Chem. Rev. **1991**, *91*, 335–362

Preparation, Properties, and Reactions of Carbonyl Oxides

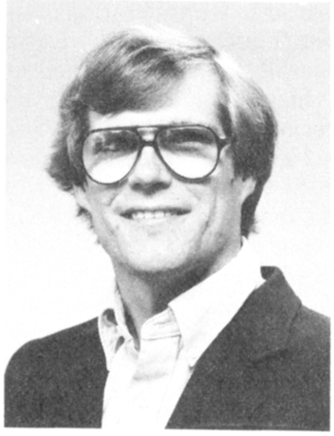
WILLIAM H. BUNNELLE

Department of Chemistry, University of Missouri—Columbia, Columbia, Missouri 65211

Received August 17, 1990 (Revised Manuscript Received November 15, 1990)

Contents

- I. Introduction 335
- II. Computational Studies 336
  - A. Ab Initio Calculations 336
  - B. Semiemprical Calculations 337
  - C. Reaction Energetics and Dynamics 338
- III. Preparation of Carbonyl Oxides 339
  - A. Alkene Ozonolysis 339
  - B. Carbonyl Oxides from Carbene–O_2 Reactions 343
  - C. Singlet Oxygen Reaction with Diazoalkanes 346
  - D. Photooxygenation of Other C=X Systems 346
  - E. Carbonyl Oxides from Furan Endoperoxides and Other 1,2,4-Trioxolanes 347
- IV. Reactions of Carbonyl Oxides 348
  - A. Nucleophilic Trapping 348
  - B. Cycloadditions 349
    - 1. Cycloaddition with the C=O Group 349
    - 2. Cycloadditions to Alkenes 351
    - 3. Other Dipolarophiles 352
    - 4. Dimerization 352
  - C. Isomerization of Carbonyl Oxides 352
    - 1. Syn–Anti Stereoisomerism 352
    - 2. Cyclization to Dioxirane 354
    - 3. Tautomerization of Carbonyl Oxides 355
  - D. Oxygen-Transfer Reactions 356
    - 1. Models for Biochemical Oxidations 356
    - 2. Oxygen Atom Loss 356
    - 3. Alkene Epoxidation 357
    - 4. Baeyer-Villiger Oxidation 358
    - 5. Oxidation at Sulfur 359
- V. Conclusion 360



Bill Bunnelle was born in Chicago in 1955. He received the bachelor's degree in chemistry from Wittenberg University (Ohio) and went on to graduate work at The University of Chicago with Philip Eaton, completing the Ph.D. in 1982. After three years on the faculty at the College of William and Mary in Virginia, he moved to the University of Missouri—Columbia where he is presently Assistant Professor of Chemistry. His research interests lie in the area of synthetic and mechanistic organic chemistry, with a current emphasis on studies of the formation and reactions of novel peroxides from alkene ozonolysis. Untold sacrifices have been made in his behalf by his wife Leslie and sons, Eric and Kurt, and this effort is dedicated to them.

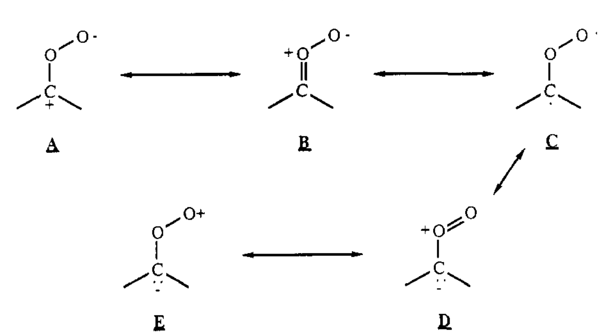
I. Introduction

In 1949, Criegee postulated the existence of carbonyl oxides as intermediates in the ozonolysis of alkenes.[1] During the next three decades, vigorous effort was directed at verifying the "Criegee mechanism" for alkene ozonolysis. By the mid 1970's, the basic Criegee mechanism had been confirmed, although subtle features such as the stereoselectivity of the process continue to stimulate refinements of the mechanistic scheme. Most impressively, sufficient evidence was accumulated to confirm beyond any reasonable doubt the involvement of carbonyl oxide in this process, even though the intermediate could not be detected directly. This effort has been clearly documented in Bailey's recent monographs.[2]

During the last 10–15 years, much more has been learned about the structure, reactivity, and nature of carbonyl oxides. New methods for the generation of these species have permitted their spectroscopic characterization, and sophisticated computational techniques have shed light on the structural and electronic features of these systems and helped to define the likely modes of reactivity for these intermediates. The role of carbonyl oxides has been expanded to include a prominent involvement in the chemistry of urban air pollution,[3] and as chemical mimics of biological oxygen transfer systems.[4] Finally, the recent development of the chemistry of dioxiranes, the cyclic isomers of carbonyl oxides, has stimulated a great deal of interest in the relationships between these species. The chemistry of dioxiranes has been the subject of recent reviews.[5]

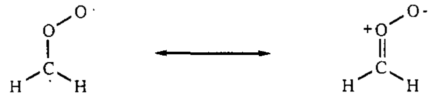
The electronic nature and structure of the carbonyl oxide intermediate has intrigued chemists for years, and has generated a certain amount of confusion. The original formulation as a zwitterion (A, or the resonance form B), has perhaps been most comfortable to organic chemists, since it permits a convenient "Lewis-dot" representation (B) which adequately accounts for much of the observed chemistry. Thus, as outlined below, carbonyl oxides readily add nucleophiles at carbon, and engage in cycloadditions as typical 1,3-dipoles. On the other hand, high-level computational methods consistently demonstrate that carbonyl oxides are more properly represented by a singlet diradical ground state (C). While the significance of the difference between structures such as B and C is discussed more fully be-

0009-2665/91/0791-0335$09.50/0



(1)

low, it will be noted here that the conflict over electronic structures has led to a proliferation of nomenclature for these systems. Thus, while carbonyl oxide is probably the most generally recognized term, and will be used throughout this review, the association of this name with a zwitterionic structure has led some authors to refer to these as dioxymethylenes or peroxymethylenes, more in accord with the diradical representation C. Others choose more simply (and with appropriate recognition for the founder of this field) to call this class of compounds "Criegee intermediates". For indexing purposes, *Chemical Abstracts* uses, unfortunately, two nomenclature systems. Thus, the parent compound is indexed either under the heading "methyl, dioxy-" (corresponding to the diradical structure **1a**) or as the derivative "oxonium, hydroxymethylene-, hydroxide, inner salt" (corresponding to the zwitterion **1b**). Other derivatives have been indexed under one or the other system, but not necessarily both. This is clearly an area where greater uniformity would be desirable. Since the current view of carbonyl oxides favors a diradical structure, nomenclature systems which reflect this can be recommended, but it must be recognized that the zwitterionic formulation (especially for structural representations which may influence the way these compounds are indexed) is deeply ingrained in common usage, and it is probably unrealistic to expect immediate consensus on this point. Throughout this review, the diradical structural representation will be used. Except for the simplest carbonyl oxides, the Chemical Abstracts names are too cumbersome for frequent reference. Instead, these derivatives will be named as "oxide" derivatives of the corresponding carbonyl compound, or by listing the substituents with the root "carbonyl oxide".



(2)

1a

(Dioxymethyl)

1b

Hydroxymethyleneoxonium hydroxide, inner salt

Carbonyl oxides have been implicated in a number of different processes involving a broad range of reaction types, and covering the gamut of temperatures and physical states. As a result, these intermediates have been studied from a variety of perspectives. Three distinct experimental regimes can be identified: the gas-phase chemistry of carbonyl oxides, investigations of these intermediates generated in frozen, inert matrices, and processes involving carbonyl oxides which occur in solution. Such a division is, however, artificial, since there is considerable overlap for the chemistry observed under these different reaction conditions. Certainly, investigations in each area have produced results which are important to the other two. Previous reviews have focused on aspects of gas-phase[3,6] and solution-phase[2,7] ozonolysis. More recently, Kafafi, Martinez, and Herron[8] have provided a concise summary of the major reaction pathways to and from the Criegee intermediate. Likewise, Sander's very recent review[9] focuses on the spectroscopic characterization of carbonyl oxides, particularly in matrix isolation. The object of the present article is to provide a broader overview of the recent developments in the chemistry of carbonyl oxides. Particular emphasis is placed on features which control the reactivity of carbonyl oxides under various conditions, and especially the connections between results obtained in gas-phase, matrix, and solution studies. The organization of topics reflects this emphasis—a systematic survey of the methods for generation of carbonyl oxides, and a summary of the known reactions are presented with appropriate juxtaposition of relevant results from matrix, solution, or gas-phase experiments.

II. Computational Studies

A. Ab Initio Calculations

Quite a large number of computational studies of the ozonolysis reaction, and of the carbonyl oxide intermediate in particular, have been reported over the past 20 years,[10-23] Since it is only recently that direct experimental detection of carbonyl oxides has become possible, and because relatively limited structural data is so far available from those studies, theoretical calculations have played a significant role in the development of questions relating to the structure and reactivity of carbonyl oxides. Accurate computations can provide much insight regarding the energetics of these species, including an assessment of the likely reactivity patterns, which has otherwise been difficult to obtain. On the other hand, progress toward the development of reliable theoretical models has been hard-won. Carbonyl oxides have turned out to provide a difficult challenge for computational methods. Calculations based solely on restricted Hartree–Fock (RHF) theory[10] are not suitable for compounds like 1, since the RHF method has a built in bias toward zwitterionic (closed-shell) states. In addition, corrections to account for electron correlation are required.[11-15]

Harding and Goddard[13] found that generalized valence bond (GVB-CI) calculations described the ground state of 1 as a singlet diradical (**1a**), while the zwitterionic form **1b** was found to be an excited state some 92 kcal/mol higher in energy. The authors considered this energy difference, however, to be artifically large and carried out a simple model calculation which provided a revised estimate for the radical–zwitterion energy difference of about 23 kcal/mol.[13] Moreove, it was concluded that substituent or solvent effects could reduce this gap substantially, even to place the zwitterion lower in energy than the singlet biradical. Thus, the electronic nature of the carbonyl oxides may depend critically on their environment.

More recently, high-level calculations, starting with either the restricted (RHF)[15,19] or unrestricted (UHF)[8,14,16] Hartree–Fock wave function, with increasing elaborate correction for electron correlation by

TABLE I. Ab Initio Geometries^a and Energies^b for Dioxymethyl

method	OO length	CO length	CH (syn)	CH (anti)	COO angle	HsCO angle	HaCO angle	energy	ref
RHF/DZ	1.48^c	1.44^c	1.09^c	1.09^c	115			−188.43780	10
6×6CI/4-31G//RHF/STO-3G	1.269	1.367			117.5	120^c	120^c	−188.27181	11a
GVB(3)-CI/DZ+P	1.362	1.343	1.08^c	1.08^c	116.6	120^c	120^c	−188.75614	13b
UHF-CI/4-31G//UHF/4-31G	1.367	1.384			114.0	113.7		−188.52930	14b
MP2/6-31G*	1.295	1.297	1.083	1.079	120.3	118.0	114.3	−189.05283	15a
MC-CI/DZ+P//MCSCF/DZ+P	1.262	1.277	1.09^c	1.09^c	119.3			−188.98630	12a
CASSCF/DZ+P	1.313	1.275	1.068	1.065	119.5	119.1	118.5	−188.96420	12b
UMP3/6-31G*	1.292	1.325		1.082	117.1	118.2	114.7	−189.04040	8
MP4/6-31G*	1.329	1.274	1.086	1.083	119.2	118.6	115.3	−189.07021	19b
MP4(SDTQ)/6-31G**	1.306	1.314	1.081	1.077	119.8	118.3	114.3	−189.10975	15b
QCISD(T)/6-31G**	1.356	1.287	1.080	1.078	119.1	118.8	115.3	−189.11139	15b

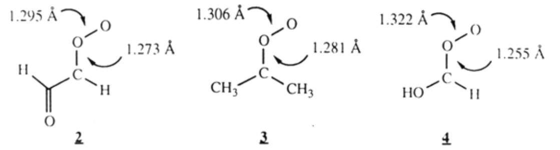
^{a} Bond distances are in Angstroms, bond angles in degrees. ^{b} Energies in Hartree. ^{c} Parameter not optimized.

either peturbation (Rayleigh–Schrödinger–Møller–Plesset (RSMP), hereafter MP) or configuration interaction (CI) techniques, have been used for theoretical studies of 1. For comparison, optimized geometric parameters from some of these studies are collected in Table I. It can be seen that a fairly consistent geometry for 1 emerges. In all cases, the molecule is planar, with bond angles near 120°. The CO and OO bond distances are approximately equal, each fluctuating around 1.3 Å, depending on the exact method. The computed geometries are consistent with significant double bond character for both C–O and O–O. This has been interpreted in terms of an electronic structure representing a superposition of the resonance forms **1a** and **1b**, i.e., a singlet biradical admixed with a zwitterion. Thus, for Cremer's QCISD(T) calculations,[15b] the CO length is somewhat shorter than that found by Goddard for the GVB diradical state **1a**, as expected for some contribution of the zwitterion form **1b**. Unfortunately, the precise bond distances for the heavy atoms are quite sensitive to the computation method employed, and no distinct trend is discernible. For example, Cremer's calculations with second-order Møller–Plesset perturbation theory (MP2) lead to nearly identical distances for the CO and OO bonds.[15a] Improvement to the MP4(SDQ) (single, double, and quadruple excitations included) level results in lowering of the total energy, along with a shorter CO bond and lengthening of the OO bond.[19b] On the other hand, inclusion of triple excitations at the MP4 level (MP4(SDTQ)) causes a reversal in the relative lengths of CO vs OO bond. An alternate method for computating correlation energy is quadratic configuration interaction. When this is applied using single, double, and triple excitations (QCISD(T)), the carbonyl oxide structure has bond distances CO > OO. At present, there seems to be no clear choice as to which method is superior, or which geometry is more reasonable. The QCISD(T) total energy is lower than that for MP4(SDTQ), and so Cremer argues in favor of this method,[15b] in part because the calculated geometry implies a larger contribution of the zwitterionic structure **1b**. Nevertheless, the fact that the different computational methods do not appear to converge on a consistent structure is disconcerting, and so evaluation of the extent of zwitterion vs diradical character on the basis of geometry remains somewhat arbitrary.

As mentioned in the introduction, the conflict over representation of the carbonyl oxide as diradical vs zwitterion has definitely had a significant impact on nomenclature. Although at first glance one might expect dramatically different reactivity for a diradical vs a zwitterion, in fact, as Bailey has pointed out,[2] these represent points on a continuum of electronic structure, and we can actually anticipate varying reactivity profiles depending on the circumstances. Thus, as Cremer has stated,[15a] the question of diradical vs zwitterionic ground state becomes somewhat academic. As described above, high-level ab initio calculations uniformly predict that the carbonyl oxide electronic structure is best represented as a superposition of biradical and zwitterionic states—both characters are expressed, although the former presumably dominates. The difference in energy between UHF and RHF wavefunctions has been proposed as a measure of diradical character; by this criterion, a carbonyl oxide is consideratly less diradicaloid than, e.g., ozone.[16] Furthermore, it has been concluded that substituent and solvent effects can cause emergence of dominant zwitterionic character.[17]

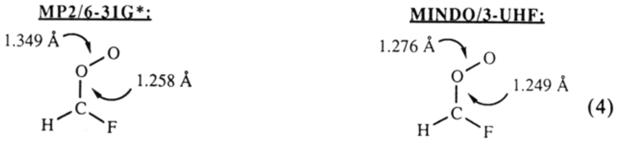
B. Semiempirical Calculations

The computational complexity of ab initio methods has restricted most of this work to the parent carbonyl oxide 1, although some extensions to include methyl and fluoro substituents have been reported.[15a,18–20] Generally speaking, is is not practical at present to carry out reasonable ab initio calculations on substituted carbonyl oxides, such as those for which experimental characterization data is available. In these cases, a reliable semiempirical approach, which could accommodate large organic substituents with reasonable economy, is needed. Hull had used Dewar's MINDO/3 in an early computational study of 1 and found that inclusion of 2 × 2 configuration interaction was necessary to obtain a reasonable geometry.[21] MINDO/3 without CI leads to a structure which greatly exaggerates the zwitterionic character for 1,[21,22] as is typical for RHF methods (see above). Cremer, Schmidt, Sander, and Bischof[23] have surveyed a number of semiemprical methods (including MNDO and AM1, among others), and find that the MINDO/3 description of the carbonyl oxide electronic structure is significantly improved at the UHF level. Using the MINDO/3–UHF method, these authors have calculated geometries, energies, and charge and spin distributions for a variety of substituted carbonyl oxides. Except for very strong π-donors, the carbonyl oxide system retains the diradical character on substitution, including alkyl, aryl, carbonyl, and fluoro groups. In accord with the ab initio results for 1, MINDO/3–UHF reveals a strong spin polarization in the π-system of the substituted carbonyl oxide—excess spin density is concentrated on the OO group and, with opposite spin, at carbon. Thus, the ground state appears as a singlet diradical as in **1a**. Nevertheless, contributions to the electronic character as described in structures A, B, D, and E are manifested in a predictable way: π-acceptors withdraw electron density from the system, and increase the contribution of structures like D and E. Although prevailing diradical character is still evident for **2**, an increase in the CO and decrease in the OO bond lengths compared to **1** are consistent with increased involvement of E. Alkyl substituents (and weak π-donors) should favor contributions from resonance forms A and B; i.e., they should increase the zwitterionic character. Indeed, Goddard predicted that dimethyl substitution on the carbonyl oxide would suffice to bring about degeneracy of the zwitterionic and biradical states.[13b] According to the MINDO/3–UHF results,[23] the ground state of dimethylcarbonyl oxide **3** is still predominantly a singlet diradical, although a lengthening of the CO bond was taken as evidence for increased contribution from structure A. Finally, for strong π-donors such as OH or NH_2, the ground state is zwitterionic, as revealed by the fact that the UHF wavefunction collapses to the RHF solution.[16] The charge distribution and geometry for **4** is in accord with the zwitterionic structures A and B.



2 3 4 (3)

It appears that the semiempirical calculations can provide useful insight into systems for which ab initio methods will be too cumbersome. On the other hand, it is necessary to establish the limitations of the MINDO/3–UHF method, particularly where direct comparison with ab initio results can be made. For example, the optimized geometry of fluoro-substituted carbonyl oxide **5** determined at the MP2/6–31G* level[19b] can be compared with the MINDO/3–UHF results.[23]



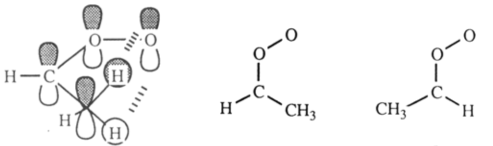
5 5 (4)

While there is reasonable agreement for the CO bond distance between the two methods, the reproducibility of the OO bond length is not especially good. An even greater difference is noted for the difluoro carbonyl oxide **6**. For this case, even the ab initio geometry,

6 6 (5)

obtained at the UHF/3-21G level,[20] is not totally reliable; the importance of using more flexible basis sets and correlation corrections has already been discussed. The calculated OO bond is unreasonably long (1.774 Å). Better results are obtained by using the GVB(2)/6-31G* treatment—optimization at this level leads to an OO distance of 1.468 Å. Thus, the ab initio calculations predict an incremental lengthening of the OO bond with fluorine substitution (note that substitution by F in the anti position causes a larger increase in OO bond distance than for the syn position).[19b] This trend is not reproduced well by the MINDO/3–UHF results. Perhaps more important is the observation that even the ab initio energies are remarkably insensitive to the OO bond distance. Thus, the GVB(2)/6-31G* energy using the optimized geometry (OO = 1.468 Å) from that method is only 2.1 kcal/mol lower than a similar, single-point calculation using the 3-21G geometry (OO = 1.774 Å).[20] This example demonstrates clearly the difficulty in obtaining precise, reliable bond distances for carbonyl oxides and provides a caveat for interpretations of electronic character and reactivity based on bond distances for these systems.

Other points of comparison for ab initio and the semiempirical method are calculations of the methyl-substituted carbonyl oxides. Two stereoisomers, syn and anti (**7** and **8**, respectively) are possible. Ab initio calculations (6-31G*, MP2) indicate that the syn isomer is 3.3 kcal/mol more stable than is the anti isomer.[15a] This result, opposite to what might be expected on the basis of steric considerations, is attributed in part to a stabilizing interaction of the π-orbital on the terminal oxygen with the methyl orbitals of π-symmetry. This interaction, possible only for the syn isomer, leads to a cyclic aromatic-type sextet, as evidenced by positive orbital populations between the hydrogen atoms and the terminal oxygen atom. The MINDO/3–UHF does not reproduce this effect, as the anti isomer is determined to be 0.2 kcal/mol more stable than the syn isomer.[23] Therefore, while the semiempirical method will surely be useful for evaluating trends in substituent effects, extreme care must be exercised when using this method to analyze more subtle features of carbonyl oxide structure.



7 8 (6)

C. Reaction Energetics and Dynamics

Computational methods have been especially useful for exploring the energetics of reactions which form carbonyl oxides, as well as subsequent transformations of these reactive intermediates. A particularly useful presentation is the energy diagram in Figure 1, which follows that due to Kafafi et al.,[8] with minor modifications. This chart outlines some of the energetic relationships among carbonyl oxide, its precursors, and its products. Of particular interest is the relationship between the carbonyl oxide **1** and its cyclic isomer, the dioxirane **9**. Ab initio,[10,12,13,15a,19b] semiempirical,[21,22] and thermochemical[6a,13b] calculations all place **9** at least 30 kcal/mol lower in energy than **1**. Results from Cremer's study of the conversion of **1** to **9** are used here:[19b] the reaction is exothermic by 31.3 kcal/mol, and has an activation barrier of 22.8 kcal/mol. This large activa-

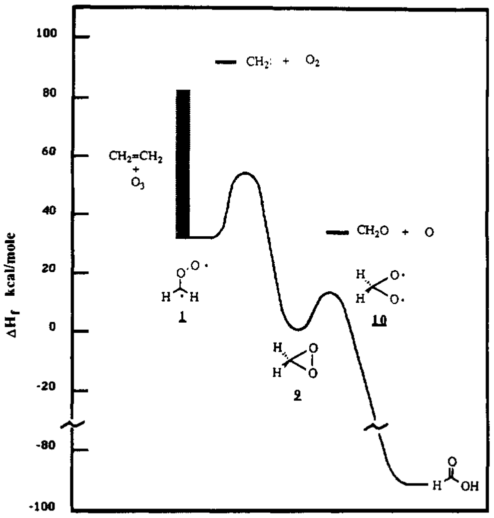


Figure 1. Energy relationships on the CH_2O_2 surface.

tion barrier would seem to rule out isomerization of 1 to 9 in the face of competitive bimolecular processes, at least for a thermally equilibrated carbonyl oxide. Consideration of the energetics of carbonyl oxide forming processes, however, indicates that it is possible for 1 to be formed with considerable excess energy. If this internal energy is not dissipated efficiently (via collisional deactivation, etc.), a vibrationally excited carbonyl oxide may isomerize to the dioxirane. For example, the ozonolysis of ethene leads to equal amounts of formaldehyde and carbonyl oxide 1, with an overall exothermicity of 45–50 kcal/mol.[24,25] Depending on the partitioning of this excess energy between the products, and further on the efficiency of collisional deactivation, the carbonyl oxides can be formed with sufficient internal energy to isomerize spontaneously. The available energy is indicated in the diagram by the shaded bar. The reaction of methylene with oxygen is still more exothermic, and the product carbonyl oxide can be produced with considerable excess energy, as indicated by the mark on the diagram.

Under conditions where the initially formed carbonyl oxide retains enought of the excess internal energy, then, isomerism to the dioxirane is possible. Of course, the exothermicity of this cyclization implies that the dioxirane will be formed with a large amount (ca. 50 kcal/mol, taking account of the activation barrier) of internal energy, and will react further. Cleavage of the OO bond to form methylenebis(oxy) 10 has a barrier of only 10–12 kcal/mol; the energy needed to dissociate the weak OO bond is nearly counterbalanced by relief of ring strain.[8] Rearrangement of methylenebis(oxy), by 1,2-hydrogen atom shift, generates formic acid with an exothermicity of over 100 kcal/mol. In the absence of mechanisms for quenching this "hot" acid, further dissociation (to H_2, CO, CO_2, H_2O, H, OH, etc.) is energetically feasible.[6a]

Other fates of the carbonyl oxide can be considered. In the absence of coreactants, it is possible for the carbonyl oxide to eject an oxygen atom. On the basis of the heats of formation for CH_2O and O, this reaction should be slightly endothermic (1.4 kcal/mol). The activation energy is not known. Kafafi et al. conclude that, for dioxymethyl, the loss of oxygen atom does not compete with isomerism to dioxirane, and so the activation barrier must be larger than for 1 → 9 (>23 kcal/mol).[8] This process may become important for other carbonyl oxides.

The diagram in Figure 1 is meant to provide the reader with a general feeling for the relative energetics of some of the processes involving carbonyl oxides. Substituent groups can alter relative energies, and changes in reaction conditions can open up new avenues for reaction. A great deal of experimental data pertaining to the formation and reactivity of carbonyl oxides is available and is the subject of the remainder of this article.

III. Preparation of Carbonyl Oxides

A. Alkene Ozonolysis

Historically, the most important method for generating carbonyl oxides is that which prompted Criegee to postulate their existence in the first place, namely alkene ozonolysis. A very large body of mechanistic work has since confirmed the basic features of the Criegee mechanism including the intermediacy of the carbonyl oxide in this process.[2,7] This is all the more remarkable since, under the conditions of alkene ozonolysis, the carbonyl oxide cannot be detected directly. Nevertheless, the weight of circumstantial evidence is overwhelmingly in support of the Criegee mechanism, which is shown below.

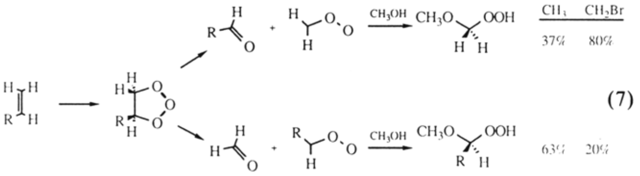
The carbonyl oxide is produced by fragmentation of a primary ozonide (PO, 1,2,4-trioxolane). This process, which occurs spontaneously at the temperatures (≥−80 °C) usually employed for alkene ozonolysis, can be viewed as a retro [3 + 2] dipolar cycloreaction[26] and is generally considered to be a concerted process. Cleavage of the PO produces one equivalent each of a carbonyl compound and a carbonyl oxide. For a substituted PO, this is a complicated event. Two modes of fragmentation are possible, each leading to a different carbonyl oxide–carbonyl pair. Moreover, if the substituents on the carbonyl oxide are not identical, two stereoisomers (syn and anti) are possible. In general, then, the ozonation of an alkene can lead to up to four different carbonyl oxide intermediates, subject to the controlling features of PO fragmentation.

With regard to the generation of carbonyl oxides by alkene ozonolysis, then, we must consider the importance of stereochemistry and regiochemistry in this process. From extensive studies of the stereoselectivity of alkene ozonolysis, it is clear that stereoisomerism is an important feature of the carbonyl oxide intermediate. Thus, the general result that cis and trans alkenes form different mixtures of cis and trans final ozonides (that is, some transmission of stereochemistry occurs) can only be accomodated within the Criegee mechanism if the carbonyl oxide carries stereochemical information (clearly, the carbonyl partner cannot). Very sensible models, which account for the transfer of stereochemistry via the Criegee mechanism, have been developed,[27] and a detailed computational study has provided additional refinements and some new insights.[28] For thorough discussions of these developments, the reader is directed to recent reviews.[2,7]

Notwithstanding the importance of carbonyl oxide stereochemistry, there has been to date no definite stereochemical assignment for any carbonyl oxide. Direct experimental verification of the syn-anti stereoisomerism of carbonyl oxides remains a challenge for the future. We will return to the issue of carbonyl oxide stereochemistry in section IV.C.1.

A number of investigations have focused on the regioselectivity of PO cleavage.[29-40] In general, these studies have involved ozonolysis of substituted alkenes in a hydroxylic solvent, normally methanol. Under these conditions, the carbonyl oxide is intercepted by addition of the solvent, forming the corresponding α-methoxy hydroperoxide. Various control experiments have indicated that the solvent has a negligible effect on the rate or mode of PO decomposition, and that trapping of the carbonyl oxide is essentially quantitative.[29d] In most cases, the α-methoxy hydroperoxides are reasonably stable, and can be quantified by a number of methods. The proportion of the two possible α-methoxy hydroperoxides (measured directly or inferred from the ratio of the carbonyl partners), then, is directly related to the partitioning of the PO fragmentation to the respectively carbonyl oxides.

The most extensive studies are those carried out by Fliszár and associates in the lates 1960's.[29] These have been described in detail elsewhere,[2,7] but some of the general features will be summarized here. For the most part, one can make a reasonable prediction of the preferred direction of PO cleavage based on the inductive effects of the alkene substituents. Thus, electron-donors tend to be incorporated into the carbonyl oxide and electron-withdrawing groups turn up mainly in the carbonyl fragment. Thus, 1-alkenes (e.g., propene) are found to lead to an excess of the substituted carbonyl oxide, while allyl bromide shows the opposite regioselectivity.[29d]



(7)

As these examples indicate, it is not at all unusual for both carbonyl oxides to be formed in significant amounts, and the preference for one over the other actually represents a very small energy difference (<1 kcal/mol) between the competing pathways.

The use of substituent inductive effects alone to predict PO cleavage is certainly naive, and it is indeed surprising that this model works as well as it does. Excellent correlations of the regioselectivities of PO fragmentation with electron donation by substituents (as measured by Hammett[29a-c] and Taft[29c-e] parameters) have been obtained, consistent with the effects expected for stabilization of a zwitterionic carbonyl oxide. It is less clear how these results fit with the current view that carbonyl oxides are best described as polar, singlet diradicals. In particular, electron density calculations do not show the carbon center of these species to be electron deficient.[23] On the other hand, a more "correct" theoretical interpretation of substituent directive effects is not yet available. PO decomposition is a very complex process. For many, but not all primary ozonides, cleavage to carbonyl oxide is probably an exothermic process.[24,25,29] According to the Hammond postulate, these should have a transition state which resembles the PO. As Cremer has pointed out, however, there are four conformers of the PO which have the proper orbital alignment for the [3 + 2] cycloreversion (Figure 2), and therefore there are four transition states which must be considered.[28] Unfortunately, reliable computations of the transition state properties for this process are not yet practical, because of the prohibitive cost involved in using the large basis sets with the multideterminant approach which is required for accurate results.[28]

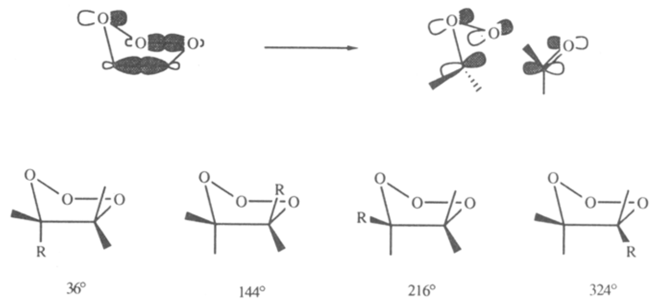
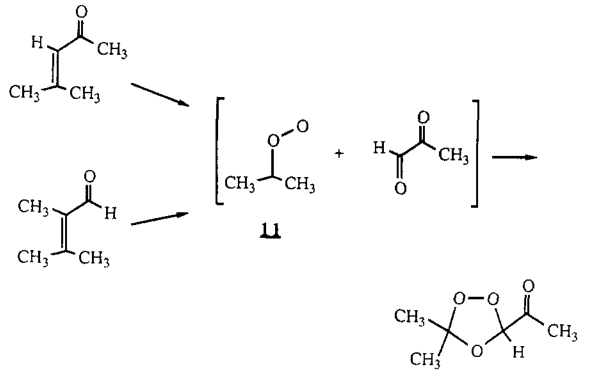


Figure 2. The orbital alignment for PO cleavage and the four substituted PO conformers, each identified with a puckering coordinate. See ref 28b.

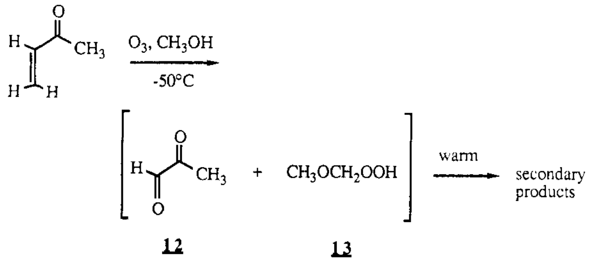
In order to approximate transition-state properties, recourse can be made to an analysis of the respective PO conformers. Cremer has examined the effect of a methyl group on the computed structure and energy of the PO[28b] and has carried out a similar analysis for fluorine.[19a] He found that conformational interconversion among the four transition-state-like geometries is a low-energy process, and so conformational preference is not a determining feature, at least for these groups. Furthermore, the substituent exerts a significant effect on the electronic energy of the PO, and this depends strongly on the precise PO conformation. Thus, a substituent will affect the HOMO energy differently for each of the four "transition-state" conformers of the substituted PO. The extent to which these effects are retained in the true transition states is difficult to estimate and must be balanced against the development of product-stabilizing features, dipole–dipole interactions, and the like. Since the energy differences between the various paths are quite small to begin with, and since too little is known about other types of substituents or how to assess the interplay between two or more groups, reliable predictions of regioselectivity based on theory are not yet possible.

As a practical matter, it would be very desirable to identity alkene substituents which have a directing effect powerful enough to ensure that only one of the possible carbonyl oxides is produced on ozonolysis. In particular, groups that have a high propensity for incorporation in the carbonyl fragment are useful, since these would permit the selective preparation of any desired carbonyl oxide by choice of the appropriately substituted starting alkene. Ideally, the carbonyl product containing the directing group will be inert, so that the subsequent chemistry of the carbonyl oxide can be explored with minimal interference. During the past several years, several auxiliary groups of this type have been developed, and their use has facilitated the study of carbonyl oxide chemistry under ozonolysis conditions.

On the basis of inductive effect arguments, an acyl substituent should exhibit a strong bias against incorporation in the carbonyl oxide. In fact, Fliszár and Granger[29c] found instead that ozonation of α,β-unsaturated ketones in methanol gave high yields of the aldehyde derived from the β-carbon—the inference is that the ketocarbonyl oxide is formed preferentially. This selectivity was attributed to resonance stabilization of the carbonyl oxide, as indicated above (presumably, the argument refers to stabilization developed at the transition state of the PO cleavage). This result stands in contrast to the early observation of von Bornhaupt[31] that trimethylacrolein and mesityl oxide form the same final ozonide: the most economical explanation is that fragmentations of the primary ozonides each proceed to give the dimethyl carbonyl oxide **11** and methylglyoxal, that is, with the carbonyl oxide derived from the β-carbon. More recent studies by Griesbaum et al. also support the inductive directing effect for an acyl substituent,[32,33] and provide some explanation for the different results obtained from earlier investigations. For example, ozonolysis of methyl vinyl ketone in methanol/$CDCl_3$ at −50 °C gives 86% of the products corresponding to generation of the carbonyl oxide at the methylene (β) position, ultimately leading to **13**.[32] It is particularly important that the cold reaction mixture is *immediately* analyzed by NMR, for it is found that the product composition changes substantially if the reaction mixture is allowed to warm to room temperature. The higher temperatures initiate a series of secondary reactions between **12** and **13**, and these initial products are nearly completely consumed. In a separate series of experiments, it was shown that the trapping products of keto carbonyl oxides are likewise unstable.[32,33] Therefore, in contrast to the stability of product mixtures from ozonation of other alkanes in methanol, those from α,β-unsaturated ketones decompose readily. This will lead to errors in analyses carried out at room temperature, as has been common,[29,30] and so the results from the low-temperature NMR studies must be considered more reliable.



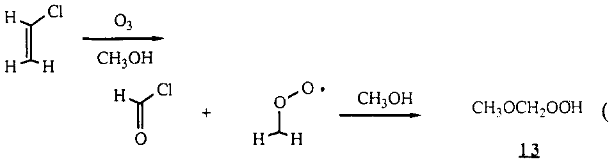
(8)



(9)

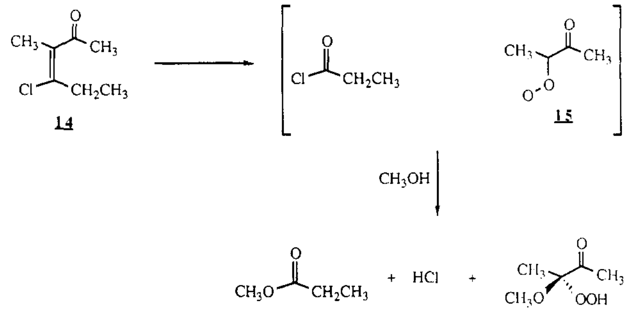
The acyl group, then, influences PO fragmentation in line with its electron-withdrawing character and is a reasonably effective directing group for carbonyl oxide formation. Nevertheless, the α-dicarbonyl byproduct is certainly not inert, and so this system is less useful for isolating the reactivity patterns of the carbonyl oxide.

Primary ozonides from vinylic halides fragment with good to excellent regioselectivity, in favor of an acyl halide–carbonyl oxide pair.[34,35] A particularly nice example of this effect is the basis of a useful preparative route to methoxymethyl hydroperoxide, the methanol adduct with dioxymethyl.[34b] Cleavage of the vinyl chloride PO occurs with apparently complete regioselectivity for the primary products shown. Dioxymethyl is captured by methanol, and formyl chloride decomposes to CO and HCl. Neutralization of the latter provides nearly pure **13**.



(10)

An instructive example is provided by **14**, where the directive effect of chloride is measured against that of an acetyl group.[33b] Here, as for other systems, the chloride effect dominates completely, directing PO cleavage to the keto carbonyl oxide **15** with high regioselectivity.



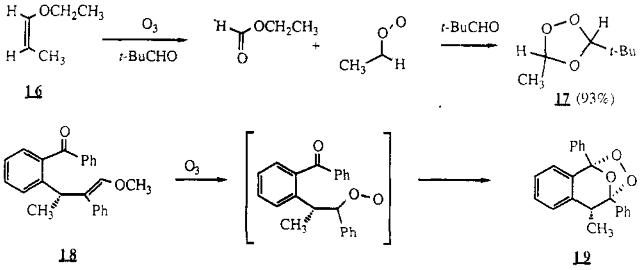
(11)

Clearly, the vinyl chloride system is an extremely potent regiocontrol element for PO fragmentation, and has been used effectively in this manner. One possible disadvantage to this method is the inevitable production of HCl from secondary reactions of the acyl chloride byproducts. Since the peroxide products of ozonation are often acid-labile, it may be necessary to buffer the reaction medium, e.g. with sodium bicarbonate.

A directive effect similar to the halides is found for alkoxy substituents. Ozonolysis of vinyl ethers proceeds with virtually complete regioselectivity to the carbonyl oxide–ester pair.[36-39] Since esters are stable compounds with a relatively low reactivity toward carbonyl oxides, this is a good method for the selective generation of carbonyl oxides with minimal interference from the byproduct.

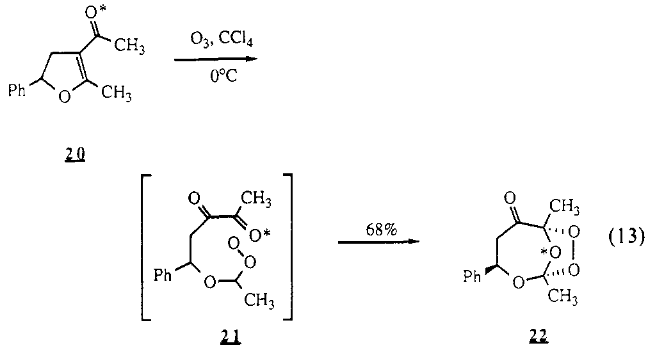
The methanol trapping procedure has been used to verify the high regioselectivity for cleavage of both cyclic[37] and acyclic[38] vinyl ethers. In nonparticipating solvents, the carbonyl oxide can be intercepted with an external aldehyde ("crossed" ozonide formation, **16** → **17**)[38c] or trapped with a suitably placed group in an intramolecular reaction, e.g., **18** → **19**.[39b]

In contrast to these results, conversion of the dihydrofuranyl ketone **20** to the "slipped" alkoxy ozonide **22** was found to proceed via the ester oxide **21**.[40] In this case, the intermediate carbonyl oxide cannot be trapped by methanol, since intramolecular reaction is apparently



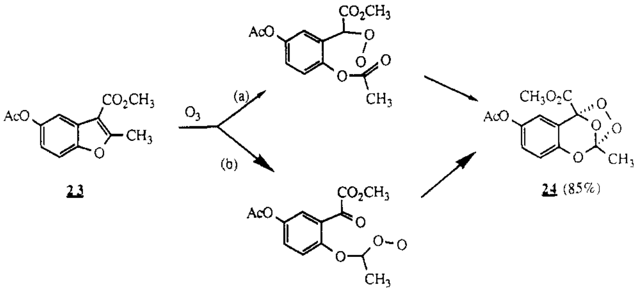
(12)

much faster. The incorporation of the acetyl group of **20** in the ozonide system for **22** does, however, permit this question to be resolved by ^{17}O-labeling, as outlined below.[40b]



(13)

Undoubtedly, the course of the fragmentation of **20** is governed by the directive effect of the acyl substituent also present. In this case, in contrast to the conversion of **14** to **15** noted above, the acyl group effect overrides that of the vinyl ether. The relatively efficient formation of final ozonides from other vinylogous esters and carbonates[40a,41,42] may be additional examples of this effect. For conversion of **23** to **24**, the ozonide could result from recombination of either pair of Criegee cleavage products (carbonyl oxide–ester from path a, ketone–ester oxide from path b). Since it is known that

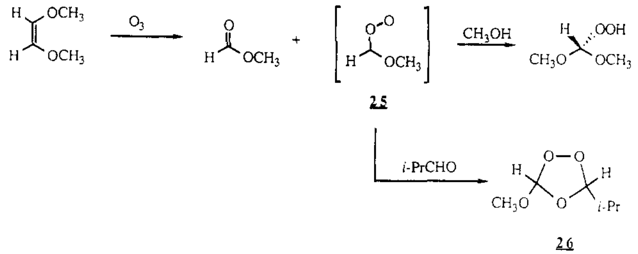


(14)

cycloaddition of carbonyl oxides with esters is not generally facile, it is likely that path a does not contribute substantially and that PO cleavage favors path b. This proposal should be tested with appropriate trapping experiments.

An unambiguous route to alkoxycarbonyl oxides (ester oxides) has been reported by Kuczkowski.[43] Thus, *Z*-1,2-dimethoxyethane (the *E* isomer reacts similarly) fragments according to the Criegee pathway, which must give equal amounts of methyl formate and the methoxycarbonyl oxide **25**. This was characterized as its adduct with methanol. In nonreactive solvents, **25** could be trapped by added aldehydes to form the alkoxy ozonides **26**.

The results for more highly substituted analogues are variable.[44] Ozonation of *E*-dimethoxystilbene in



(15)

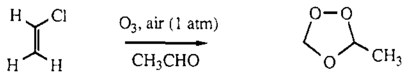
methanol leads to α,α-dimethoxybenzyl hydroperoxide, the ester oxide trapping product. In contrast, the *Z* isomer leads to a different set of products, produced by a non-Criegee pathway. Similarly, ozonolysis of tetramethoxyethene fails to give any of the dialkoxycarbonyl oxide.[44]

For alkene ozonation in the gas phase, the very large exothermicity of the reaction comes into play.[3,6,8] Since the PO is formed with a great deal of excess energy and since this energy is not efficiently dissipated, the fragmentation to carbonyl oxide is considerably less regioselective than for the corresponding reaction in solution. For example, nearly equal proportions of the Criegee fragments are formed from isobutene in the gas phase;[45] the reaction in solution provides 77% selectivity for the more substituted carbonyl oxide.[29d] Moreover, the carbonyl oxide retains substantial internal energy, which affects its subsequent chemistry. In fact, for gas-phase alkene ozonolysis, only a fraction of the theoretical amount of carbonyl oxide can be trapped, for example, as a final ozonide.[45–54] The possible intervention of other PO fragmentation processes (which do not involve the carbonyl oxide) has been considered, but the current interpretation is that the Criegee mechanism is still the dominant process.[3,6] It has been determined that a large fraction of the carbonyl oxide is produced in an excited state(s) from which unimolecular decomposition, rearrangement, etc. is very rapid, and therefore cannot be trapped in biomolecular processes.[46] Some of the carbonyl oxide, however, is sufficiently long lived that it can be intercepted in bimolecular reactions, typically oxygen transfer to SO_2[47–49] or scavenging by aldehydes.[50–54] The fraction of trappable carbonyl oxide is a function of the total system pressure, as would be expected since collisional energy transfer should be an important mode of energy dissipation for the "hot" carbonyl oxide. At low pressure (4 Torr), nearly all of the carbonyl oxide is consumed via unimolecular processes.[45,46] As the total pressure is increased, the proportion of "stabilized" carbonyl oxide rises and then levels out at a limiting value near that at atmospheric pressure[48]—this is referred to as the branching ratio. The branching ratio is a function both of the carbonyl oxide and of the process by which it is produced. Some representative values are presented in Table II. It can be seen that, for gas-phase ozonolysis of ethene, some 60% of the initially formed dioxymethyl is "hot" and is irretrievably consumed through unimolecular decomposition. About 40% is sufficiently stabilized that it can be engaged in bimolecular reactions. The situation with vinyl chloride is somewhat more complicated. In contrast to the results in solution (see above), both PO cleavage channels operate in the gas phase.[54] This is consistent with the idea noted above that the "hot" PO should exhibit less

TABLE II. Branching Ratios for Stabilized Carbonyl Oxide from Ozonolysis at Atmospheric Pressure

alkene	carbonyl oxide	trapping agent	branching ratio	ref
ethene	CH_2–O–O	SO_2	38–40%	48, 50a
		CH_2O	35 ± 5%	50, 51b
ethene-*d*$_4$	CD_2–O–O	SO_2	39%	48a
vinyl chloride	CH_2–O–O	CH_3CHO	25%	54
		SO_2	23%	48a
trans-2-butene	CH_3CH–O–O	SO_2	18%	48a
			43–45%	47
cis-2-butene	CH_3CH–O–O	HCHO, SO_2	18%	51a
			40–46%	47
tetramethylethylene	$(CH_3)_2C$–O–O	HCHO	30%	51c
trans-dichloroethylene	HC(Cl)–O–O	C_2H_6, HCHO	~30%	52, 53

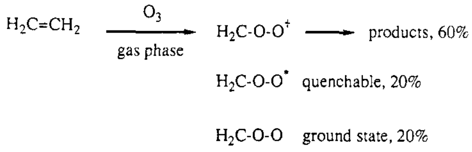
discrimination between the regioisomeric fragmentation paths. In this case, the CH_2OO channel predominates 3:1 over the ClCHOO channel. By trapping with ethanal, a 19% yield of **27** was obtained, which implies a branching ratio *for CH_2OO* of 25%.[54] The branching



(16)

27 (19%)

ratio for ClCHOO could not be determined since the trapping product was considered to be unstable. The lowered proportion of stabilized CH_2OO from the ozonolysis of vinyl chloride as compared to ethylene can be attributed to the greater exothermicity of the former reaction, leading to a higher fraction of "hot" intermediates. Similarly, the increased exothermicity for ozonolysis of the other alkenes in Table II may account for the lowered branching ratios relative to ethene. Of course, this argument is somewhat oversimplified. A properly detailed analysis will require more information about the partitioning of the excess PO internal energy among the various Criegee cleavage products, and particularly calls for an improved understanding of the correlations between the relevant energy states of PO and carbonyl oxide. In this connection, it is worth pointing out an interesting feature in the ozonolysis of ethene. It has been shown[48b] that the fraction of trappable carbonyl oxide does not approach zero at low pressure, as is observed for other alkenes. Instead, an extrapolated value of ~20% is projected at zero pressure, suggesting that this proportion of CH_2OO is produced "cold", without need for collisional stabilization, while another 20% (for a total of ~40%) is vibrationally excited, but quenchable at atmosphere pressure.



(17)

B. Carbonyl Oxides from Carbene–O_2 Reactions

Although the evidence for the involvement of carbonyl oxides in alkene ozonolysis is quite compelling, the chances for direct observation of the intermediates under these conditions are slim. This is because the rate of decomposition of the primary ozonide is generally slower than the subsequent reactions of the carbonyl oxide, and so the concentration of carbonyl oxide is always quite small.

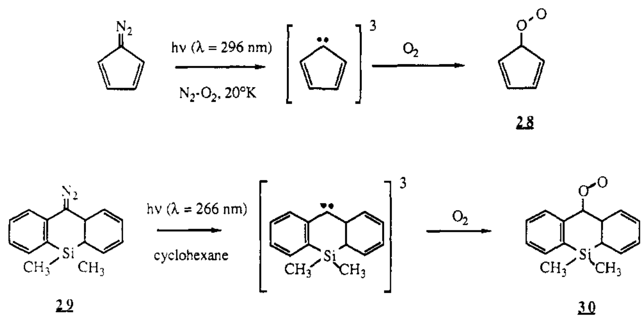
TABLE III. Spectroscopic Parameters for Carbonyl Oxides in Matrix Isolation

carbonyl oxide	$\lambda_{max}(\pi\rightarrow\pi^*)$, nm	ν_{O-O}, cm^{-1}	ref
28	420	1014	58
31	422	897	63b,c
32	460	898 881	61a,b
44	582	931	68
45	445	938	61a,b
46	395	1016 1007	61b,c
47	387	915 890	63a,c
48	406	931 901	64
49	400	890	67
50	462	1045 1034	66
51	378	1009 943	65
52	–	1049 997	65

Alternate methods for generation of the carbonyl oxide are much more suited for this purpose. The photooxidation of diazoalkanes was considered by Kirmse et al.[55] to involve an intermediate carbonyl oxide, a proposal supported by the isolation of a ketone diperoxide (carbonyl oxide dimer) by Bartlett and Traylor.[56] Following these leads, Murray and Suzui[57] demonstrated that the carbonyl oxide could be intercepted by reaction with external aldehydes to form the corresponding 1,2,4-trioxolanes (final ozonides). This important result clearly established the connection between the photooxygenation process and alkene ozonolysis, with strong implication for the intermediacy of the carbonyl oxide in both reactions.

The photooxidation of diazo compounds proceeds in two distinct steps: photoextrusion of N_2 to provide a carbene, which then combines with oxygen to form the carbonyl oxide. In the absence of oxygen, of course, only the first step occurs, and the carbenes so obtained can be monitored by using such techniques as matrix isolation or time-resolved spectroscopy. If oxygen is present, the lifetime of the carbene is shortened, and its decay coincides with the appearance of a new species, assigned the carbonyl oxide structure. A most important feature of this process is that the rate of formation of the carbonyl oxide is fast compared to its lifetime, and so this product will accumulate. A critical advance in the study of carbonyl oxides has come in the last decade with the investigation of the carbene–oxygen reaction by matrix isolation or flash photolysis/time-resolved spectroscopy. The details of these methods as applied to the characterization of carbonyl oxides has been nicely reviewed by Sander.[9] Only a summary of the results will be provided here.

The first direct observations of carbonyl oxides by each of these methods were reported in 1983. Bell and Dunkin[58] provided IR evidence for the formation of **28** from photolysis of diazacyclopentadiene in a frozen matrix of N_2–O_2 (9:1). At almost the same time, Iwamura et al. reported that flash photolysis of **29** in oxygenated cyclohexane gave rise to a transient species with λ_{max} = 425 nm, which was assigned to the carbonyl oxide **30**.[59] Since these initial reports, a large number of carbonyl oxides have been studied by one or the other of these techniques.[60–75] These are presented in Chart



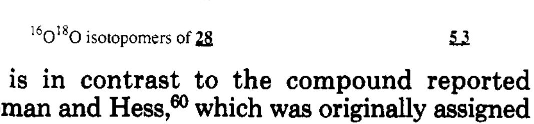
(18)

I, and a summary of some relevant spectral data is given in Tables III and IV.

As is evident from the tables, the carbonyl oxides are characterized by an absorption in the 380–460 nm range. The absorption does not change substantially between the matrix and solution for those two carbonyl oxides (**31** and **32**) studied in both environments. Moreover, **32** is reported to provide virtually identical spectra in 1,1,2-trichlorofluoroethane (Freon 113), benzene, and acetone, even though the half-life of this species is strongly solvent dependent.[70] The observed absorbance is assigned to a $\pi \rightarrow \pi^*$ transition in accord with CNDO/S computations which also predict $n \rightarrow \pi^*$ transitions in the region 600–800 nm.[23] The latter absorption is very weak and has not been directly measured experimentally, but their presence is indicated by the fact that photochemical conversions of the carbonyl oxide (discussed further in section IV.C.2) can be initiated by irradiation in this range.[63-66]

To date, UV–vis spectra have been obtained only for carbonyl oxides with conjugated π-systems. The only nonconjugated system to be studied is **52**; in this case, the low yield of carbonyl oxide prevents determination of the UV–vis spectrum.[65] It is worth noting that CNDO/S calculations predict that **1** will have λ_{max} = 384 nm,[23] and so it should be feasible to monitor even these simpler carbonyl oxides spectroscopically.

Infrared spectroscopy has been used to characterize carbonyl oxides in matrix isolation. Isotope labeling with ^{18}O in one or both oxygens has been used to assign vibrational bands as well as to confirm structure. Thus, for **28** the IR bands at 1014, 947, and 940 cm^{-1} exhibit a large shift (−28, −22, and −15 cm^{-1}, respectively) on double labeling with ^{18}O and are therefore assigned to vibrations with considerable O–O stretching component.[58] There are two $^{16}O^{18}O$ isotopomers for this species, as evidenced by the fact that the band at 1014 cm^{-1} is split into two (1001 and 995 cm^{-1}), clearly indicating that the oxygen atoms are not equivalent.



(19)

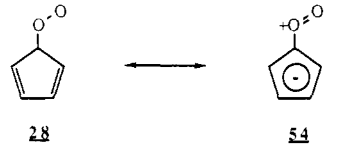
This is in contrast to the compound reported by Chapman and Hess,[60] which was originally assigned the carbonyl oxide structure **28**. Subsequent work demonstrated that only one $^{16}O^{18}O$ isotopomer is formed,[62] and so the oxygen atoms are equivalent, as in the dioxirane structure **53**.

TABLE IV. Spectroscopic and Kinetic Parameters for Carbonyl Oxides in Solution

carbonyl oxide	solvent	$\lambda_{max}(\pi \rightarrow \pi^*)$, nm	k_{O_2}, $M^{-1}\,s^{-1}$	$2k/\epsilon l$, s^{-1} [a]	ref
30	cyclohexane	425	2×10^9		59
31	CH_3CN	410	5×10^9	1.44×10^3	69
32	freon 113	450	1.4×10^9		70
33	CH_3CN	401		8.1×10^3	72
34	CH_3CN	409	2.2×10^9	1.99×10^3	72
35	freon 113	418			72
36	CH_3CN	428		3.1×10^3	72
37	CH_3CN	415			72
38	CH_3CN	410		1.25×10^3	72
39	CH_3CN	405		1.87×10^3	72
40	CH_3CN	390	3.4×10^8		72
41	freon 113	410	8.6×10^8	6.6×10^4	74
42	cyclohexane	435	3.5×10^9	3.2×10^5	71
43	CH_3CN			3.0×10^2	72

[a] Bimolecular rate constant for disappearance of the carbonyl oxide. These are listed for l = 10 cm. The value for ϵ is usually not determined, but refers to the molar absorptivity of the carbonyl oxide at the λ_{max}.

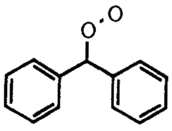
All of the carbonyl oxides characterized so far have an absorbance in the 900–1000 cm^{-1} region which is attributable to a vibration involving O–O stretch, in reasonable accord with the calculated spectrum for **1**.[76] The exact position of this band depends on the carbonyl oxide substituents. In general, electron-withdrawing substituents tend to shift the O–O absorption to higher frequency. This is in accord with an increased shift of electron density to the carbon center, with development of some O–O double bond character, as for resonance form D. Thus, for the series **31**, **51**, and **52**, an incremental shift of ~50 cm^{-1} is found for replacement of phenyl by trifluoromethyl.[65] For **28**, significant contribution of the resonance form **54** might be expected, and indeed the O–O frequency for **28** is higher than for **45** and **32**, where cyclopentadienide character should be less important. Such comparisons can be hazardous, however, since the "O–O stretch" is in fact a more complicated vibration, and a change in structure may change the O–O stretching character of this band as well. Thus, while Sander has shown through comparison of the isotope shifts that the O–O contribution is similar among **31**, **51**, and **52**,[65] the isotope shift for **28** is somewhat lower,[58] indicating that this is a less-pure O–O stretch, and no data are yet available for **45** and **32**. It can be noted parenthetically that oxygen-transfer experiments involving **28** do not indicate a strong contribution from resonance forms like **54** (see further section IV.D.5).

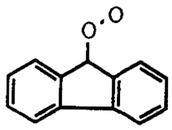


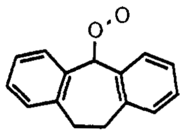
(20)

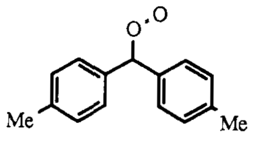
Sander has carried out a detailed study of isotope substitution of benzophenone oxide (**31**), and was able to assign nearly all of the bands in the spectrum.[63c] Of some interest is the location of the C–O stretching band, since this should provide some experimental bearing for assessment of the extent of double bond character for this system. No distinct CO stretching band is observed—this vibration is strongly coupled to the adjacent C–C stretching modes. Calculations for **1** indicate, however, that the C–O stretching frequency is 1116 cm^{-1}, close to that for a C–O single bond.[76]

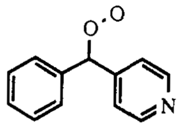
CHART I

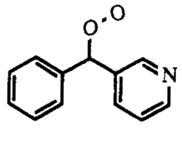

31

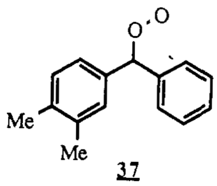

32

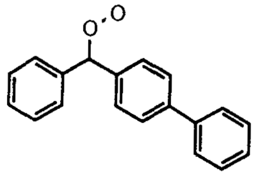

33

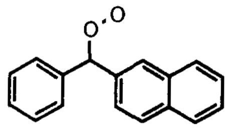

34

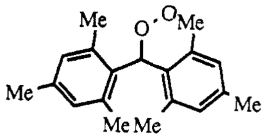

35

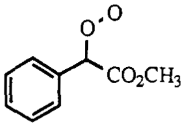

36

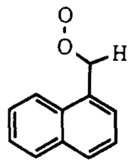

37

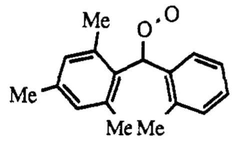

38

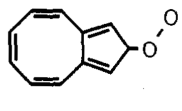

39

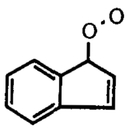

40

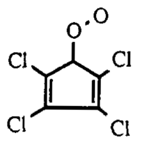

41

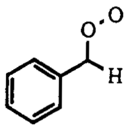

42

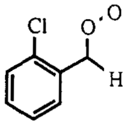

43

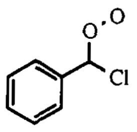

44

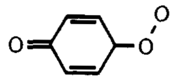

45

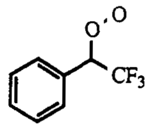

46

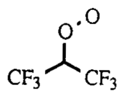

47


48


49


50


51


52

Of the carbene precursors to the carbonyl oxides in Tables III and IV, all have triplet ground states with the exception of phenylchlorocarbene (the precursor to **49**), which is a singlet. Matrix-isolated phenylchlorocarbene (PhCCl), in contrast to all of the other carbenes, reacts only slowly with oxygen, and the carbonyl oxide accumulates over 6 h at 35 K.[67] Under conditions where the triplet carbenes are completely converted to carbonyl oxide, PhCCl does not react perceptibly.[64] This result is consistent with the formulation of the carbonyl oxide ground state as a singlet—only the triplet carbene-(triplet) oxygen reaction has a spin-allowed pathway to a single product; the singlet carbene-triplet oxygen reaction cannot proceed directly to the singlet product.[61a]

Absolute rate constants for the carbene-oxygen reaction in solution can be determined by the use of laser flash photolysis with fast time-resolved spectroscopy. At room temperature, the second-order rate constants are close to 10^9 M^{-1} s^{-1}, near the diffusion-controlled rate. Compared to the time scale of their formation, the carbonyl oxides are quite long-lived (10^{-5}–10^{-3} s), and so their subsequent reactions are kinetically different. In fact, the decay time for carbonyl oxides frequently exceeds the time domain of the laser photolysis system. In these cases, conventional flash photolysis[72] or optical modulation spectroscopy[73] have been used to monitor the decay kinetics. For most of the carbonyl oxides, the decay is best fit to a second-order rate law,[71-74] indicating a bimolecular decomposition pathway. For benzophenone oxide (**31**), the ketone is the major product at room temperature.[73] A bimolecular process involving O_2 extrusion has been suggested—this is presented in section IV.D.2. Most

TABLE V. Kinetic Parameters for Carbonyl Oxide Reactions in Solution

carbonyl oxide	solvent	trapping agent	k_{trap}, $M^{-1} s^{-1}$	ref
30	cyclohexane	CH_3OH	1.8×10^5	*a*
31	CH_3CN	CH_3CHO	3.1×10^6	72
		$PhCH_2CHO$	2.1×10^6	72
		n-octanal	2.0×10^4	73
32	freon-113	CH_3CHO	1.21×10^9	70
		$PhCH_2CHO$	5×10^8	70
		n-octanal	4.5×10^7	70
33	CH_3CN	CH_3CHO	4.7×10^5	72
		$PhCH_2CHO$	2.9×10^5	72
34	CH_3CN	CH_3CHO	4.5×10^6	72
41	freon-113	CH_3OH	3.4×10^6	74

[a] Estimated from data in ref 59.

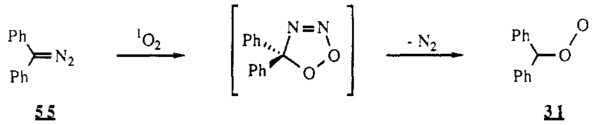
importantly, the direct observation of the carbonyl oxide permits determination of the kinetics for reactions so well known from alkene ozonolysis—the second-order rate constants for reaction of carbonyl oxides with aldehydes (as in the final step of the Criegee mechanism) vary considerably with the structure of the carbonyl oxide, as well as the aldehyde (see Table V). Likewise, it has been possible to extract the rate constant for methanol trapping of a carbonyl oxide.[74] The prospects for this kind of rate data are exciting. In particular, the large effects of structure on reactivity, already apparent from the limited data in Table V, will undoubtedly be very useful in developing a better understanding of the mechanistic details of the carbonyl oxide reactions.

Fessenden and Scaiano used dielectric loss measurements to determine the dipole moments for benzophenone oxide (**31**) and dibenzosuberone oxide (**33**).[75] The experimental values, 4.0 and 3.8 D, respectively, provide an assessment of the electronic distribution in carbonyl oxides. While the observed dipole moments for **31** and **33** are considerably larger than would be expected for a simple peroxy radical, they are less than that estimated ($\mu \sim 5.0$ D) for a true zwitterion. The difference in dipole moment between **31** and benzophenone ($\Delta\mu \sim 1.1$ D) is similar to that calculated for dioxymethyl (**1**, $\mu = 3.5$ D)[13b] compared to formaldehyde ($\mu = 2.34$ D).[77] The interpretation is that these carbonyl oxides are highly polar diradicals, in accord with the theoretical results.

The reaction of CH_2 with O_2 has been studied in the gas phase[78] and in a low-temperature matrix.[79] In neither case was the carbonyl oxide detected. The reaction is highly exothermic (see Figure 1), and so the carbonyl oxide would rearrange rapidly to formic acid. In the matrix-isolation experiment, Lee and Pimentel observed luminescence which they assigned to transitions from the excited A'^1A' state of formic acid, indicating that nearly all of the excess energy ($\Delta H = -181$ kcal/mol) of the CH_2–O_2 reaction is conserved in this excited state.[79] Fragmentation of the excited formic acid gives rise to a number of products, some of which are also observed in the gas-phase ozonation of ethylene.[80] Likewise, products consistent with the decomposition from the excited states of formic acid are obtained in the gas-phase methylene–oxygen reaction.[78] The amount of ground-state formic acid is increased in the presence of water vapor. At least two effects are in play: the H_2O appears to be an effective quencher of excited formic acid, and also serves to quench a precursor of the formic acid, probably dioxymethyl. This is demonstrated by the production of monolabeled formic acid when $H_2{}^{18}O$ is used.[78] Since no doubly labeled acid is obtained, O exchange of formic acid is ruled out. A complexation–quenching of the excited dioxymethyl has been proposed.

C. Singlet Oxygen Reaction with Diazoalkanes

Despite the obvious utility of the carbene–oxygen reaction for generating carbonyl oxides, there are some limitations to this process. Conditions must be controlled so that the intermediate carbene reacts with oxygen before it is consumed in other processes. Carbenes that rearrange rapidly or solvents which will react with the carbene must be avoided. For example, attempts to generate a carbonyl oxide in the presence of methanol, in order to study the trapping reaction, will be complicated by competitive reaction of the carbene with the alcohol.[74] An alternate method, which promises to circumvent many of these problems, was developed by Higley and Murray.[81] Oxidation of diazo compounds with singlet oxygen leads to carbonyl oxides, which can be trapped with aldehydes to form ozonides. The proposed mechanism for this transformation involves cycloaddition of singlet oxygen to the diazoalkane, followed by extrusion of N_2 from the intermediate diazadioxolene:[81,82]

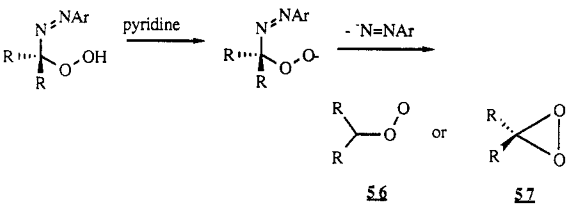


(21)

Significantly, the carbene intermediate is avoided, and so aliphatic carbonyl oxides can be prepared by this method. Recently, Scaiano et al. have shown that intermediates generated by this method could be observed by time-resolved spectroscopy.[69b] Here, laser pulses ($\lambda \approx 590$ nm) are used to generate singlet oxygen (methylene blue sensitizer) in the presence of diazoalkane **55**. Reaction of singlet oxygen with **55** is very rapid and proceeds with extrusion of N_2 to the carbonyl oxide **31** as the first detectable product. Through comparison of the electronic spectrum ($\lambda_{max} = 410$ nm), as well as quenching rate constants, the authors were able to show that the intermediate obtained by sensitized irradiation (the "single route") was identical with that obtained earlier by direct photolysis of **55** in the presence of oxygen (the carbene–oxygen reaction, the "triplet route"). Similar results have been obtained for other aryl carbonyl oxides.[70,72] As Scaiano points out, the singlet route offers distinct advantages for the generation of carbonyl oxides in solution. Thus, it is possible to generate fluorenone oxide (**32**) in 2-propanol solution by the singlet route;[70] this cannot be done via the triplet route since the carbene would be completely consumed by reaction with the solvent. Therefore, the singlet route offers great potential for the exploration of the behavior of carbonyl oxides in reactive solvents (alcohols), and especially for the study of simpler alkyl carbonyl oxides.

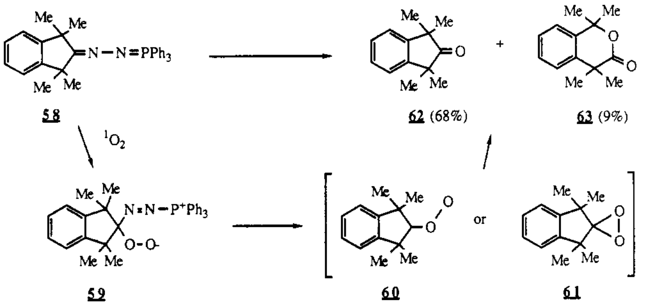
D. Photooxygenation of Other C=X Systems

Singlet oxygen reacts with a variety of C=X (X = heteroatom) systems, including azines, hydrazones, and sulfur ylides to give peroxidic intermediates which are capable of oxygen-transfer reactions. Several possible structures have been considered for these intermediates, including carbonyl oxides or the isomeric dioxiranes. For example, Tezuka and Iwaki have reported that the base-induced decomposition of α-azo hydroperoxides,[83] prepared by photooxidation of hydrazones, generates an oxidizing species which epoxidizes alkenes stereospecifically. Electron-deficient alkenes do not react. The reactive species is believed to be either the carbonyl oxide **56** or the dioxirane **57**. The stereospecificity of oxygen transfer, as well as the electrophilicity of the intermediate, are more consistent with a dioxirane,[5] though this point bears further study.



(22)

Ando and co-workers have found that the sensitized oxidation of the phosphazine **58** leads to a mixture of the indanone **62** (68%) and the corresponding lactone (**63**, 9%).[84] Since the reaction is inhibited by *p*-dimethoxybenzene (an electron-transfer quencher), the authors propose that oxidation proceeds by initial electron transfer from azine to singlet oxygen, followed by radical recombination to the zwitterion **59**. This can fragment to liberate the carbonyl oxide **60** or, alternatively, to the dioxirane **61**. One of these is presumably the precursor to the lactone. The peroxide intermediate could be diverted by reaction with methyl phenyl sulfoxide—the sulfone is produced, with a corresponding decrease in the lactone yield. A similar mechanism has been reported for the photooxidation of adamantanone azine;[85] in this case, the involvement of a carbonyl oxide intermediate was established by trapping with methanol.

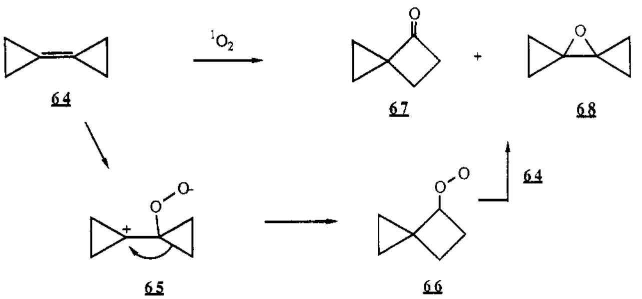


(23)

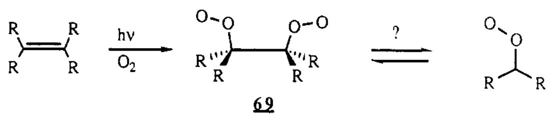
A variety of ylides react with singlet oxygen to give species capable of oxygen transfer to sulfides. Directly analogous mechanisms have been proposed and either the carbonyl oxide or the dioxirane may be involved as the oxygen-transfer agent.[86]

Certain alkylidenecyclopropanes react with singlet oxygen to give products indicative of a carbonyl oxide intermediate. Addition of singlet oxygen to **64** provides the peroxycyclopropylcarbinyl cation **65**. This rearranges to the carbonyl oxide **66**, which transfers oxygen to **64**, providing **67** and **68**.[87b]

Finally, Martinez[88] has suggested a unified mechanism for the matrix photooxidation of alkenes which invokes the intermediacy of carbonyl oxides from cleavage of a *vic*-bisperoxy radical **69**. The reverse reaction is considered to be facile. This may be a possibility in the confinement of a solid matrix, but the dimerization of carbonyl oxides in solution proceeds through a formation of C–O bonds (head-to-tail).



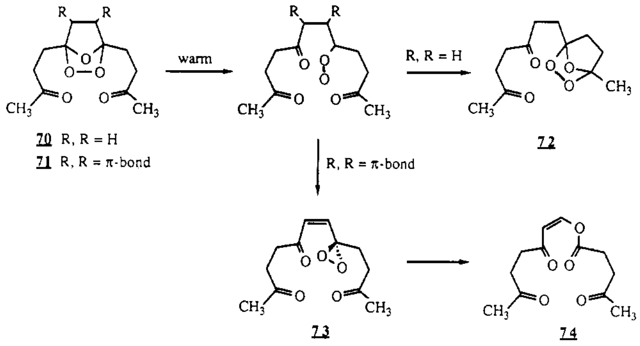
(24)



(25)

E. Carbonyl Oxides from Furan Endoperoxides and Other 1,2,4-Trioxolanes

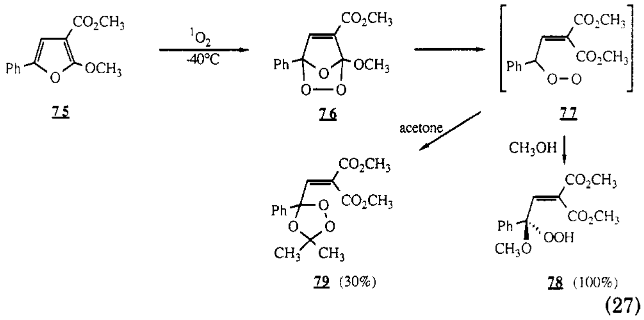
Adam and Rodriguez have observed that furan endoperoxides can act as oxygen-transfer systems in epoxidation, sulfoxidation, and Baeyer-Villiger reactions.[89] Direct oxygen transfer by the endoperoxide itself is considered unlikely, since reaction only occurs at temperatures where the peroxide is thermally unstable. A ring opening of the peroxide is proposed to provide a carbonyl oxide, which serves as the active oxygen-transfer agent. It is interesting to note that the ring opening of the furan endoperoxide, which is actually an ozonide, corresponds to a formal reverse of the carbonyl oxide–carbonyl cycloaddition:



(26)

Trapping experiments, designed to assess the involvement of a carbonyl oxide in this process, gave very striking results.[89b] Thus, thermolysis of **70** leads to formation of the rearranged ozonide **72**, corresponding to intramolecular capture of the carbonyl oxide intermediate. In contrast, the unsaturated analogue **71** rearranged to the ester **74** and gave none of the ozonide expected from trapping of a carbonyl oxide. The interpretation is that the carbonyl oxide from **71** is kinetically labile and rearranges to the dioxirane **73**. Baeyer-Villiger rearrangement of **73** would then lead to **74**. The difference in behavior between these compounds is apparently due to the electron-withdrawing conjugation in **71** which is not present in the saturated system **70**. This subtle effect underscores the close relationship between carbonyl oxides and their dioxirane isomers.

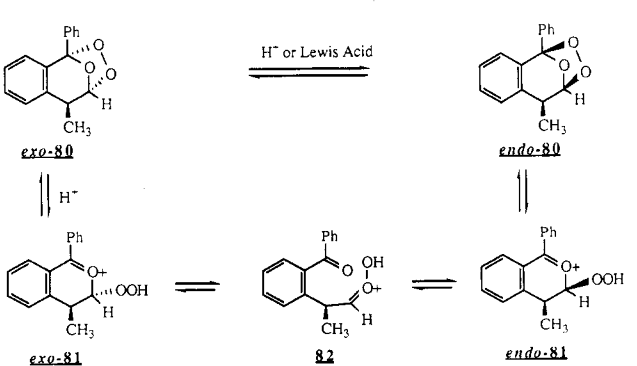
Carbonyl oxides have been invoked in the decomposition of other furan endoperoxides. Recent work by Scarpati and associates reveals clear evidence for the production of carbonyl oxides during the photooxygenation of certain α-methoxyfurans.[90] Reaction of 75 with ${}^1O_2$ in methanol proceeds quantitatively to the α-methoxy hydroperoxide 78, the solvent trapping product of carbonyl oxide 77. When the photooxygenation is carried out in acetone, the carbonyl oxide is trapped as the ozonide 79. In nonreacting solvents, the unstable endoperoxide 76 is produced—this reacts quantitatively on addition of methanol to give 78, establishing 76 as the likely precursor to 77.[90b] Formation of the carbonyl oxide is strongly influenced by substituents on the endoperoxide. In particular, an electron-withdrawing group at the 5-position completely inhibits opening to the carbonyl oxide.[90c] The origin of this effect is not well understood.



(27)

Oxazole endoperoxides rearrange to triamides in a synthetically useful process. Ring opening to the carbonyl oxide, exactly analogous to 76 → 77, has been suggested as a possible mechanism.[91]

Protic and Lewis acids catalyze the equilibration of the endo–exo ozonides *endo*-80 and *exo*-80, leading Nojima to propose the involvement of a complexed carbonyl oxide in this process.[92a] The benzylic C–H does not exchange when deuterated acid is used, ruling out a simple epimerization at this center. Instead, endo–exo isomerization requires inversion at the ozonide (bridgehead) carbons; this can occur only if one C–O bond to each is broken. According to ab initio calculations,[92b] protonation of the peroxide will cause facile ring opening to the carboxonium species 81.



(28)

Further cleavage of this intermediate to the protonated carbonyl oxide 82 occurs more slowly, and reverse of this process after C–C bond rotation accounts for the stereoisomerization. A similar complexed carbonyl oxide is implicated in the acid-mediated dimerization of certain ozonides. Lewis acid complexes analogous to 81 can be isolated. In at least some cases, these react by ring opening to the acid complex of the carbonyl oxide.[92c,d]

IV. Reactions of Carbonyl Oxides

A. Nucleophilic Trapping

The most common nucleophile trapping reaction of carbonyl oxides is, by far, the formation of α-methoxy hydroperoxides with methanol. The reaction has been used extensively to verify the production of carbonyl oxides, and several examples of this type have already been discussed. Higher alcohols, water, carboxylic acids, ammonia, and cyanide are among other nucleophiles which have been used to trap carbonyl oxides.[2] Niki et al. have studied the reaction of oxygen nucleophiles with carbonyl oxides, and determined the order of reactivity:[93]

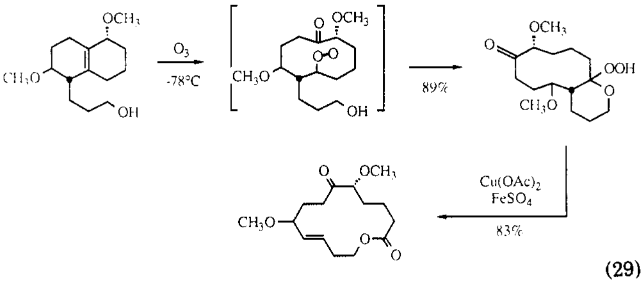
$$\mathrm{MeOH} > \mathrm{EtOH} > n\text{-}\mathrm{PrOH} > i\text{-}\mathrm{PrOH} > \mathrm{H_2O} > t\text{-}\mathrm{BuOH} > \mathrm{CH_3CO_2H}$$

The alcohol reactivities correlate with various solvent polarity parameters, although it is likely that steric effects are also important. The relatively low reactivity of water and acetic acid was attributed to increased strength of the OH bond in these compounds, and a cyclic transition state for simultaneous delivery of O and H was suggested.

More recently, a second-order rate constant of 3.44×10^6 M^{-1} s^{-1} has been measured for the reaction of 41 with methanol at room temperature.[74] Data for direct comparison with other alcohols is not available, but the relatively long half-live for fluorenone oxide (32) in 2-propanol (≥55 μs)[70] suggests that this solvent is less reactive ($k \approx 10^5$ M^{-1} s^{-1}).

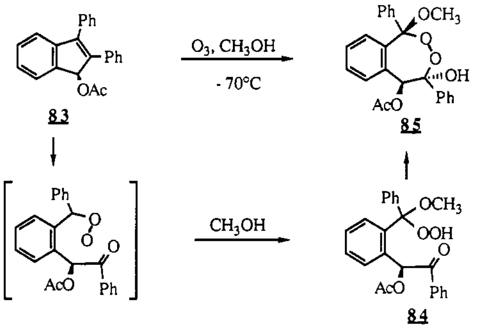
Schreiber[94] recognized the symmetry-breaking property of alkene ozonolysis—the equivalent olefinic carbons of a symmetric, cyclic alkene are converted to different functional groups: in methanol, these are a carbonyl and an α-methoxy hydroperoxide. In conjunction with procedures to selective modify one or the other of these groups, the method provides for the controlled preparation of linear molecules with differentiation of the terminal functionality. Of course, for nonsymmetric alkenes, one can also exploit the regioselectivity of primary ozonide fragmentation to control the development of new functionality.

The intramolecular trapping of a carbonyl oxide by a suitably tethered alcohol is likewise very efficient: Schreiber has made good use of the β-scission chemistry of hydroperoxides in a beautifully clever route to macrocyclic lactones:[95]



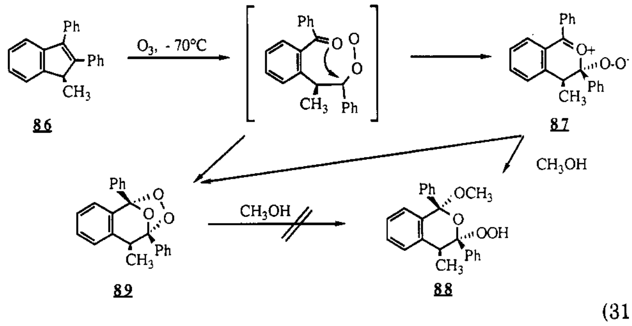
(29)

Under the right circumstances, other groups can participate in the nucleophilic trapping of carbonyl oxides. Nojima and co-workers have found that, with cyclic olefins, ozonation in methanol can lead to a variety of complex peroxides involving participation of both Criegee fragments along with the solvent.[96,97] The conversion of **83** to **85** probably proceeds by the usual addition of methanol to carbonyl oxide to form the α-methoxy hydroperoxide **84**, which then closes to the hemiacetal **85**.



(30)

A different trapping mode is indicated by the structure of **88**, obtained on ozonation of **86** in methanol. In this case, the carbonyl oxide is captured by intramolecular addition of the carbonyl oxygen, followed by reaction with the solvent. This process is especially interesting in that it exemplifies a combination of carbonyl oxide with a carbonyl group which does not result in cycloaddition. In fact, this represents the first step of a nonconcerted cycloaddition—in principle, the zwitterion **87** could close to form the ozonide **89**. In fact, in nonnucleophilic solvents, the ozonide is obtained directly. The ozonide is stable in methanol, confirming that it is not the precursor to **88** and supporting the idea of a stepwise mechanism for combination of carbonyl oxide with a carbonyl group. This is discussed more fully in the next section.



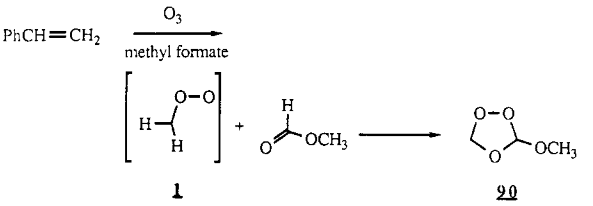
(31)

B. Cycloadditions

As typical 1,3-dipoles, carbonyl oxides participate in the cycloaddition chemistry characteristic of this class of reactive intermediates. The best-known reaction of this type is the cycloaddition with carbonyl compounds to give ozonides (1,2,4-trioxolanes), but a number of other π-bonded systems have also been found to be suitable dipolarophilic partners.

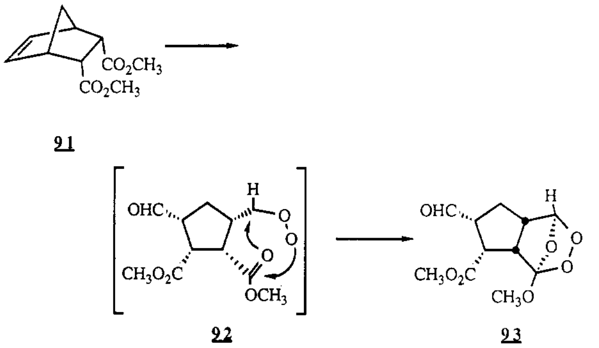
1. Cycloaddition with the C=O Group

As a general rule, ozonide formation is efficient only for cycloaddition of carbonyl oxide with aldehydes. Ketones are considerably less dipolarophilic, and good yields of ozonides are limited to special situations involving particularly reactive ketones, intramolecular reactions, or where the ketone is used as the reaction solvent and is therefore present in large concentration.[2] Esters are even less reactive than ketones, and in fact have been used as "nonparticipating" solvents for ozonolysis. In 1984, Keul and Kuczkowski showed that, under favorable conditions, carbonyl oxides would react with esters.[38,98] In this case, formate esters were chosen to trap the carbonyl oxide, since these are most like aldehydes, and should have the highest dipolarophilicity. Thus, ozonolysis of styrene in methyl formate as solvent led to the isolation of 5–10% yields of the alkoxy ozonide **90**, the product from cycloaddition of dioxymethyl with the ester.[98a] Less reactive esters, such as methyl acetate, gave correspondingly lower yields. The major product (75%) from this reaction is styrene ozonide, indicating that recombination of the carbonyl oxide with the cognate aldehyde is more favorable than cycloaddition to the ester. Higher yields of the alkoxy ozonide are obtained by ozonolysis of methyl vinyl ether in methyl formate—in this case, the PO fragments with high selectivity to dioxymethyl and methyl formate. Under these conditions, a 29% yield of the alkoxy ozonide **90** is obtained.[38a]



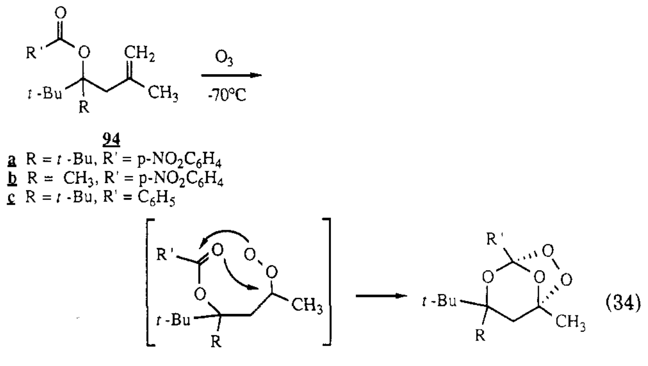
(32)

Odinokov et al. found that ozonation of the cyclopentadiene–maleic ester adduct **91** gave 15% of the crystalline ozonide **93**, resulting from intramolecular cycloaddition of the nascent carbonyl oxide with the adjacent ester group.[99] An interesting feature of this transformation is the competition of the ester and the aldehyde within **92** for the carbonyl oxide; cycloaddition with the aldehyde is sterically difficult, and so intramolecular reaction takes place at the ester.



(33)

Ozonolysis of the homoallylic ester **94a** proceeds to the bicyclic alkoxy ozonide **96a** via an unusually efficient intramolecular carbonyl oxide–ester cycloaddition.[100] The high yield for formation of **96a** is due to a fortuitous coincidence of steric and electronic effects. The steric influence of the *gem*-di-*tert*-butyl group is to restrict the conformations of **95a** to those which place the carbonyl oxide in close proximity to the ester, thereby favoring cyclization. Replacement of one of the *tert*-butyl groups by methyl restores enough conformational flexibility so that intramolecular cycloaddition is no longer preferred: **94b** gives none of **96b**. Likewise, the electron-withdrawing effect of the *p*-nitro substituent is critical, since the analogous benzoate derivative **94c** does not form ozonide. It is clear



94

a R = t-Bu, R' = p-NO₂C₆H₄
b R = CH₃, R' = p-NO₂C₆H₄
c R = t-Bu, R' = C₆H₅

95 → **96a** (86%) (34)

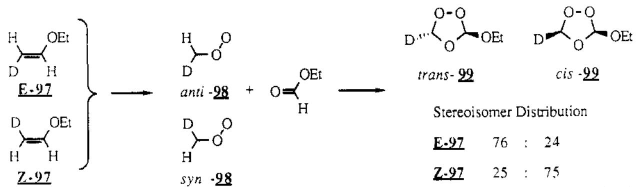
from these examples that, despite the uniquely efficient conversion of **94a** to **96a**, the carbonyl oxide–ester cycloaddition is not a favorable process. In general, one can expect that other, competing reactions of the carbonyl oxide will be more facile, and alkoxy ozonide yields will be low.

In principle, the yield of ozonides from alkene ozonolysis would be improved if side reactions of the intermediate carbonyl oxide could be reduced. One strategy to accomplish this is to immobilize the alkene during ozonolysis—the carbonyl oxide and carbonyl cleavage products will be likewise immobilized, in close proximity to one another, which should favor their recombination to ozonide. Silica gel has been used as a support material for this purpose,[101] but the most spectacular success has come with Griesbaum's use of powdered polyethylene as an inert support.[102,103] The "dry ozonolysis" technique has already been used to prepare a large number of ozonide types for which conventional solution methods fail, including those from tetrasubstituted alkenes, large-ring cycloalkenes, vinyl chlorides, ethers, and esters. Undoubtedly, this method will continue to provide access to new classes of substituted ozonides.

Cycloadditions of carbonyl oxides to carbonyl groups have been variously described as concerted, biradical, or zwitterionic processes. On the basis of thermochemical considerations, Nangia and Benson conclude that, at least for cycloaddition to aldehydes, biradical pathways will not compete with a concerted cycloaddition.[24] This is, of course, an orbital symmetry allowed [$_\pi4 + _\pi2$] process, which may involve considerable variation in the degree of synchronicity for the forming bonds. Experimental study of the mechanism is complicated by several factors. For example, solvent cage effects are often significant for ozonide formation from alkenes. Particularly in nonpolar solvents, a significant proportion of ozonide results from in-cage recombination of the fragments from the same PO. This can be rationalized in terms of the dipole–dipole interaction between carbonyl oxide and its carbonyl partner, which favors the head-to-tail orientation appropriate for cycloaddition. Solvents of higher permittivity can stabilize these polar intermediates, facilitating escape from the solvent cage. Indeed, the proportion of ozonide which forms outside of the original solvent cage is found to increase with solvent polarity.[7]

Reaction stereoselectivity is a useful probe of reaction mechanism. For alkene ozonolysis, some transmission of alkene stereochemistry to the final ozonide is observed, since cis and trans alkene stereoisomers tend to give different cis/trans ozonide mixtures. The interpretation is not entirely straightforward, since both the stereoselectivity of the PO fragmentation (formation of syn vs anti carbonyl oxide) and that of the subsequent cycloaddition come into play. Explanations for the overall stereoselectivity of alkene ozonolysis based on both concerted and stepwise cycloaddition steps have been advanced. These have been reviewed elsewhere.[2,7]

We focus here on the question of concertedness for the carbonyl oxide–carbonyl cycloaddition. The most compelling evidence in favor of concerted reaction comes from Kuczkowski and associates.[104,105] An especially striking result is the finding that the stereolabeled ethyl vinyl ethers **97** lead to complementary distributions of stereolabeled ozonides (**99**).[104] It is known that

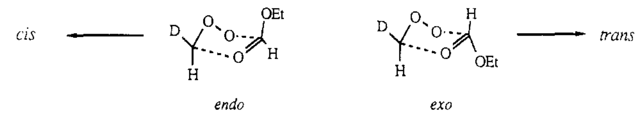


Stereoisomer Distribution

E-97	76	24
Z-97	25	75

(35)

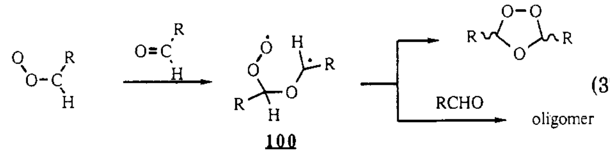
the PO cleavage is highly selective for formation of dioxymethyl,[38] and so the product distribution reflects stereoselective formation and cycloaddition of the stereolabeled carbonyl oxides *syn*- and *anti*-**98**. The preservation of stereochemistry in this system is remarkable, since even a totally concerted cycloaddition reaction could wash out the stereochemical differences. For example, assuming that PO cleavage is entirely stereospecific (say, *E*-**97** leads exclusively to *anti*-**98**; the argument holds regardless of the stereochemical assignment), concerted recombination of carbonyl oxide with ethyl formate can occur in either an endo or an exo mode. As indicated, these lead to different stereoisomers of the ozonide product. Therefore, the 3:1 stereospecificity for the overall process is the *lower* limit for any individual step and is entirely consistent with a sequence of concerted processes. On the other hand, a stepwise cycloaddition process can only account for these results if it is assumed that ring closure is faster than single bond rotations.



(36)

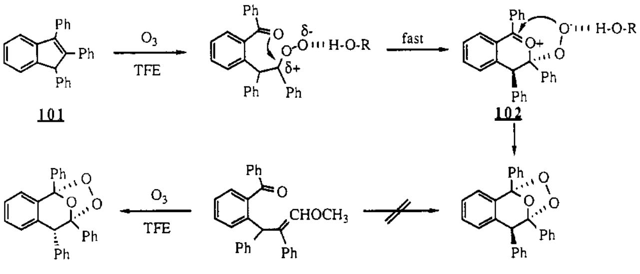
Further evidence in favor of a concerted cycloaddition comes from a study of kinetic secondary isotope effects (KSIE) on the process.[105] By analysis of the isotope composition of ozonides from ethylene-1,1-d_2 in the presence of varying amounts of acetaldehyde, an inverse deuterium KSIE was established for the carbonyl oxide in the cycloaddition.[105a] Similarly, an inverse KSIE was demonstrated for the carbonyl component as well.[105c] Since an inverse KSIE is generally associated with change in carbon hybridization from sp^2 to sp^3, these results imply that cycloaddition involves development of bonding for both carbon centers at the transition state, that is, a concerted reaction.

While this constitutes strong evidence for a concerted mechanism for some carbonyl oxide–carbonyl cycloadditions, a very substantial case has been made for the operation of a stepwise process for others.[106–108] For instance, it is known that yields of ozonides are drastically reduced, and the amount of peroxide oligomer correspondingly increased, when alkene ozonolysis is carried out with aldehyde as the solvent. This is difficult to reconcile with a concerted mechanism where increased aldehyde concentration should enhance carbonyl oxide recombination to ozonide. The implication is that an ozonide precursor is diverted to the oligomer. Murray has pointed out that the "added aldehyde effect" can be explained by assuming a stepwise carbonyl oxide–carbonyl cycloaddition process.[106] In this view, the intermediate, formulated as **100** according to the suggestion of Harding and Goddard,[13b] could undergo ring closure to the ozonide, or, in the presence of excess aldehyde, further additions to give oligomeric products.



(37)

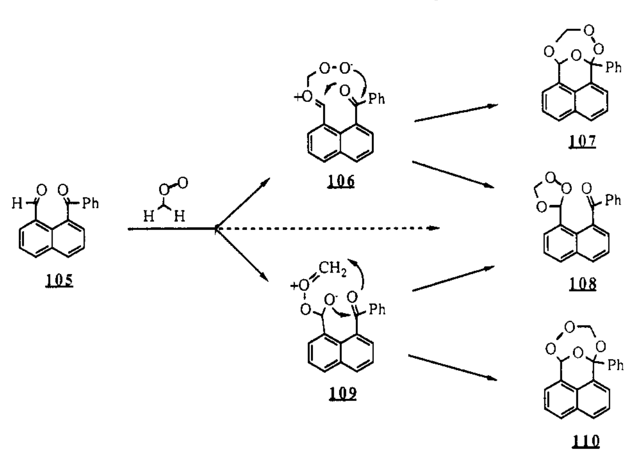
In order to account for solvent effects on the yields and stereochemistry of ozonide formation, Nojima has proposed that the cycloaddition reaction occurs by a stepwise mechanism involving a zwitterionic intermediate.[96,107] A remarkable result is the enhanced yield of ozonides in protic, but weakly nucleophilic solvents such as 2,2,2-trifluoroethanol (TFE).[107c] The authors' rationale is that the electrophilicity of the carbonyl oxide is enhanced by solvation, and this facilitates nucleophilic addition of the carbonyl group to provide the zwitterion **102**. In nucleophilic solvents like methanol, this intermediate can be trapped (as for **86** → **88**, see above), but in TFE the peroxide closure to **103** is preferred. An interesting "memory effect" is observed in the ozonolysis of **101** and **104**. Although both of these



(38)

should give the same carbonyl oxide intermediate, they lead to nearly opposite stereoisomer distributions in the ozonide product. This is considered to involve a very rapid cyclization onto the solvated carbonyl oxide, before substantial conformational change in this sterically encumbered system can occur. Since the orientation of groups in the cyclic alkene is very different than in the open-chain compound **104**, cyclization proceeds with opposite stereochemical results.

Relevant to the scenario for oligomer formation outlined above, the sequential capture of two carbonyl groups by a carbonyl oxide has been reported very recently.[108] Dioxymethyl (from ozonolysis of ethyl vinyl ether) reacts with **105** to produce a variety of products, including **107**, **108**, and **110**. Formation of the "[3 + 2 + 2]" product **107** most likely proceeds from the zwitterionic intermediate **106**, with capture by the carbonyl group competing with closure to **108**. The regioisomeric peroxide **110** could arise by initial addition to dioxymethyl by the ketone carbonyl, with subsequent closure as for **107**. Alternatively, the authors suggest that the carbonyl oxide adds as a nucleophile to the aldehyde to give the zwitterion **109**, which cyclizes as shown.



(39)

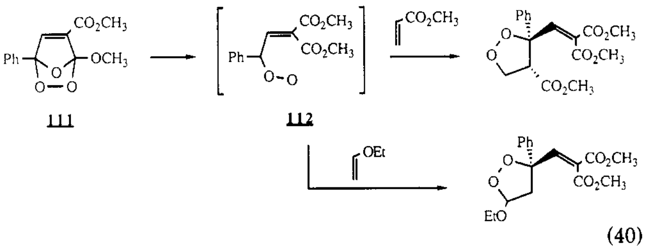
On the basis of the experiments describe dhere, three possible modes of cycloaddition for carbonyl oxides with carbonyl groups can be identified. For less-substituted systems, including ethylene, a concerted cycloaddition is likely. For other alkenes, it is apparent that a stepwise process operatres, and that either of the C–O bonds may be formed first. The situation is obviously complicated, and not enough data is yet available to define clear trends. Likewise, the intermediates have been variously described as diradicals or zwitterion, and this distinction will undoubtedly depend on variables such as structure and solvent. Finally, the sensitivity of carbonyl oxide reaction to structural features is evident in the fact that the second-order rate constant for reaction of **32** with acetaldehyde is three orders of magnitude larger than for **33** (see Table V).

2. Cycloadditions to Alkenes

The ready availability of ozonides from alkene ozonolysis has stimulated attempts to convert these to other, less accessible peroxides. The Nojima group was developed a route to 1,2-dioxolanes through the Lewis acid mediated decomposition of ozonides in the presence of alkenes.[109] This reaction involves the formation of an acid-complexed carbonyl oxide, as discussed in section III.E, which undergoes stepwise addition to the alkene.

During their study of vinyl ether ozonation, Keul and Kuczkowski found that 1,2-dioxolanes were produced as the major products.[38,104] As described earlier, the vinyl ether fragments to dioxymethyl and an ester. Because of the low reactivity of the ester, recombination of the Criegee fragments is not efficient. Instead, the carbonyl oxide adds to unreacted vinyl ether to yield a 3-alkoxy-1,2-dioxolane. A series of competition experiments established that the vinyl ethers are reasonably good dipolarophiles toward carbonyl oxides, ranking better than ketones but not as reactive as aldehydes.[38b] The regiochemistry of carbonyl oxide addition to the vinyl ether corresponds to that expected for electrophilic addition. Stereolabeled vinyl ethers were used to show that the alkene stereochemistry is completely retained in the dioxolane product, consistent only with a concerted cycloaddition process. Similar stereospecificity is observed when alkyl substituents are present.[38c]

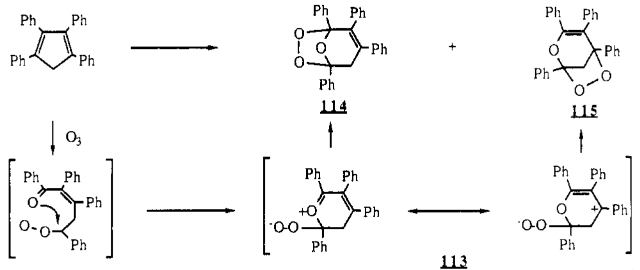
Electron-poor alkenes are also effective dipolarophiles toward carbonyl oxides, as recently demonstrated by Scarpati and co-workers.[90b] The carbonyl oxide **112**, generated by fragmentation of the furan endoperoxide **111**, was found to react with methyl acrylate as well as with ethyl vinyl ether. The reversal of regioselectivity in these two examples is notable, and is in accord with the bipolar character of the carbonyl oxide.



(40)

3. Other Dipolarophiles

For reaction of a carbonyl oxide with an α,β-unsaturated ketone, 1,2-additions to either the carbonyl group or to the alkene might be anticipated. On the other hand, the dipolar nature of carbonyl oxides raises the possibility for 1,4-addition across the enone system. In principle, this would be an orbital symmetry forbidden process, but could occur by a nonconcerted route. Nojima and co-workers have recently described such a reaction.[110] The controlled monoozonation of 1,2,3,4-tetraphenyl-1,3-cyclopentadiene leads to a mixture of the ozonide **114** and the [3 + 4] product **115**. Presumably, these form in a stepwise manner from the zwitterion **113**, which can close to either product.



(41)

Carbonyl oxides combine with other C=X π-systems to give cycloadducts. Imines[111] and thioketones[112] have been shown to react in this way. These compounds are relatively unreactive toward ozone, and so carbonyl oxides can be generated in their presence by ozonolysis of vinyl ethers. The reaction with imines is quite efficient; in fact, imines appear to be significantly more reactive than the comparably substituted ketones.[111] Most remarkable is the cycloaddition of carbonyl oxides with thioadamantanone, which occurs in preference to oxidation of the sulfur. In contrast, aryl thioketones do not form cycloadducts—the dominant reaction with carbonyl oxide is oxygen transfer to form the sulfine. This difference is attributed to the change in polarity of aryl thioketones which makes the sulfur more electrophilic, facilitating nucleophilic oxygen transfer by the carbonyl oxide.

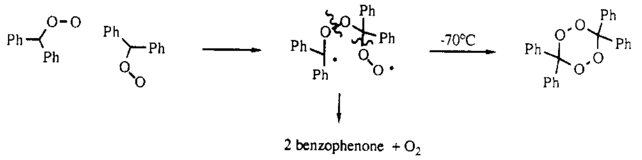
Cycloaddition of carbonyl oxide to the SO bond has been invoked as a key step in the gas-phase oxidation of SO_2 to H_2SO_4.[48,49] A cycloadduct was proposed to account for the fact that H_2SO_4 forms more rapidly than could be expected for hydration of SO_3; H_2SO_4 was considered to arise primarily from reaction of H_2O with this cycloadduct.[49] The formation of this intermediate is supported by the observation of oxygen exchange between labeled carbonyl oxide and SO_2.[48b]

Sawaki has suggested a similar process for the intriguing deoxygenation of diphenyl sulfoxide by an electron-poor carbonyl oxide.[113] The probable involvement of a cyclic adduct is supported by ^{18}O-tracer studies, which establish oxygen transfer consistent with the proposed mechanism.

4. Dimerization

A common byproduct in most condensed phase reactions of carbonyl oxides is a 1,2,4,5-tetraoxane, the carbonyl oxide dimer. These are often reasonably stable, crystalline compounds, though, as peroxides, they must be handled carefully. The concerted [3 + 3] dimerization of a carbonyl oxide is thermally forbidden, and probably occurs via a stepwise process. Typically, unsymmetrical carbonyl oxides give a mixture of *cis*- and *trans*-tetraoxanes.[114] In principle, other 1,3-dipoles should also react with carbonyl oxides. Indeed, the cycloaddition of carbonyl oxides with nitrones has been observed.[115]

In the absence of suitable coreactants, carbonyl oxide lifetimes are on the order of 10^{-5}–10^{-3} s at the typical concentrations employed.[69–74] The decomposition process has been studied by conventional flash photolysis with time-resolved spectroscopy,[72] or by optical modulation spectroscopy.[73] In most cases, bimolecular kinetics are observed for loss of carbonyl oxide. Benzophenone oxide (**31**) has been the best studied—the rate constant is somewhat less than that for a diffusion-controlled process. An activation energy of ~1.8 kcal/mol has been determined, with $\log A = 9.1$.[73] This has been interpreted in terms of a bimolecular process requiring substantial alignment of the reactants at the transition state. All of this, of course, is consistent with a dimerization process, but product studies indicate that the major product is benzophenone and oxygen,[55,73] and the dimer is only formed at low temperatures.[56] Presumably, the formation of benzophenone is accompanied by evolution of oxygen, but Bartlett and Traylor have determined that no O–O cleavage occurs.[56] The following mechanism, based on the proposal by Girard and Griller, can account for these results.[73]



(42)

C. Isomerization of Carbonyl Oxides

1. Syn-Anti Stereoisomerism

The issue of stereochemistry for carbonyl oxides is an important one, but for which there is only indirect information. It is clear that these intermediates carry stereochemical information—the different *cis*/*trans*-ozonide ratios obtained by ozonolysis of *cis*- vs *trans*-

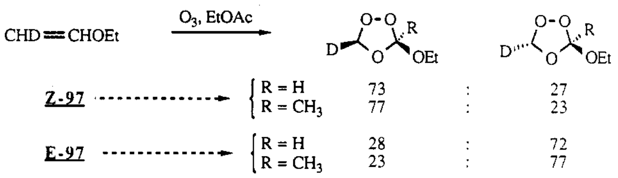
alkenes (generally, *cis*-alkene leads to a greater proportion of *cis*-ozonide, and *trans*-alkene forms more *trans*-ozonide, at least for larger substituent groups) implies that the ozonolysis intermediates also have differing stereoisomer distributions. For the Criegee mechanism, this is possible only with the carbonyl oxide. Models based on conformational analysis of the primary ozonide, and incorporating least-motion arguments in PO fragmentation, have been developed to predict the predominant carbonyl oxide geometry, and from this the resulting ozonide stereochemistry. Detailed discussions of these models are available[2,7] and will not be repeated here. One significant aspect of these stereochemical arguments is that the carbonyl oxides are configurationally stable—if syn–anti equilibration were rapid, both *cis*- and *trans*-alkenes would produce the same mixture of ozonides.

Theoretical studies of the syn/anti interconversion of carbonyl oxides indicate a substantial activation barrier for the process.[11,13,15,21] Two isomerization pathways are possible, corresponding to inversion through the central oxygen (via a linear C–O–O system) or rotation about the C–O bond. According to Cremer,[15a] the latter process is the lower energy path, with a barrier of 32.1 kcal/mol for dioxymethyl. A slightly larger barrier (35.6 kcal/mol) is predicted for the conversion of syn- to *anti*-dioxyethyl; as mentioned earlier, the syn form is more stable than the anti. The calculated energies indicate that syn–anti interconversion should be slow compared to other reactions of the carbonyl oxides, and it is reasonable to expect configurational stability for these intermediates.

Such computations, of course, refer to isolated molecules in the gas phase, and it must be kept in mind that solvation effects can dramatically alter the energetics of these processes. It is quite possible that the activation barrier for carbonyl oxide stereoisomerization is much lower in solution. Thus, Bailey has observed that the ozonide stereoisomer distributions from *cis*- and *trans*-alkenes tend to converge at higher temperatures,[116] which is attributed to partial equilibration of carbonyl oxides at the higher temperatures. An opposite shift in isomer distribution is found in the presence of certain polyalkylbenzenes. This was rationalized in terms of π-complexation with the carbonyl oxide, which either inhibited syn–anti isomerism, or afforded preferential stabilization of the anti form, or both.[116] Moreover, the rate of warmup after ozonation also influences ozonide stereochemistry. For both *cis*- and *trans*-alkenes with bulky substituents, the proportion of *cis*-alkene is higher if a very slow warmup (24 h to reach room temperature) is used.[116b,117] Since the standard models indicate that *cis*-ozonide is formed preferentially from *anti*-carbonyl oxide, these results have been taken to indicate that more *syn*-carbonyl oxide is available under the fast warmup conditions. Isomerization of some *anti*-carbonyl oxide to the more stable syn form might be possible with the higher temperatures during rapid warmup.

Nevertheless, these results are very complicated, and it is difficult to isolate the effects of possible syn–anti equilibration from other possible influences on ozonide stereochemistry. For instance, the intervention of a stepwise pathway for ozonide formation might be more significant at higher temperatures. This is reasonable if one considers that the concerted cycloaddition should have a more unfavorable entropy of activation than a stepwise reaction, and this feature will become more important at higher temperatures. The stereochemistry of a stepwise mechanism, which might therefore compete, would be determined at the final ring-closure stage and would likely favor the more stable *trans*-ozonide. In this connection, it is interesting to note that Murray has suggested, on the basis of warmup effects on ozonide stereochemistry from diisopropylethylene, that a mechanism change occurs around −60 °C.[117] Obviously, there are several possible factors influencing the ozonide stereochemistry, and it is extremely difficult to sort them out individually.

In any case, the fact that different *cis*/*trans*-ozonide mixtures are obtained from stereoisomeric alkenes is evident that carbonyl oxide syn–anti equilibration is incomplete, if it occurs at all. Keul and Kuczkowski have completed a very nice set of experiments which suggest strongly that syn–anti interconversion is insignificant for dioxymethyl.[104] As described in section IV.B.1, the 3:1 stereospecificity for ozonide formation from stereolabeled ethyl vinyl ether indicates a high degree of concert for the formation and cycloaddition of the stereolabeled carbonyl oxides, and also places an upper limit on the extent of their interconversion. Virtually the same 3:1 stereospecificity is obtained in pentane and in ethyl formate as solvent. If syn–anti equilibration were important, a change in stereochemistry might be expected for the more polar solvent. In addition, when ethyl acetate is used as the solvent, both alkoxy ozonides are obtained, and both with 3:1 stereospecificity. The invariance of this ratio to changes in solvent and dipolarophile is a strong indication that stereoisomer equilibration does not occur. Interestingly, a similar isomer distribution was obtained when dioxymethyl was generated from the corresponding labeled styrene or 1-hexene. This suggests that the carbonyl oxides are formed with very high stereoselectivity, and that the 3:1 ratio of products reflects competition between endo and exo transition states for the ozonide-forming cycloaddition, as discussed above. An assignment for the stereochemistry of the carbonyl oxides must be tentative, but assuming that the bulky substituent prefers the equatorial position for all three PO's, the prediction is that the *E*-labeled alkenes will lead to the *anti*-carbonyl oxide, and the *Z*-alkene to the syn isomer.[104] If this is correct, the major cycloaddition pathway with ethyl formate is via the exo transition state.



(43)

A similar study with the stereoisomeric 1-ethoxypropenes can, in principle, permit a similar analysis of the possibility for syn–anti interconversion for dioxyethyl.[38c] The situation here, however, is considerably more complex. In particular, it is no longer reasonable to assume similar reactivity for syn and anti stereoisomers, nor will the stereoisomeric primary ozonides form or fragment with the same rates. A computer program was developed to model the kinetics of the process, and rate constants were determined which would allow the best fit to the experimental yields.[38c] Although the system could not be determined uniquely, the model does predict partial stereospecificity (4:1) for carbonyl oxide formation, and implies that the carbonyl oxides are configurationally stable. Clearly, more studies are needed which will address this question, and allow study of more substituted systems.

Obviously, direct observation of the dynamics of syn and anti isomers of carbonyl oxides would be an ideal solution. This has not yet been achieved. Nevertheless, Sander has found two distinct bands for O–O stretch in the IR spectrum of matrix-isolated dioxyphenylmethyl (**47**), which might be attributed to the presence of syn and anti stereoisomers of this species.[63c] On the other hand, for **51**, where stereoisomerism is also possible, only one band is observed.[65]

2. Cyclization to Dioxirane

A most intriguing aspect of carbonyl oxide chemistry is the connection of these compounds with their cyclic isomers, the dioxiranes. The very recent development of dioxiranes as potent oxygen-transfer agents has stimulated much interest in the similarities, and especially the differences, between these classes of molecules. In this section, the isomerization of carbonyl oxides to dioxiranes will be considered.

Can carbonyl oxides be converted to dioxiranes? The answer is clearly that they can, under the right circumstances. As discussed in section II.C, the isomerization of carbonyl oxide to dioxirane is thermodynamically favorable, but involves a substantial activation barrier. For ground-state dioxymethyl in solution, unimolecular transformation to dioxirane is too slow to be competitive with other processes. On the other hand, carbonyl oxides produced in the gas phase, whether by alkene ozonolysis or by carbene–O_2 reaction, retain substantial excess internal energy which is not efficiently dissipated. This is evident from the discussion in Section III.A, where it was pointed out that a large fraction of the carbonyl oxide produced in the gas phase cannot be trapped as such. Instead, this portion of the intermediate reacts further through numerous unimolecular isomerization and fragmentation channels. In at least some cases, these involve conversion of the carbonyl oxide to a dioxirane. Thus, for the ozonolysis of ethene, the products include CO, CO_2, H_2O, H_2, and formic acid.[36,46,50] These are considered to arise via conversion of "hot" dioxymethyl to thermally excited dioxirane, which isomerizes to an excited state of formic acid.[6] Fragmentation and quenching of this intermediate accounts for many of the observed products. Because of the exothermicity of its formation, the dioxirane should be very short-lived. It is therefore somewhat of a paradox that dioxirane has been detected in the gas phase from ozonation of ethene at low temperature.[118] It has been suggested that this may have been produced by an indirect pathway.[8]

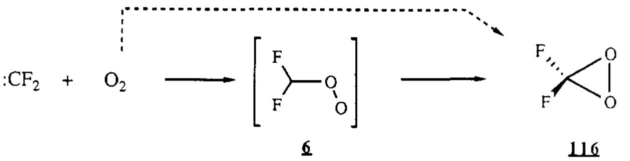
Isomerization to dioxirane appears to be a dominant process for "hot" dioxymethyl, but becomes relatively less important for substituted carbonyl oxides produced by gas-phase ozonation. For the ozonation of *trans*-2-butene, the dioxirane channel is still operable, but other processes compete.[46d] With dimethylcarbonyl oxide, from ozonation of tetramethylethylene, the dioxirane pathway does not contribute significantly.[46c] The products arise largely from tautomerization, to be discussed in the next section.

The conversion of carbonyl oxides to dioxiranes can be accomplished photochemically, as has been demonstrated for several matrix-isolated species.[61–68] In fact, the extreme photolability of carbonyl oxides requires that particular care be exercised in their preparation and characterization. In oxygen-rich matrices, it is important to use low-wavelength irradiation ($\lambda \leq 300$ nm) to effect generation of the carbene precursor, which reacts with available oxygen to form the carbonyl oxide. Light of longer wavelength will be absorbed by the carbonyl oxide, and will cause isomerization to the dioxirane and other products. This was a problem encountered in an attempted preparation of cyclopentadienone oxide (**28**);[60] the actual product was later shown to be the isomeric dioxirane **53**.[62] Alternatively, the carbene can be generated in more lightly O_2-doped matrices, and the carbonyl oxide generated in the dark by annealing the matrix to permit diffusion of oxygen to the carbene. Photoisomerization can be selectively induced by irradiation[63,65,66] with visible light ($\lambda \approx 600$ nm)—this apparently is the domain of the $n \rightarrow \pi^*$ transition for the carbonyl oxide, and the dioxirane product is transparent in this region, minimizing further photochemistry. The dioxiranes, in turn, can be photolyzed at ~400 nm; rearrangement to esters is a major reaction pathway.[59,61–68]

For some carbonyl oxides, photoisomerization to the dioxirane is quite inefficient. Especially for carbonyl oxides with one hydrogen substituent, a significant side reaction is the photoextrusion of an oxygen atom from the carbonyl oxide, producing the corresponding aldehyde.[63,64] The oxygen atoms so produced can combine with unreacted carbene when the matrix is annealed—chemiluminescence observed during this process has been attributed to this reaction.[63–65]

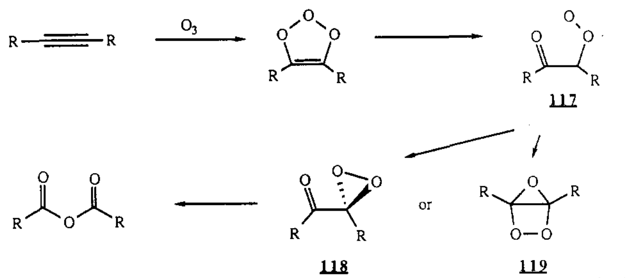
The formation of esters as byproducts in the solution-phase reactions of carbonyl oxides raises the question as to whether dioxiranes are involved in these conversions. Sawaki and associates have studied the mechanism of ester production from the photooxygenation of diazoalkanes.[119,120] Isotope tracer experiments established that oxygen scrambling was complete—a unimolecular process, including the involvement of a dioxirane, was therefore ruled out. In fact, crossover experiments established that the ester alkyl groups were also scrambled intermolecularly, and a radical chain mechanism, not involving a carbonyl oxide, was proposed for ester formation.[120]

While these results seem to rule out dioxirane formation for many carbonyl oxides, some special cases exist where ring closure might be favorable. The reaction of difluoromethylene with oxygen has been reported to provide an intermediate which epoxidizes alkenes stereospecifically.[20] This is a result more typical of dioxiranes than of carbonyl oxides.[5] Moreover, ab initio calculations indicate that the isomerization of carbonyl oxide to dioxirane is facilitated by the presence of π-donors such as F,[19b] and for the difluorocarbonyl oxide **6**, closure should be fast. Therefore, the weight of the evidence falls in favor of difluorodioxirane **116** as the active oxygen-transfer agent. This might be formed directly from the CF_2–O_2 reaction, or proceed via **6**.



(44)

Dioxiranes have also been proposed as one of the intermediates in the ozonation of certain alkynes. A mechanism for alkyne ozonation is illustrated below.

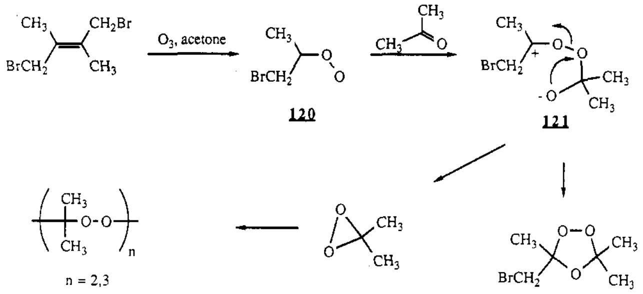


(45)

Ring opening of the initially formed 1,2,3-trioxolene provides the acylcarbonyl oxide **117**, which can cyclize either to the 2,3,5-trioxabicyclo[2.1.0]pentane **119** or to dioxirane **118**. Both of these intermediates can be expected to isomerize to the anhydride, a usual end product of the reaction.[121] Keay and Hamilton[122] determined that two unstable intermediates capable of alkene epoxidation were produced in the ozonation of 2-butyne. The first, which decomposed at temperatures above −50 °C, was assigned the 1,2,3-trioxolene structure, and the second species, stable to −15 °C, was tentatively identified as the dioxirane **118**. Ando et al. have presented NMR evidence that the low-temperature oxidant is in fact the trioxabicyclo[2.1.0]pentane (**119**), which was found to decompose at −50 °C.[123] This assignment is also favored by Pryor, Govindan, and Church, who studied the reaction by ESR in the presence of spin traps.[124] These workers also found that the −15 °C oxidant formed an acetyl spin adduct, which they considered to arise from **118**. This assignment is in line with the earlier IR study of DeMore and Lin, which showed that the anhydride precursor contained a carbonyl group.[125] One inconsistency, however, is evident. Keay and Hamilton found that the −15 °C peroxide transferred oxygen to alkenes in a nonstereospecific fashion.[122] This does not fit well with the current picture of dioxiranes as highly stereospecific oxidants,[5] and this point must be rectified before the dioxirane intermediate can be accepted.

If the assignment is correct, the implication is that the acylcarbonyl oxide can isomerize to the dioxirane. No computational results are available, but Cremer has indicated that π-acceptors should raise, not lower, the activation barrier for direct ring closure.[19b] Itoh and co-workers have studied the decomposition of **41** (see Chart I): there is no evidence for dioxirane formation from this ester-substituted carbonyl oxide.[74] It is, of course, possible that species like **119** might rearrange to the dioxirane, and this could provide an alternate route to the dioxirane. Finally, in this connection it is interesting to review the mechanistic dichotomy observed by Adam (Section III.E): the saturated endoperoxide **70** rearranges via a carbonyl oxide, while the unsaturated analogue **71** appears to isomerize to the dioxirane.[89b] It can be noted that **71** opens to a vinylogous acylcarbonyl oxide, and dioxirane formation might be expected on that basis.

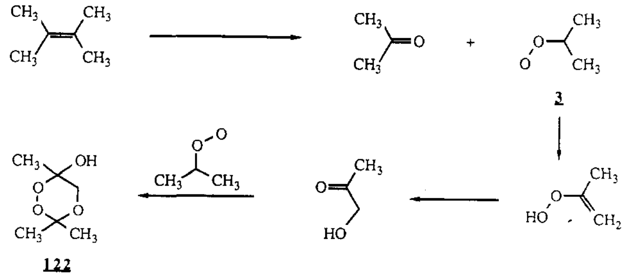
Other pathways for conversion of a carbonyl oxide to a dioxirane may be available under certain conditions. Murray and Agarwal have carried out the ozonation of *E*-1,4-dibromo-2-butene in acetone, and have identified acetone diperoxide and triperoxide among the products.[126] The symmetric alkene can give only the brominated carbonyl oxide **120**, and this must transfer peroxide to the solvent. The authors propose that the products arise from dimerization and trimerization of dimethyldioxirane, which they consider to arise from stepwise addition of **120** to acetone. The intermediate zwitterion **121**, from nucleophilic addition of the carbonyl oxide to acetone, can close to form the ozonide, or proceed to dimethyldioxirane by extrusion of bromoacetone. Two features of this mechanistic scheme should be emphasized: first, it reaffirms the involvement of nonconcerted pathways in ozonide formation, and second, it outlines an alternative route from carbonyl oxides to dioxiranes which may be more favorable than direct unimolecular cyclization. This is an intriguing possibility which deserves further study to establish its viability and generality.



(46)

3. Tautomerization of Carbonyl Oxides

For carbonyl oxides with α-protons, tautomerization becomes a competitive isomerization pathway. Story and Burgess first demonstrated intervention of this process in the ozonation of tetramethylethylene in acetone solution.[127] The isolation of **122** along with a smaller amount of hydroxyacetone is rationalized by tautomerization of the initially formed dimethylcarbonyl oxide **3** to 2-hydroperoxypropene, followed by isomerization of this to hydroxyacetone. This ketol captures the carbonyl oxide, accounting for the observed product. Interestingly, hydroxyacetone has also been reported as a major decomposition product of dimethyldioxirane, and might be an alternative route to these products.[128] That reaction, however, occurs over

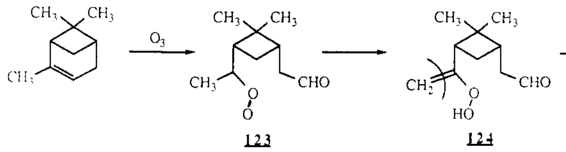


(47)

a period of several hours to room temperature, and does not appear to be rapid enough to contribute to the formation of **122** under the ozonolysis conditions.

Tautomerization appears to be the dominant process in the gas-phase ozonolysis of tetramethylethylene. At low pressure (4 Torr), where little of the dimethylcarbonyl oxide is collisionally stabilized, kinetic modeling leads to an estimate that 80% of the carbonyl oxide follows the tautomerization pathway, while isomerization to dioxirane is negligible.[46c] Similar results were obtained from studies at atmospheric pressure, where that portion of carbonyl oxide not collisionally stabilized was found to decompose via tautomerization.[51c] The situation for methylcarbonyl oxide from ozonation of *trans*-2-butene is more complex, but modeling studies suggest that both the dioxirane and the tautomerization pathways are operable.[46d]

The tautomerization process has been implicated in the atmospheric ozonation of certain terpenes.[129] Thus, ozonlysis of α-pinene in humid air leads to significant amounts of dioxymethyl Eq(48) (1), as evidenced by trapping products. While 1 cannot be produced directly from Criegee-type cleavage of α-pinene, this species can arise by tautomerization of the carbonyl oxide **123** and further ozonolysis of the hydroperoxy alkene **124**.



(48)

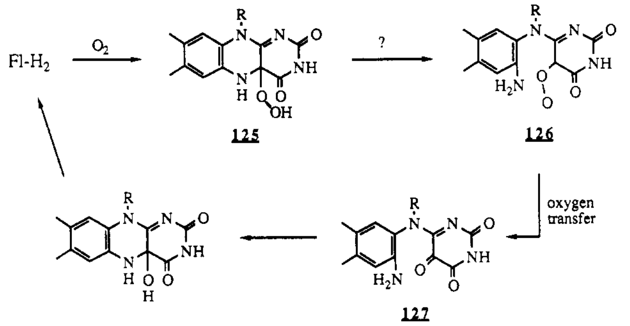
D. Oxygen-Transfer Reactions

In recent years, the recognition that carbonyl oxides are easily accessible, highly reactive peroxides has brought to the fore intensive study of their oxygen-transfer chemistry. Considerable effort has been directed at characterizing the oxidation chemistry of carbonyl oxides, differentiating it from the similar reactivity of dioxiranes and other peroxides, and establishing the pertinence of these processes to biological oxygenations and to problems in atmospheric environmental chemistry. Some of these reactions have been mentioned earlier. A more systematic overview follows.

1. Models for Biochemical Oxidations

Much of the interest in carbonyl oxides as oxygen-transfer agents relates to their apparent character as *oxenoids*,[4] that is, the ability to effect transfer of a singlet oxygen atom to suitable substrates. In this respect, the oxygen transfers are considered similar to the range of reactions for singlet carbenes: C–H insertion, addition to alkenes, and formation of arene oxides. The significance of these reactions is that they resemble a varity of processes carried out by oxygenase enzymes, and carbonyl oxides have been considered as possible models for these enzyme systems.[130]

Hamilton first proposed the involvement of carbonyl oxides in the action of the aromatic hydroxylase flavoenzymes.[4,131] These "mixed-function oxidases" use a bound flavin cofactor to react with O_2 and to deliver one oxygen to an aromatic ring, generating water with the other. Reaction of O_2 with dihydroflavin is known to provide the 4a-hydroperoxide **125**. Hamilton suggested that this intermediate could ring open to the acylcarbonyl oxide **126**, which would be the actual oxygen-transfer agent. Reclosure and dehydration provides oxidized flavin, which is turned over by reduction.



(49)

This proposal was based on the premise that a hydroperoxide like **125** would not be a good hydroxylating agent. Support for the oxenoid character of species like **126** was gained by the observation of phenol hydroxylation and alkene epoxidation by an intermediate in the ozonolysis of 2-butyne, presumed to be an acylcarbonyl oxide.[131b] Subsequent work, however, has cast doubt on that assignment (see section IV.C.2). Moreover, detailed studies of enzyme models based on modified flavins have demonstrated that hydroperoxides like **125** are actually very good oxygen donors,[132] and there is no need to postulate ring opening to carbonyl oxide. In addition, an intermediate observed spectroscopically in the flavoenzyme system cannot be reconciled with the involvement of ring-opened forms like **127**.[133]

An analogous proposal for the involvement of carbonyl oxides in pteridine-dependent monooxygenases is likewise unconfirmed by experiment.[130b] Nevertheless, the concept of carbonyl oxides as oxenoid species has greatly stimulated interest in their oxygen-transfer potential and has led to the discovery of a number of intriguing processes.

2. Oxygen Atom Loss

Under certain conditions, carbonyl oxides can fragment by ejection of an oxygen atom to produce the corresponding carbonyl compound. While not, strictly speaking, an oxygen transfer process, this can be an important reduction pathway for carbonyl oxides and is included here.

The gas-phase (1 atm) reaction of CH_2 with O_2 leads to "hot" dioxymethyl (the reaction is exothermic by 60 kcal/mol, see Figure 1); among the decomposition products are ozone and formaldehyde.[78] These are formed by fragmentation of dioxymethyl to formaldehyde and an oxygen atom, which recombines with O_2 to provide ozone. This decomposition mode is not easily accessible in this system, amounting to an estimated[8] 1–5% of the total carbonyl oxide consumption. A substantial activation barrier is indicated by the fact that dioxymethyl produced in the less-energetic ethene ozonolysis does not produce oxygen atoms at a detectable level.[53]

Likewise, the extent of O-atom formation from the gas-phase ozonation of *trans*-2-butene has been placed at 5% or less.[46d] This increases to 20% for dimethylcarbonyl oxide from ozonolysis of tetramethylethylene at low pressure (4 Torr).[46c] At atmospheric pressure, however, this pathway is not detected.[51c] Apparently, that fraction of carbonyl oxide which expels O atoms at 4 Torr is collisionally stabilized at the higher pressure and no longer has sufficient excess energy to cross the activation barrier for this process. Oxygen atom production from *trans*-dichloroethene is more efficient, amounting to 20% even at atmospheric pressure.[53]

Ketones have typically been observed as byproducts in the carbene–O_2 reaction in frozen matrices. Since bimolecular combination of the type **31** → (2 benzophenone + O_2) (Section IV.B.4) is improbable under matrix-isolation conditions, it is likely that the ketone is formed by unimolecular O-atom ejection from the carbonyl oxide. Sander has studied this reaction in some detail.[63–65] The generation of carbonyl oxides in inert matrices invariably produces some oxygen atoms. This can arise from scission of the initially formed "hot" carbonyl oxide, as well as from cleavage of the carbonyl oxide induced by the photolysis used to generate the carbene precursor. The photoejection of oxygen from carbonyl oxides competes with isomerization to the dioxirane, and this is sometimes the dominant reaction. For example, no dioxirane is detected from irradiation of **52**. Only hexafluoroacetone is obtained.[65]

The oxygen atom is generally considered to reside in the ground $O(^3P)$ state,[63a] although spin conservation arguments suggest that this is not the form produced initially.[8] Some of the oxygen atoms are lost by recombination to O_2, and in matrices with high O_2 content, formation of ozone has been observed.[63,64,68] Perhaps the most interesting process is the strong chemiluminescence observed on annealing these matrices. Sander has shown that this luminescence is most reasonably attributed to combination of oxygen atoms in the matrix with unreacted carbene.[63c] This produces the carbonyl compound in an electronically excited state, and the observed emission corresponds to phosphorescence of this species.

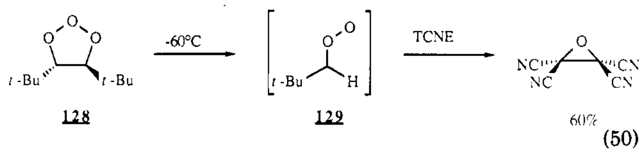
One curious feature of the competition between the dioxirane and O-atom pathways for decomposition of carbonyl oxides can be noted. For the photochemical conversion in frozen matrices, the O-atom splitting predominates over isomerization to dioxirane for those carbonyl oxides where one substituent is hydrogen.[63] This is opposite to the trend noted for the fragmentation of "hot" carbonyl oxides produced in gas-phase ozonolysis. For these, replacement of alkyl groups by H leads to increased importance of the dioxirane isomerization pathway.[46] No direct correlation should be expected, since these represent very different types of reactions, but this observation may have some implications for the nature of the excited states involved in these processes.

3. *Alkene Epoxidation*

In 1963, Criegee and Günther reported that ozonolysis of tetramethylethylene in the presence of tetracyanoethylene (TCNE) does not give peroxide products.[134] Instead, acetone and tetracyanoethylene oxide are obtained in nearly quantitative yield. Since TCNE does not react with ozone under the conditions of the experiment, it was concluded that one of the peroxidic intermediates from ozonation of tetramethylethylene was capable of effecting epoxidation of TCNE. Kwart and Hoffman[135] pointed out that the tautomeric form of a peracid, which they considered to be involved in alkene epoxidation, was in fact a carbonyl oxide and suggested that it is the carbonyl oxide which is the oxygen-transfer agent in alkene ozonations. Epoxide formation has also been attributed to intermediates in the ozonation of alkynes[121–124] and haloalkenes[136]—these might be due to carbonyl oxides, but this is not certain. From the discussion in Section IV.C.2, it is possible that some of these might involve dioxiranes or other peroxidic species. The reaction is more readily studied when carbonyl oxides are prepared by methods not involving ozonolysis. Murray et al. demonstrated that the carbonyl oxide from singlet oxygenation of diazodiphenylmethane is indeed capable of alkene epoxidation.[137] For the dialkyl olefins studied here, epoxidation is much less efficient than with TCNE. Nevertheless, oxygen transfer from the carbonyl oxide does occur, and the epoxidation is partially stereospecific: trans olefins give trans epoxides while cis olefins give predominately cis epoxides. The partial erosion of stereochemistry with cis alkenes can be contrasted with the high stereospecificity obtained from dioxirane epoxidation—Murray has suggested that this criterion may be useful for differentiation of carbonyl oxides and dioxiranes.[5a] Interestingly, Murray et al. have observed a significantly lower transmission of stereochemistry in epoxidation by photochemically produced carbonyl oxide compared to that formed with thermally generated singlet oxygen (from $(PhO)_3PO_3$), and suggest that higher electronic states of the carbonyl oxide (with a different pattern of stereoselectivity) may be involved in the former case.[137] Of course, photochemical excitation of carbonyl oxides is now known to produce dioxiranes and/or oxygen atoms; since the former should enhance the stereospecificity of epoxidation, it is conceivable that the loss of stereochemistry might be due to contribution by O-atom addition to the alkene.

Sawaki et al. found that allylic H abstraction and C=C cleavage products were produced along with epoxides from reaction of carbonyl oxides with alkenes.[22] This might be interpreted in terms of radical character for the carbonyl oxide, but the low yield of the products leaves open the possibility that side reactions not involving the carbonyl oxide are dominant. Singlet oxygen, used to generate the carbonyl oxide, reacts with cyclohexene to give a product distribution similar to (and with higher total yield) that obtained for this alkene in the presence of diazofluorene, underscoring this point.

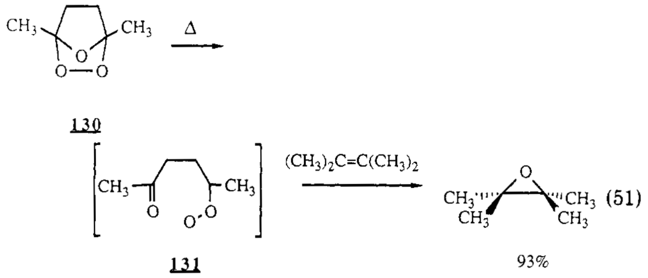
Pryor and Govindan have studied the decomposition of ozone-free solutions of the primary ozonide of *trans*-di-*tert*-butylethylene (**128**).[138] This unusually



(50)

stable 1,2,3-trioxolane fragments normally at −60 °C to *tert*-butyl carbonyl oxide **129**. In neat cyclohexene, only a trace of epoxide is obtained. In contrast, TCNE is epoxidized efficiently (60% yield) by **129**. The implication here is that carbonyl oxides are nucleophilic oxygen-transfer agents toward alkenes.

On the other hand, Adam and Rodriguez have obtained high yields of tetramethylethylene oxide from the intermediate formed on thermolysis of **130**.[89a] This is most reasonably the carbonyl oxide **131**, by analogy to that from 71, indicated through intramolecular trapping (section III.E). Likewise, Nojima and coworkers have demonstrated an intramolecular oxygen delivery from a carbonyl oxide to a vinyl ether.[139] These results indicate that even electron-rich alkenes can be oxidized efficiently under some circumstances.



130

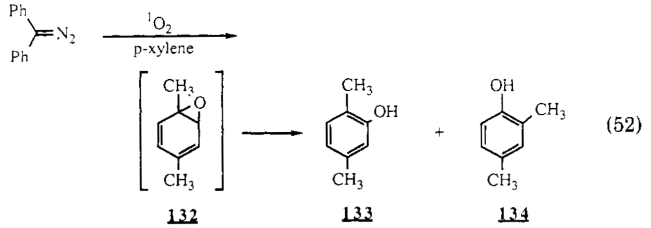
131

(51)

Alkene epoxidation by a carbonyl oxide has been studied theoretically by Cremer and Bock.[140] A concerted mode for oxygen transfer was identified and could be described as an S_N2-type attack of the alkene on the terminal oxygen of the carbonyl oxide. Analysis of the electron density in the transition state reveals the oxenoid character of this process. A polarization of the carbonyl oxide π-density toward the terminal oxygen atom (approaching a zwitterionic state) is balanced by withdrawal of the O-O σ-electrons to the central oxygen, ultimately resulting in O-O cleavage. Depending on the alkene, different frontier orbital overlaps can dominate. For electron-poor alkenes, interaction of the carbonyl oxide HOMO (compromising the enhanced π-density at the terminal oxygen) with the alkene LUMO is most significant, while the π HOMO of electron-rich olefins can interact strongly with a low-lying σ^* (O-O antibonding) orbital of the carbonyl oxide. Thus, both kinds of interactions can facilitate epoxidation, and help to explain why both electron-rich and electron-deficient alkenes are readily epoxidized.

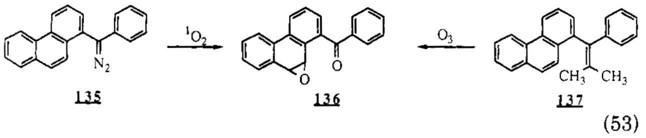
A special class of epoxidations is the hydroxylation of aromatic rings. A key experiment involved the demonstration that fluorenone oxide effects the conversion of 4-[^{2}H]anisole to 4-hydroxyanisole with significant retention of the deuterium label.[141] This is clear evidence for a hydroxylation mechanism which proceeds by formation of the arene oxide, followed by rearangement including the NIH shift, as observed for many microsomal oxidations.

Murray's group has carried out extensive studies of arene oxidation by carbonyl oxides.[142-144] Sensitized photooxygenation of diazodiphenylmethane in the presence of naphthalene gives an 85:15 mixture of α- and β-naphthols, consistent with the formation of naphthalene 1,2-oxide.[142a] Similarly, oxidation of p-xylene leads to a mixture of xylols, **133** and **134**, for which the latter must arise from NIH shift of methyl in the intermediate epoxide **132**.[142] Intramolecular oxygen transfer has been observed.[143c] In the case of **135**, the K-region arene oxide **136** is obtained in 7% yield after treatment with $^1O_2$. The same product was formed in the ozonolysis of **137**: when this alkene is immobilized on silica gel during ozonolysis, the arene oxide **136** is still produced, supporting an intramolecular path for oxygen delivery.[143c]



132 133 134

(52)



135 136 137

(53)

The electronic character of carbonyl oxide for arene oxidation was investigated by Agarwal and Murray.[144] The yields of naphthols from a series of substituted diphenyl carbonyl oxides could be correlated with substituent σ constants in a Hammett plot. The slope so obtained ($\rho = +0.93$) indicates that the carbonyl oxide acts as an electrophilic oxidant in these transformations. This, of course, is not consistent with the zwitterionic structure for a carbonyl oxide, but can be rationalized within the framework of carbonyl oxides as an oxenoid species. With naphthalene as substrate, the arene HOMO-carbonyl oxide LUMO interaction should dominate. In this situation, the electrophilic character of the carbonyl oxide should be expressed.

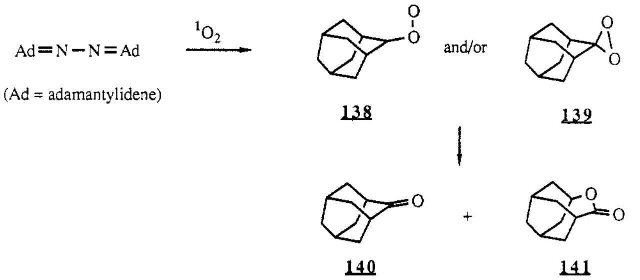
4. Baeyer-Villiger Oxidation

The Baeyer-Villiger oxidation of ketones to esters and lactones is a useful sythetic transformation. The reaction is also known in biological systems and can be considered an oxenoid process.[130a] Indeed, several of these are mediated by flavin-dependent monooxygenase enzymes, as for arene hydroxylation. In view of the activity of carbonyl oxides for the latter reaction, similar efficacy for Baeyer-Villiger oxidation might be anticipated. Although Baeyer-Villiger-type products are frequently observed in alkene ozonolysis, it is often difficult to determine whether these are derived through oxygen transfer from a carbonyl oxide or from some other intermediate.

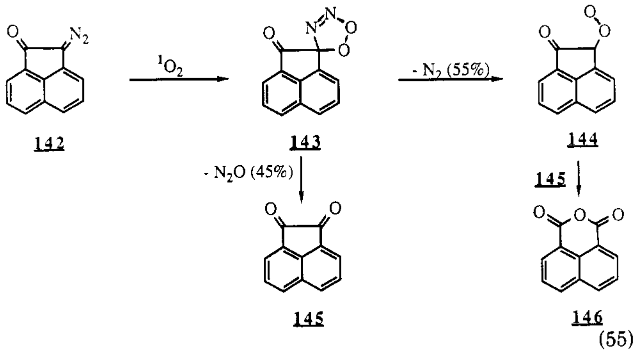
Here again, the generation of carbonyl oxides by photooxygenation of diazoalkanes helps to simplify a potentially complicated situation. This method has been used by Ando and associates in a study of oxygen transfer to silyl ketones.[145,146] Efficient conversion to the corresponding silyl esters was achieved with benzophenone oxide. Aryl silyl ketones react more readily than alkyl silyl ketones, leading the authors to suggest that delocalization of negative charge by the ketone substituent facilitates the rearrangement. The proposed mechanism involves nucleophilic addition of carbonyl oxide to the silyl ketone, followed by C-to-O migration of the silyl group, and elimination of benzophenone.[145]

Rearrangement of a silyl carbonyl oxide, obtained from photooxygenation of the corresponding silyldiazoalkane, to the silyl ester was also reported, and an intramolecular pathway was suggested.[146] Oxygen-tracer experiments,[120] however, are not consistent with this interpretation. Scrambling of the oxygens rules out a unimolecular rearrangement. On the other hand, crossover experiments indicate that transfer of oxygen from silyl carbonyl oxide to silyl ketone does not occur.[146b] Most likely, a radical chain decomposition of the diazoalkane as proposed by Sawaki[120] is responsible for the formation of these silyl esters, and carbonyl oxides do not play a significant role.

Photooxidation of adamantanone azine leads to mixture of adamantanone (**140**) and the lactone **141**, and a unimolecular rearrangement of the carbonyl oxide **138** or the isomeric dioxirane **139** was proposed to account for this.[85] A similar mechanism has been suggested for photooxygenation of 7-diazo-8-acenaphthenone (**142**).[147] An intermolecular oxygen transfer was considered unlikely in each case because the yield of oxidation products did not increase when excess ketone (**140** or **145**) was added. Sawaki's isotope tracer studies, however, rule out a unimolecular rearrangement for each of these reactions.[120] Moreover, in the case of **142**, the failure of added ketone to increase product yield is nicely explained by the observation that the evolved gases from photooxidation contain both N_2O (45%) and N_2 (55%), comparable to the product ratio **145**:**146**.[120] Therefore, much of the singlet oxygen–diazoalkane adduct **143** decomposes by loss of N_2O to provide the diketone **145**. The yield of carbonyl oxide is limited at the photooxidation stage and is already trapped efficiently by intermolecular reaction with **145**, so additional diketone has little effect. Ketones such as adamantanone have been shown to be readily oxidized by other carbonyl oxides,[89] and it may be concluded that these are intermolecular Baeyer-Villiger oxidations.



(54)



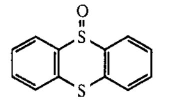
(55)

5. Oxidation at Sulfur

Organosulfur compounds are good acceptors for a variety of oxygen-transfer species, and carbonyl oxides are no exception. Sulfides and sulfoxides can be added to alkenes during ozonation, and function as efficient scavengers for carbonyl oxides. The formation of carbonyl oxides from other sources has likewise been probed by addition of sulfides or sulfoxides;[85,86] inhibition of reaction products in the presence of sulfoxide is taken as evidence that these are formed via a carbonyl oxide. Obviously, such determinations are sensitive to the involvement of other oxygen-transfer agents, for example dioxiranes, which might also be intercepted by these trapping agents. One particular advantage of sulfur compounds for the study of oxygen transfer is the range of oxidation levels at sulfur, with the attendant changes in electronic character of this center, which permits a rather detailed study of electronic character of these intermediates.

Sulfides and sulfoxide substituent effects have been used to gauge the reactivity of carbonyl oxides in oxygen transfer. As suggested by the results from alkene epoxidation described above, carbonyl oxides are capable of displaying a range of behaviors—the particular mode of reactivity which is expressed will depend to a large extent on substituent effects and on the reaction partner. Carbonyl oxides generally react faster with sulfoxides than with sulfides, and this has led to their characterization as nucleophilic species. Fluorenone oxide (**32**) exhibits nucleophilic character in reactions with substituted aryl sulfoxides, as evidenced by the positive value ($\rho = 0.26$) for a Hammett correlation.[22] On the other hand, benzophenone oxide (**31**) reacts with aryl sulfides as an electrophilic oxygen donor,[148] demonstrating that the electronic nature of the carbonyl oxide is not simply defined. Electron-withdrawing substituents on the carbonyl oxide do seem to enhance the electrophilic character of these species: trifluoroacetophenone oxide (**51**) reacts as an electrophile with both sulfides and sulfoxides.[113] Likewise, Ando has found that an acylcarbonyl oxide exhibits increased reactivity toward sulfides (electrophilic reaction) comparable to that with sulfoxides.[149]

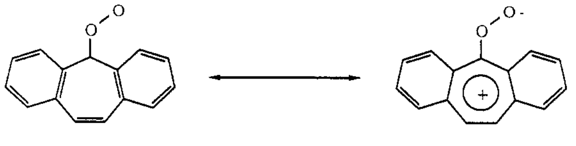
Adam has introduced thianthrene-5-oxide as a standard to measure electronic character in oxygen transfers.[150] The premise is that electrophiles will tend to react at the sulfide center of **147**, while nucleophiles will attack the sulfoxide group. The X_{SO} scale has been defined as the fraction of nucleophilic attack of **147**, and should vary between 0 (totally electrophilic reaction) and 1 (completely nucleophilic character). The scale has been calibrated against a number of common oxidants and shown to be useful for discriminating these systems.



147

(56)

A number of carbonyl oxides have been studied. In general, carbonyl oxides are determined to be nucleophilic by this method, having X_{SO} values in the range 0.8–1.0. Predictable variations can be observed: *tert*-butyl carbonyl oxide **129** ($X_{SO} = 0.94$) is more nucleophilic than benzophenone oxide (**31**, $X_{SO} = 0.83$), and the high nucleophilicity for dibenzotropone oxide (**148**, $X_{SO} = 1.0$) compared to dibenzosuberone oxide (**33**, $X_{SO} = 0.83$) can be attributed to a strong contribution of the aromatic resonance form shown. On the other hand, aromaticity should render cyclopentadienone oxide (**28**) electrophilic. This is not the case ($X_{SO} = 0.87$), and so



(57)

the contribution from resonance form **54** is not pronounced.

(58)

28 54

One potential use of the X_{SO} scale is in the differentiation of carbonyl oxides from other peroxide systems, especially dioxiranes. This remains a challenge. The X_{SO} scale has some promise in this area, since X_{SO} values for carbonyl oxides are generally larger than those for dioxiranes. Nevertheless, some difficulties remain. The X_{SO} values for dioxiranes (0.57–0.67) are higher than should be expected for these distinctly electrophilic species.[5a] Conjugative interaction between the sulfide and sulfoxide groups of **147** may alter their reactivity. Moreover, reaction at the sulfoxide can be electrophilic, and this would inflate the X_{SO} values for electrophiles.

V. Conclusion

Investigation of carbonyl oxides continues to present challenges for all comers. Tremendous progress has been made in the last 15 years; as always, there is much more to be learned. The discovery and development of new methods for the preparation of these reactive intermediates, and the application of sophisticated experimental and computational techniques to their characterization have paced recent advances and promise to play an increasingly large role in the future. The existence of carbonyl oxides from a variety of sources has been firmly established, and a number of reactivity patterns have been identified. Future work holds answers to subtler questions relating to mechanistic detail, stereoisomerism, excited-state chemistry, and the details of electronic structure, to name a few.

Acknowledgments. I thank Professors Rainer Glaser and John Adams of this department for many helpful discussions. Our own work in the area of carbonyl oxide chemistry has been possible through support from the University of Missouri Research Council and the National Science Foundation (Grant No. CHE-8806198), for which I am very grateful.

References

(1) Criegee, R.; Wenner, G. *Chem. Ber.* **1949**, *564*, 9.

(2) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic: New York, 1978; Vol. 1; 1982; Vol. 2.

(3) (a) Atkinson, R.; Carter, W. P. L. *Chem. Rev.* **1984**, *84*, 437. (b) Atkinson, R.; Lloyd, A. *J. Phys. Chem. Ref. Data* **1984**, *13*, 315.

(4) Hamilton, G. A. In *Molecular Mechanisms of Oxygen Activation*; Hayashi, O., Ed.; Academic: New York, 1974, pp 245–283.

(5) (a) Murray, R. W. *Chem. Rev.* **1989**, *89*, 1187. (b) Murray, R. W. In *Molecular Structure and Energetics. Unconventional Chemical Bonding*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988; Vol. 6, pp 311–351. (c) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* **1989**, *22*, 205.

(6) (a) Herron, J. T.; Martinez, R. I.; Huie, R. E. *Int. J. Chem. Kinet.* **1982**, *14*, 201. (b) Herron, J. T.; Martinez, R. I.; Huie, R. E. *Int. J. Chem. Kinet.* **1982**, *14*, 225.

(7) Kuczkowski, R. L. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; pp 197–275.

(8) Kafafi, S. A.; Martinez, R. I.; Herron, J. T. In *Molecular Structure and Energetics. Unconventional Chemical Bonding*; Liebman, J. F., Greenberg, A., Eds.; VCH Publishers: New York, 1988; Vol. 6, pp 283–310.

(9) Sander, W. *Angew. Chem., Int. Ed. Engl.* **1989**, *29*, 344.

(10) Ha, T.-K.; Kühne, H.; Vaccani, S.; Günthard, H. H. *Chem. Phys. Lett.* **1974**, *24*, 172.

(11) (a) Hiberty, P. *J. Am. Chem. Soc.* **1976**, *98*, 6088. (b) Hiberty, P. C.; Devidal, J. P. *Tetrahedron* **1979**, *35*, 1015. (c) Hiberty, P. C.; Leforestier, C. *J. Am. Chem. Soc.* **1978**, *90*, 2012.

(12) (a) Karlström, G.; Engström, S.; Jönsson, B. *Chem. Phys. Lett.* **1979**, *67*, 343. (b) Karlström, G.; Roos, B. O. *Chem. Phys. Lett.* **1981**, *79*, 416.

(13) (a) Wadt, W. R.; Goddard, W. A., III *J. Am. Chem. Soc.* **1975**, *97*, 3004. (b) Harding, L. B.; Goddard, W. A., III *J. Am. Chem. Soc.* **1978**, *100*, 7180.

(14) (a) Yamaguchi, K.; Ohta, K.; Yabushita, S.; Fueno, T. *J. Chem. Phys.* **1978**, *68*, 4323. (b) Yamaguchi, K.; Yabushita, S.; Fueno, T.; Kato, S.; Morokuma, K.; Iwata, S. *Chem. Phys. Lett.* **1980**, *71*, 563. (c) Yamaguchi, K. *J. Mol. Struct.* **1983**, *103*, 101.

(15) (a) Cremer, D. *J. Am. Chem. Soc.* **1979**, *101*, 7199. (b) Gauss, J.; Cremer, D. *Chem. Phys. Lett.* **1989**, *163*, 549.

(16) Kahn, S. D.; Hehre, W. J.; Pople, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 1871.

(17) Steinke, T.; Hänsele, E.; Clark, T. *J. Am. Chem. Soc.* **1989**, *111*, 9107.

(18) Yang, C.; You-Liang, W. *Theochem* **1990**, *204*, 285.

(19) (a) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3633. (b) Cremer, D.; Schmidt, T.; Gauss, J.; Radhakrishnan, T. P. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 427.

(20) Rahman, M.; McKee, M. L.; Shevlin, P. B.; Sztyrbicka, R. *J. Am. Chem. Soc.* **1988**, *110*, 4002.

(21) Hull, L. A. *J. Org. Chem.* **1978**, *43*, 2780.

(22) Sawaki, Y.; Kato, H.; Ogata, Y. *J. Am. Chem. Soc.* **1981**, *102*, 3832.

(23) Cremer, D.; Schmidt, T.; Sander, W.; Bischof, P. *J. Org. Chem.* **1989**, *54*, 2515.

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

(25) (a) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3627. (b) Cremer, D. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 888.

(26) This refers to the number of atoms involved in each π-system. For analyses based on the number of electrons involved, subscripts will be included. Thus, this process is a [${}_{\pi}4 + {}_{\pi}2$] transformation.

(27) (a) Bailey, P. S.; Ferrell, T. M. *J. Am. Chem. Soc.* **1978**, *90*, 899. (b) Lattimer, R. P.; Kuczkowski, R. L.; Gillies, C. W. *J. Am. Chem. Soc.* **1974**, *96*, 348.

(28) (a) Cremer, D. *J. Am. Chem. Soc.* **1981**, *103*, 3619. (b) Cremer, D. *J. Chem. Phys.* **1979**, *70*, 1911.

(29) (a) Fliszár, S.; Granger, M. *J. Am. Chem. Soc.* **1969**, *91*, 3330. (b) Fliszár, S., Renard, J. *Can. J. Chem.* **1967**, *45*, 533. (c) Fliszár, S.; Granger, M. *J. Am. Chem. Soc.* **1970**, *92*, 3361. (d) Fliszár, S.; Renard, J. *Can. J. Chem.* **1970**, *48*, 3002. (e) Fliszár, S.; Renard, J.; Simon, D. Z. *J. Am. Chem. Soc.* **1971**, *93*, 6953. (f) Renard, J.; Fliszár, S. *J. Am. Chem. Soc.* **1970**, *92*, 2628.

(30) Yamamoto, Y.; Niki, E.; Kamiya, Y. *J. Org. Chem.* **1981**, *46*, 250.

(31) Unpublished work cited by Criegee: Criegee, R. *Adv. Chem. Ser.* **1959**, *21*, 133.

(32) Griesbaum, K.; Zwick, G. *Chem. Ber.* **1986**, *119*, 229.

(33) (a) Griesbaum, K.; Zwick, G.; Agarwal, S.; Keul, H.; Pfeffer, B.; Murray, R. W. *J. Org. Chem.* **1985**, *50*, 4194. (b) Griesbaum, K.; Bandopadhyay, A. R. *Can. J. Chem.* **1987**, *65*, 487.

(34) (a) Keul, H.; Griesbaum, K. *Can. J. Chem.* **1980**, *58*, 2049. (b) Meister, M.; Zwick, G.; Griesbaum, K. *Can. J. Chem.* **1983**, *61*, 2385. (c) Griesbaum, K.; Greinert, R. *Chem. Ber.* **1989**, *123*, 391.

(35) Gillies, C. W.; Kuczkowski, R. L. *Isr. J. Chem.* **1983**, *23*, 446.

(36) Kuczkowski, R. L. In *Advances in Oxygenated Processes*; Baumstark, A. L., Eds.; JAI Press: Greenwich, CT, Vol. 3, in press.

(37) Thompson, Q. E. *J. Org. Chem.* **1962**, *27*, 4498.

(38) (a) Keul, H.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1984**, *106*, 5370. (b) Keul, H.; Choi, H.-S.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3365. (c) Wojciechowski, B. J.; Pearson, W. H.; Kuczkowski, R. L. *J. Org. Chem.* **1989**, *54*, 115.

(39) (a) Nakamura, N.; Nojima, M.; Kasubayashi, S. *J. Am. Chem. Soc.* **1987**, *109*, 4969. (b) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799.

(40) (a) Bunnelle, W. H.; Meyer, L. A.; Schlemper, E. O. *J. Am. Chem. Soc.* **1989**, *111*, 7612. (b) Bunnelle, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 7613.

(41) (a) Bernatek, E.; Thoresen, F. *Acta Chem. Scand.* **1955**, *9*, 743. (b) Bernatek, E.; Bø, I. *Acta Chem. Scand.* **1959**, *13*, 337. (c) Bernatek, E.; Hvatum, M. *Acta Chem. Scand.* **1960**, *14*, 836. (d) Bernatek, E. *Ozonation in the Naphthoquinone and Benzofuran Series*; Oslo University Press: Oslo, Norway, 1960. (e) Bernatek, E.; Ledaal, T.; Steinsvik, S. *Acta Chem. Scand.* **1961**, *15*, 429.

(42) Schank, K.; Schuhknecht, C. *Chem. Ber.* **1982**, *115*, 2000.
(43) Wojciechowski, B. J.; Chiang, C.-Y.; Kuczkowski, R. L. *J. Org. Chem.* **1990**, *55*, 1120.
(44) Kopecky, K. R.; Molina, J.; Rico, R. *Can. J. Chem.* **1987**, *67*, 2234.
(45) Herron, J. T.; Huie, R. E. *Int. J. Chem. Kinet.* **1978**, *10*, 1019.
(46) (a) Herron, J. T.; Huie, R. E. *J. Am. Chem. Soc.* **1977**, *99*, 5430. (b) Martinez, R. I.; Herron, J. T.; Huie, R. E. *J. Am. Chem. Soc.* **1981**, *103*, 3807. (c) Martinez, R. I.; Herron, J. T. *J. Phys. Chem.* **1987**, *91*, 946. (d) Martinez, R. I.; Herron, J. T. *J. Phys. Chem.* **1988**, *92*, 4644.
(47) Cox, R. A.; Penkett, S. A. *J. Chem. Soc. Faraday Trans. 1* **1972**, *68*, 1735.
(48) (a) Hatakeyama, S.; Kobayashi, H.; Akimoto, H. *J. Phys. Chem.* **1984**, *88*, 4736. (b) Hatakeyama, S.; Kobayashi, H.; Lin, Z.-Y.; Takagi, H.; Akimoto, H. *J. Phys. Chem.* **1986**, *90*, 4131.
(49) Martinez, R. I.; Herron, J. T. *J. Environ. Sci. Health* **1981**, *A16*, 623.
(50) (a) Su, F.; Calvert, J. G.; Shaw, J. H. *J. Phys. Chem.* **1980**, *84*, 239. (b) Kan, C. S.; Su, F.; Calvert, J. G.; Shaw, J. H. *J. Phys. Chem.* **1981**, *85*, 2359.
(51) (a) Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P. *Chem. Phys. Lett.* **1977**, *46*, 327. (b) Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P. *J. Phys. Chem.* **1981**, *85*, 1024. (c) Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P.; Hurley, M. D. *J. Phys. Chem.* **1987**, *91*, 941.
(52) Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P. *Environ. Sci. Technol.* **1983**, *17*, 312A.
(53) Niki, H.; Maker, P. D.; Savage, C. M.; Breitenbach, L. P.; Martinez, R. I. *J. Phys. Chem.* **1984**, *88*, 766.
(54) Zhang, J.; Hatakeyama, S.; Akimoto, H. *Int. J. Chem. Kinet.* **1983**, *15*, 655.
(55) Kirmse, W.; Horner, L.; Hoffmann, H. *Justus Liebigs Ann. Chem.* **1958**, *614*, 19.
(56) Bartlett, P. D.; Traylor, T. G. *J. Am. Chem. Soc.* **1962**, *84*, 3408.
(57) Murray, R. W.; Suzui, A. *J. Am. Chem. Soc.* **1971**, *93*, 4963.
(58) Bell, G. A.; Dunkin, I. R. *J. Chem. Soc., Chem. Commun.* **1983**, 1215.
(59) Sugawara, T.; Iwamura, H.; Hayashi, H.; Sekiguchi, A.; Ando, W.; Liu, M. T. H. *Chem. Lett.* **1983**, 1261.
(60) Chapman, O. L.; Hess, T. C. *J. Am. Chem. Soc.* **1984**, *106*, 1842.
(61) (a) Dunkin, I. R.; Bell, G. A. *Tetrahedron* **1985**, *41*, 339. (b) Bell, G. A.; Dunkin, I. R.; Shields, C. J. *Spectrochim. Acta* **1985**, *41A*, 1221. (c) Dunkin, I. R.; Bell, G. A.; McCleod, F. G.; McCluskey, A. *Spectrochim. Acta* **1986**, *42A*, 567.
(62) Dunkin, I. R.; Shields, C. J. *J. Chem. Soc., Chem. Commun.* **1986**, 154.
(63) (a) Sander, W. *Angew. Chem.* **1985**, *97*, 964; *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 988. (b) Sander, W. *Angew. Chem.* **1986**, *98*, 255; *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 255. (c) Sander, W. W. *J. Org. Chem.* **1989**, *54*, 333.
(64) Sander, W. W. *Spectrochim. Acta* **1987**, *43A*, 637.
(65) Sander, W. W. *J. Org. Chem.* **1988**, *53*, 121.
(66) Sander, W. W. *J. Org. Chem.* **1988**, *53*, 2091.
(67) Ganzer, G. A.; Sheridan, R. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1986**, *108*, 1517.
(68) Murata, S.; Tomioka, H.; Kawase, T.; Oda, M. *J. Org. Chem.* **1990**, *55*, 4502.
(69) (a) Werstiuk, N. H.; Casal, H. L.; Scaiano, J. C. *Can. J. Chem.* **1984**, *62*, 2391. (b) Casal, H. L.; Sugamori, S. E.; Scaiano, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 7623.
(70) Casal, H. L.; Tanner, M.; Werstiuk, N. H.; Scaiano, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 4616.
(71) Barcus, R. L.; Hadel, L. M.; Johnston, L. J.; Platz, M. S.; Savino, T. G.; Scaiano, J. C. *J. Am. Chem. Soc.* **1986**, *108*, 3928.
(72) Scaiano, J. C.; McGimpsey, W. G.; Casal, H. L. *J. Org. Chem.* **1989**, *54*, 1612.
(73) Girard, M.; Griller, D. *J. Phys. Chem.* **1986**, *90*, 6801.
(74) Fujiwara, Y.; Tanimoto, Y.; Itoh, M.; Hirai, K.; Tomioka, H. *J. Am. Chem. Soc.* **1987**, *109*, 1942.
(75) Fessenden, R. W.; Scaiano, J. C. *Chem. Phys. Lett.* **1985**, *117*, 103.
(76) Gauss, J.; Cremer, D. *Chem. Phys. Lett.* **1987**, *133*, 420.
(77) McClellan, A. L. *Tables of Experimental Dipole Moments*; Freeman: San Francisco, 1963; p 41.
(78) Hatakeyama, S.; Bandow, H.; Okuda, M.; Akimoto, H. *J. Phys. Chem.* **1981**, *85*, 2249.
(79) Lee, Y.-P.; Pimentel, G. C. *J. Chem. Phys.* **1981**, *74*, 4851.
(80) Martinez, R. I.; Huie, R. E.; Herron, J. T. *J. Chem. Phys.* **1981**, *75*, 5975.
(81) Higley, D. P.; Murray, R. W. *J. Am. Chem. Soc.* **1974**, *96*, 3330.
(82) Bethell, D.; McKeivor, R. *J. Chem. Soc. Perkin Trans. 2* **1977**, 327.
(83) (a) Tezuka, T.; Iwaki, M.; Haga, Y. *J. Chem. Soc., Chem. Commun.* **1984**, 325. (b) Tezuka, T.; Iwaki, M. *J. Chem. Soc. Perkin Trans. 1* **1984**, 2507. (c) Tezuka, T.; Otsuka, T. *Chem. Lett.* **1988**, 1751.
(84) Akasaka, T.; Sato, R.; Miyama, Y.; Ando, W. *Tetrahedron Lett.* **1985**, *26*, 843.
(85) (a) Ando, W.; Sato, R.; Sonobe, H.; Akasaka, T. *Tetrahedron Lett.* **1984**, *25*, 853. (b) Sato, R.; Sonobe, H.; Akasaka, T.; Ando, W. *Tetrahedron* **1986**, *42*, 5273.
(86) (a) Ando, W.; Kohmoto, S.; Nishizawa, K. *J. Chem. Soc., Chem. Commun.* **1978**, 894. (b) Ando, W.; Kohmoto, S.; Miyazaki, H.; Nishizawa, K.; Tsumaki, H. *Photochem. Photobiol.* **1979**, *30*, 81.
(87) (a) Akasaka, T.; Ando, W. *Tetrahedron Lett.* **1987**, *28*, 217. (b) Erden, J.; deMeijere, A. *Tetrahedron Lett.* **1980**, *21*, 2501. (c) van den Heuvel, C. J. M.; Steinberg, H.; de Boer, T. J. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 145.
(88) Martinez, R. I. *J. Phys. Chem.* **1987**, *91*, 1345.
(89) (a) Adam, W.; Rodriguez, A. *J. Am. Chem. Soc.* **1980**, *102*, 404. (b) Adam, W.; Rodriguez, A. *Tetrahedron Lett.* **1981**, *22*, 3509.
(90) (a) Graziano, M. L.; Iesce, M. R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc. Perkin Trans. 1* **1988**, 1699. (b) Graziano, M. L.; Iesce, M. R.; Cermola, F.; Giordano, F.; Scarpati, R. *J. Chem. Soc., Chem. Commun.* **1989**, 1608. (c) Graziano, M. L.; Iesce, M. R.; Cimminiello, G.; Scarpati, R. *J. Chem. Soc. Perkin Trans. 1* **1989**, 241.
(91) Wasserman, H. H.; McCarthy, K. E.; Prowse, K. S. *Chem. Rev.* **1986**, *86*, 845.
(92) (a) Miura, M.; Ikegami, A.; Nojima, M.; Kusabayashi, S.; McCullough, K. J.; Nagase, S. *J. Am. Chem. Soc.* **1983**, *105*, 2414. (b) Miura, M.; Nagase, S.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1983**, *48*, 2366. (c) Miura, M.; Nojima, M. *J. Am. Chem. Soc.* **1980**, *102*, 288. (d) Miura, M.; Nojima, M.; Kusabayashi, S.; Nagase, S. *J. Am. Chem. Soc.* **1981**, *103*, 1789.
(93) Yamamoto, Y.; Niki, E.; Kamiya, Y. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 2677.
(94) (a) Schreiber, S. L.; Claus, R. E.; Reagan, J. *Tetrahedron Lett.* **1982**, *23*, 3867. (b) Claus, R. E.; Schreiber, S. L. *Organic Syntheses*; Wiley: New York, 1990; p 168.
(95) (a) Schreiber, S. L. *J. Am. Chem. Soc.* **1980**, *102*, 6163. (b) Schreiber, S. L.; Liew, W.-F. *Tetrahedron Lett.* **1983**, *24*, 2363. (c) Schreiber, S. L.; Liew, W.-F. *J. Am. Chem. Soc.* **1985**, *107*, 2980.
(96) (a) McCullough, K. J.; Nojima, M.; Miura, M.; Fujisaka, T.; Kusabayashi, S. *J. Chem. Soc., Chem. Commun.* **1984**, 35. (b) McCullough, K. J.; Fujisaka, T.; Nojima, M.; Kusabayashi, S. *Tetrahedron Lett.* **1988**, *29*, 3375.
(97) Pierrot, M.; El Idrissi, M.; Santelli, M. *Tetrahedron Lett.* **1989**, *30*, 461.
(98) (a) Keul, H.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1984**, *106*, 3383. (b) LaBarge, M. S.; Keul, H.; Kuczkowski, R. L.; Wallasch, M.; Cremer, D. *J. Am. Chem. Soc.* **1988**, *110*, 2081.
(99) (a) Odinokov, V. N.; Kukovinets, O. S.; Khalilov, L. M.; Tolstikov, G. A.; Kosnikov, A. Y.; Lindeman, S. V.; Struchkov, Y. T. *Tetrahedron Lett.* **1985**, *26*, 5843. (b) Odinokov, V. N.; Kukovinets, O. S.; Botsman, L. P.; Khalilov, L. M.; Tolstikov, G. A.; Kosnikov, A. Y.; Lindeman, S. V.; Struchkov, Y. T. *Zh. Org. Khim.* **1986**, *23*, 995; *J. Org. Chem. USSR (Engl. Trans.)* **1986**, *23*, 897.
(100) Bunnelle, W. H.; Schlemper, E. O. *J. Am. Chem. Soc.* **1987**, *109*, 612.
(101) (a) Aronovitch, C.; Tal, D.; Mazur, Y. *Tetrahedron Lett.* **1982**, *23*, 3623. (b) Den Besten, I. E.; Kinstle, T. H. *J. Am. Chem. Soc.* **1980**, *102*, 5969.
(102) (a) Griesbaum, K.; Volpp, W.; Greinert, R. *J. Am. Chem. Soc.* **1985**, *107*, 5309. (b) Griesbaum, K.; Volpp, W. *Angew. Chem.* **1986**, *98*, 108; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 81. (c) Griesbaum, K.; Volpp, W. *Chem. Ber.* **1988**, *121*, 1795. (d) Griesbaum, K.; Volpp, W.; Greinert, R.; Greunig, H.-J.; Schmid, J.; Henke, H. *J. Org. Chem.* **1989**, *54*, 383.
(103) (a) Griesbaum, K.; Volpp, W.; Huh, T.-S.; Jung, I. C. *Chem. Ber.* **1989**, *122*, 941. (b) Griesbaum, K.; Greinert, R. *Chem. Ber.* **1990**, *123*, 391.
(104) Keul, H.; Kuczkowski, R. L. *J. Org. Chem.* **1985**, *50*, 3371.
(105) (a) Choe, J.-I.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1983**, *105*, 4839. (b) Choe, J.-I.; Painter, M. K.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1984**, *106*, 2891. (c) Fong, G. D.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1980**, *102*, 3763.
(106) (a) Su, J.-S.; Murray, R. W. *J. Org. Chem.* **1980**, *45*, 678. (b) Murray, R. W.; Su, J.-S. *J. Org. Chem.* **1983**, *48*, 817.
(107) (a) Miura, M.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Org. Chem.* **1985**, *50*, 1504. (b) Nakamura, N.; Nojima, M.; Kusabayashi, S. In *The Role of Oxygen in Chemistry and Biochemistry (Studies in Organic Chemistry)*; Ando, W., Moro-oka, Y., Eds.; Elsevier: Amsterdam, 1988; Vol. 33, pp 129–132. (c) Nakamura, N.; Fujisaka, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 1799.
(108) Sugimoto, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1990**, *112*, 3690.

(109) Yoshida, M.; Miura, M.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1983**, *105*, 6279.

(110) Mori, M.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1987**, *109*, 4407.

(111) Mori, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1550.

(112) Tabuchi, T.; Nojima, M.; Kusabayashi, S. *J. Chem. Soc., Chem. Commun.* **1990**, 625.

(113) Ishiguro, K.; Hirano, Y.; Sawaki, Y. *Tetrahedron Lett.* **1987**, *28*, 6201.

(114) (a) Murray, R. W.; Lin, J. W.-P.; Grumke, D. A. *Adv. Chem. Ser.* **1972**, *112*, 9. (b) Chiang, C.-Y.; Butler, W.; Kuczkowski, R. L. *J. Chem. Soc., Chem. Commun.* **1988**, 465.

(115) Mori, M.; Sugiyama, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 6884.

(116) (a) Bailey, P. S.; Rustaiyan, A.; Ferrell, T. M. *J. Am. Chem. Soc.* **1976**, *98*, 639. (b) Bailey, P. S.; Ferrell, T. M.; Rustaiyan, A.; Seyhan, S.; Unruh, L. E. *J. Am. Chem. Soc.* **1978**, *100*, 894.

(117) Murray, R. W.; Hagen, R. *J. Am. Chem. Soc.* **1971**, *93*, 1098.

(118) (a) Lovas, F. J.; Suenram, R. D. *Chem. Phys. Lett.* **1977**, *51*, 453. (b) Martinez, R. I.; Huie, R. E.; Herron, J. T. *Chem. Phys. Lett.* **1977**, *51*, 457. (c) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1978**, *90*, 5117.

(119) (a) Sawaki, Y.; Ishiguro, K. *Tetrahedron Lett.* **1984**, *25*, 1487. (b) Ishiguro, K.; Tomizawa, K.; Sawaki, Y.; Iwamura, H. *Tetrahedron Lett.* **1985**, *26*, 3723.

(120) Ishiguro, K.; Hirano, Y.; Sawaki, Y. *J. Org. Chem.* **1988**, *53*, 5397.

(121) (a) Yang, N.-C.; Libman, J. *J. Org. Chem.* **1974**, *39*, 1782. (b) Jackson, S.; Hull, L. A. *J. Org. Chem.* **1976**, *41*, 3340. (c) Jenkins, J. A.; Mendenhall, G. D. *J. Org. Chem.* **1981**, *346*, 3997.

(122) Keay, R. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1976**, *98*, 6578.

(123) Ando, W.; Miyazaki, H.; Ito, K.; Auchi, D. *Tetrahedron Lett.* **1982**, *23*, 555.

(124) Pryor, W. A.; Govindan, C. K.; Church, D. F. *J. Am. Chem. Soc.* **1982**, *104*, 7563.

(125) DeMore, W. B.; Lin, C.-L. *J. Org. Chem.* **1973**, *38*, 985.

(126) Murray, R. W.; Agarwal, S. K. *J. Org. Chem.* **1985**, *50*, 4698.

(127) (a) Story, P. R.; Burgess, J. R. *J. Am. Chem. Soc.* **1967**, *89*, 5726. (b) Story, P. R.; Burgess, J. R. *J. Am. Chem. Soc.* **1968**, *90*, 1094.

(128) Baumstark, A. L.; Beeson, M.; Vasquez, P. C. *Tetrahedron Lett.* **1989**, *30*, 5567.

(129) Gäb, S.; Hellpointner, E.; Turner, W. V.; Korte, F. *Nature* **1985**, *316*, 535.

(130) (a) Walsh, S. T.; Chen, Y.-C. J. *Angew. Chem.* **1988**, *100*, 342; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 333. (b) Dix, T. A.; Benkovic, S. J. *Acc. Chem. Res.* **1988**, *21*, 101.

(131) (a) Hamilton, G. A. *Progr. Bioorg. Chem.* **1971**, *1*, 83. (b) Keay, R. E.; Hamilton, G. A. *J. Am. Chem. Soc.* **1975**, *97*, 6876.

(132) Bruice, T. C. *Isr. J. Chem.* **1984**, *24*, 54.

(133) Wessiak, A.; Noar, J. B.; Bruice, T. C. *Proc. Natl. Acad. Sci. U.S.A.* **1984**, *81*, 332.

(134) Criegee, R.; Günther, P. *Chem. Ber.* **1963**, *96*, 1564.

(135) Kwart, H.; Hoffman, D. M. *J. Org. Chem.* **1966**, *31*, 419.

(136) (a) Gillies, C. W. *J. Am. Chem. Soc.* **1977**, *99*, 7239. (b) Griesbaum, K.; Brüggemann, J. *Chem. Ber.* **1972**, *105*, 3638.

(137) Hinrichs, T. A.; Ramachandran, V.; Murray, R. W. *J. Am. Chem. Soc.* **1979**, *101*, 1282.

(138) Pryor, W. A.; Govindan, C. K. *J. Am. Chem. Soc.* **1981**, *103*, 7681.

(139) (a) Nakamura, N.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1986**, *108*, 4671. (b) Nakamura, N.; Nojima, M.; Kusabayashi, S. *J. Am. Chem. Soc.* **1987**, *109*, 4969.

(140) Cremer, D.; Bock, C. W. *J. Am. Chem. Soc.* **1986**, *108*, 3375.

(141) Jerina, D. M.; Boyd, D. R.; Daly, J. W. *Tetrahedron Lett.* **1970**, 457.

(142) (a) Chaudhary, S. K.; Hoyt, R. W.; Murray, R. W. *Tetrahedron Lett.* **1976**, 4235. (b) Kumar, S.; Murray, R. W. *J. Am. Chem. Soc.* **1984**, *106*, 1040.

(143) (a) Kumar, S.; Murray, R. W. *Tetrahedron Lett.* **1980**, *21*, 4781. (b) Kumar, S.; Murray, R. W. In *Polynuclear Aromatic Hydrocarbons: Physical and Biological Chemistry*; Cooke, M., Dennis, A. J., Fisher, G. L., Eds.; Battelle: Columbus, OH, 1982; pp 575–584. (c) Murray, R. W.; Banavali, R. *Tetrahedron Lett.* **1983**, *23*, 2327.

(144) Agarwal, S. K.; Murray, R. W. *Photochem. Photobiol.* **1982**, *35*, 31.

(145) Sekiguchi, A.; Kabe, Y.; Ando, W. *J. Chem. Soc., Chem. Commun.* **1979**, 233.

(146) (a) Sekiguchi, A.; Kabe, Y.; Ando, W. *J. Chem. Soc., Chem. Commun.* **1979**, 343. (b) Sekiguchi, A.; Kabe, Y.; Ando, W. *J. Org. Chem.* **1982**, 2900.

(147) Okada, K.; Mukai, T. *Tetrahedron Lett.* **1980**, *21*, 359.

(148) Agarwal, S. K.; Murray, R. W. *Isr. J. Chem.* **1983**, *23*, 405.

(149) (a) Ando, W.; Miyazaki, H.; Kohmoto, S. *Tetrahedron Lett.* **1979**, 1317. (b) Ando, W.; Kabe, Y.; Miyazaki, H. *Photochem. Photobiol.* **1980**, *31*, 191.

(150) (a) Adam, W.; Haas, W.; Sieker, G. *J. Am. Chem. Soc.* **1984**, *106*, 5020. (b) Adam, W.; Dürr, H.; Haas, W.; Lohray, B. *Angew. Chem.* **1986**, *98*, 85; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 101.