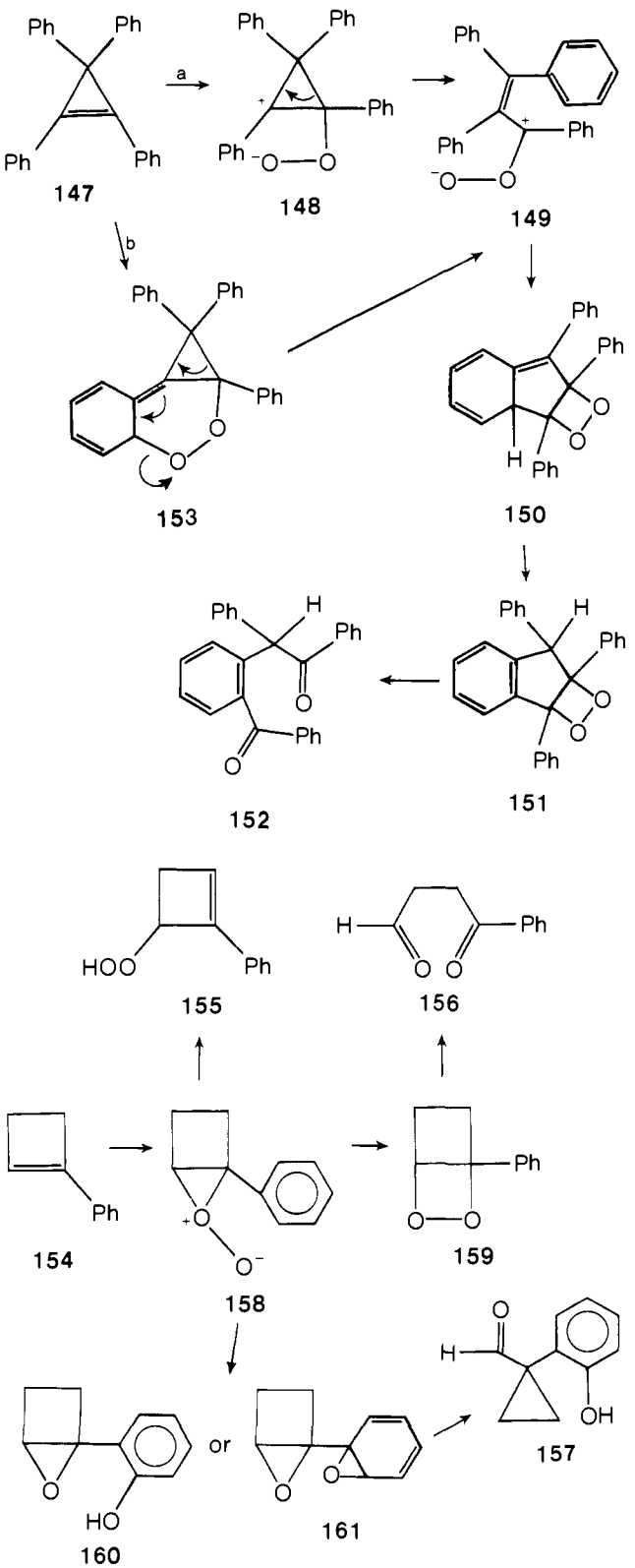
145 **146**

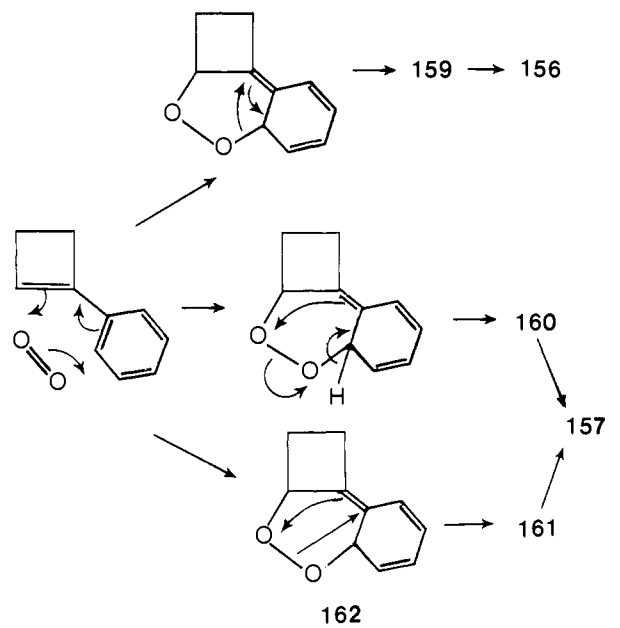
II.A that the rate of decomposition of dioxetanes is catalyzed by electron donors such as amines.[59] Hence it is not surprising that these amine dioxetanes should cleave readily at higher temperatures. At −78 °C, however, they are stable enough to be trapped by solvent or intramolecularly by alcohol or amines on a side chain.

(7) Politizer and Griffin[310,377] report that the photooxidation of tetraphenylcyclopropene (**147**) yields diketone **152** (the cleavage product of indene dioxetane **151**) as the major product. They propose that such a rearrangement requires dipolar intermediates such as zwitterion **148** which proceeds via several other intermediates (**149** and **150**) to the final observed product (path a). The reader is reminded that vinyl aromatics readily undergo a Diels–Alder reaction with $^1O_2$. Thus as inviting as this proposal may be, a more likely course of events involves (path b) initial formation of an endoperoxide (**153**) which then cleaves to zwitterion **149.** The endoperoxide and its oxidation products undoubtedly account for the large yields of polymer obtained.[347]

(8) A similar argument applies to the photooxidation of phenylcyclobutene **154** which yields hydroperoxide **155,** ketoaldehyde **156,** cyclopropanal **157,** and substantial amounts of polymer.[33] Jefford and Rimbault[33] prefer a perepoxide **158** (although a zwitterion would serve just as well) as the initially formed intermediate which rearranges to allylic hydroperoxide **155** and dioxetane **159** or undergoes inter- or intramolecular oxygenation to yield epoxycyclobutanes **160** or **161.** Either of the latter could rearrange to cyclopropanals **157,** a precedented process.

Here, too, however, a polar intermediate is not required, with the formation of an endoperoxide (**162**) much more probable. The latter could rearrange to dioxetane product **159** (see section IV.A), to a bisepoxide **161** (section IV.A) or to phenol **160.**[329] Either of the latter two compounds could rearrange to cyclopropanal **157.** (The formation of hydroperoxide **155** has been discussed in section VI.D.13.)



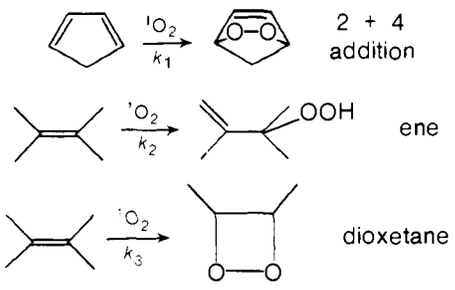


B. Evidence Supporting a Concerted Process

(1) Bartlett et al.[1b,2a] have shown (see Chart V) that all three modes of oxygen attack show nearly the same polar solvent response. Since the [2 + 4] addition is generally assumed to proceed in a concerted manner, as discussed above, a dipolar zwitterionic intermediate in dioxetane formation is improbable (at least for symmetrically substituted olefins). If, however, the transition state in all three cases occurs early and is reactant like and hence relatively nonpolar (as is indeed suggested by the MINDO/3 calculations of Dewar and Thiel[206]), then we would not expect substantially differing polar solvent responses even if ultimately polar intermediates were involved.[112a]

(2) In the case of enol ethers where ene reaction and [2 + 2] cycloaddition compete, polar solvents favor dioxetane formation (refs 1b, 2a, 51, 112, 227, 311). In the particular case of dihydropyran, a solvent effect of about 50-fold was observed between benzene and acetonitrile. In attempting to resolve this result with that cited in point 1 above, Bartlett suggested[1b,2a,311] that the significant difference between the cases must be that between symmetrical and unsymmetrical substitution at the ends

CHART V



	dodecane	acetonitrile
k_1/k_2 =	1.2	2.0

	benzene	acetone	acetonitrile
k_2/k_3 =	0.82	1.58	1.10

of the double bond. The polar solvent response, however, is not great enough to correspond to formation of a dipolar intermediate, where a range of four powers of ten is not unexpected[312] (see, however, point 1 above). It might, however, correspond to a radical reaction with substantial polar character[313] (see, however, section VI.A), or more probably to a concerted reaction with some charge transfer at the transition state.[265,266] The proposal[16] of a peroxirane as a common intermediate in the formation of dioxetane and allylic hydroperoxides might also accommodate the polar solvent dependence of dioxetane formation, although it does not predict the manner in which the partition between these products responds to the medium.

There is yet another interpretation of the results. As noted previously, MINDO/3 calculations[206] indicate that the addition of $^1O_2$ to -*E*-substituted olefins involves initial and rate-determining formation of a zwitterion. Since the transition state for this step is relatively early and nonpolar, changes in solvent should have little effect on the overall rate of conversion of dihydropyran. However, the relative amounts of dioxetane (formed directly from the zwitterion) and allylic hydroperoxides (formed via a perepoxide) should vary markedly with the polarity of the solvent since the transition states for their formation have widely different dipole moments (8.59 and 9.94 D, respectively); an increase in the polarity of the solvent should and indeed does favor formation of the dioxetane.[112a]

(3) Bartlett[1b] notes that it is suggestive that the reactivity ratio between *cis*- and *trans*-diethoxyethylenes is 3.4 in favor of the former. This evidence associates this reaction as to stereochemical dependence with the ketene [$_\pi 2_a + _\pi 2_s$] cycloadditions in direction, if not in magnitude. By way of contrast, toward hexachloropentadiene, the trans isomer reacts 13.5 times faster than the cis.

(4) As mentioned above (section VI.D.6), the photooxidation of 4-methyl-2,3-dihydro-γ-pyran[112b,227] (compound **62**) in polar solvents yields primarily dioxetane product. Its 4,4-dimethyl analog (compound **63**) yields cleavage product exclusively, as expected. Interestingly, while the secondary kinetic isotope effect (see Table I) for C_5 is inverse ($k_H/k_D \sim 0.9$), that for C_6 is normal ($k_H/k_D > 0$). These results rule out an early transition state[206] since a k_H/k_D of approximately 0.9 corresponds[314] to nearly complete rehybridization from sp^2 to sp^3. The results would also seem to rule out a simple perepoxide since for C_6 an inverse effect should have been observed. The results might well correspond to a zwitterion,[206] but the normal values are a bit troublesome.

It should be noted, however, that it is not uncommon in [2 + 2] cycloadditions for one end of a double bond to show an inverse effect, while the other shows a normal effect. Koerner von Gustorf et al.[315] reported that in the cycloaddition of azodicarboxylates with vinyl ethers, the position α to the ether shows a normal secondary isotope effect ($k_H/k_D = 1.12$), while the β position shows an inverse effect ($k_H/k_D = .83$). Similarly, Baldwin and Kapecki[373] reported that in the addition of diphenylketene to deuteriostyrenes, secondary effects for the reaction are $k_H/k_D = 0.91$ at the β position and 1.23 at the α position of styrene at 65 °C. We note, of course, that both the addition of ketene[185,316,374] and singlet oxygen to olefins have been classified as concerted [$_s 2 + _a 2$] processes. According to Baldwin and Kapecki[373] the normal value observed is a result of hyperconjugative interactions resulting from geometrical and/or orbital symmetry constraints. Alder, Baker, and Brown,[317] however, argue that the normal value observed is more likely associated with the twisting of the sp^2 carbon out of conjugation with the neighboring p orbitals as required by a $_s 2 + _a 2$ cycloaddition. Presumably the difference in moments of inertia between an RCD and an RCH group makes an important contribution to the isotope effect.

TABLE IV. Relative Rates of Photooxidation for 4,4-Dimethyl-2,3-dihydro-γ-pyran (63)

solvent	sensitizer[a]	K_{rel}	E_T[318]	$^1O_2$ lifetime[319] μs
C_6H_6	TPP	1	34.5	24
THF	TPP	1.6	37.5	
$CHCl_3$	MB	3.1	39.1	60
$CHCl_3$	TPP	3.6	39.1	60
CH_3CN	MB	6.0	46.0	30

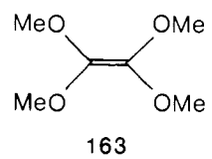
[a] TPP = tetraphenylporphyrin; MB = methylene blue.

It is also revealing that dioxetane formation seems to proceed at a faster rate as solvent polarity is increased. As seen from Table IV,[227] while the rate of photooxidation of **63** does not correlate with the singlet oxygen lifetimes for the given solvents,[319] it does correlate nicely with the solvent polarity as measured by the E_T values.[318]

Ketene additions, which as noted above, have been classified as [$_s 2 + _a 2$] processes, show a similar effect. Huisgen[320] has studied the dimerization of dimethylketene and reported that the rate of reaction increased 30-fold in going from CCl_4 to acetonitrile. They conclude that, while the reaction is probably concerted, there is unequal bond formation and partial charge separation in the transition state.[321]

C. Evidence Supporting a Charge-Transfer Mechanism

(1) A study of a series of olefins by cyclic voltametry indicates that there is a correlation between an olefin's reduction potential (olefin + $e^- \rightarrow$ [olefin]$^-$) and its mode of reaction.[322] Those olefins (e.g., compounds **163** + **164**) whose reduction potential is below that of singlet oxygen [$^1O_2 + e^- \rightarrow O_2^-$] react to give dioxetanes, while those whose reduction potential is above that of singlet oxygen are either totally unreactive or react sluggishly



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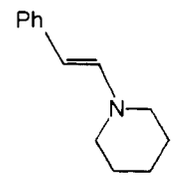

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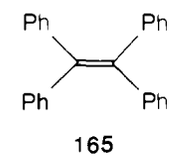

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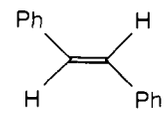

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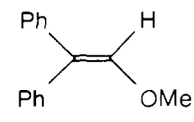

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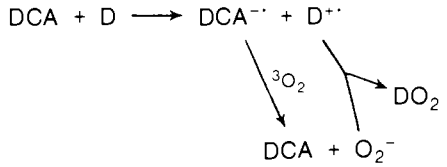
and by other modes (e.g., compounds **165–167** react by a Diels–Alder mode).

(2) Foote[271] has recently described a new type of photooxidation using electron-poor sensitizers such as dicyanoanthracene (DCA). These sensitizers appear to abstract an electron from the donor (D) to give a donor radical cation–sensitizer radical anion pair. Triplet oxygen accepts an electron from the sensitizer radical anion to give a donor radical cation–superoxide pair, which is the complex required in the singlet oxygen electron-transfer mechanism. The products of this reaction are the same as those of the donor with singlet oxygen, but the reaction does not involve singlet oxygen. It appears to proceed by way



of singlet sensitizer, and several acceptors which do not react with $^1O_2$ react well in this reaction.

Recent work by Frimer et al.[111,375] would seem to argue, however, against this electron or charge transfer as the rate-determining process in $^1O_2$ reactions. They report that acyclic 1-cyclopropyl olefins react at approximately the same rate as the corresponding methyl analogs, despite the fact that the former have substantially lower ionization potentials (IP). For example, tetramethylethylene (IP 8.30)[334] reacts three times faster than 1,1-dicylopropyl-2-methylpropene (IP 7.82).[335] Were electron or charge transfer the rate-determining step, one would have expected the vinylcyclopropane to react several orders of magnitude faster.

VIII. Conclusions

It was the hope of this author that a critical evaluation of the evidence would enable one to draw some clear conclusions regarding the mechanism of the singlet oxygen ene and dioxetane forming reactions. As the reader has by now surmised, no definite conclusions can yet be drawn. Much of the evidence is circumstantial or involves substrates with specialized physical or chemical properties which preclude ready generalization of the results. Nevertheless, some trends have emerged. For example, alkylated olefins seem to favor a concerted ene mechanism with perhaps some antarafacial component at times. For olefins such as enol ethers, in which mesomeric effects can readily come into play, the ene reaction probably proceeds via polar intermediates. However, the mechanism of [2 + 2] cycloaddition of $^1O_2$ to olefins to yield dioxetanes has still to be unraveled.

While the picture remains hazy, we trust that we have allowed future researchers to properly evaluate and analyze past and future work in this field. This should in turn allow them to plan the long-awaited decisive experiments which will, once and for all, resolve the mechanistic details of the $^1O_2$ attack on π systems.

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