

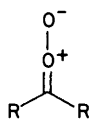
The Chemistry of Peroxonium Ions and Dioxygen Ylides

By J. C. Mitchell

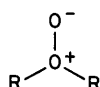
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1 Introduction

The intermediacy of carbonyl oxides (1) in ozonide formation has long been appreciated, but the wider occurrence of these species, or of 'saturated' oxo-oxonium ylides (2), and the reactivity of (1) and (2) has been recognized only recently. Similarly, discussion of the related alkoxy-oxonium (peroxonium) species (3) and (4) has only begun to appear in the last few years.

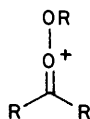


(1)



(2)

R = H or alkyl



(3)



(4)

Interest in chemical intermediates of this type has been focused primarily in the areas of ozonolysis,¹⁻³ the singlet oxygenation of alkenes,^{4,5} the alkylation of peroxides,⁶⁻⁸ and the 'oxenoid' behaviour of some biochemical systems.^{9,10} Although both dioxygen ylides and peroxonium ions have been recently (1984) observed spectroscopically at low temperature,^{7,11} no examples of stable dioxygen

¹ R. Criegee, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 745.

² A. T. Menyailo and M. V. Pospelov, *Russ. Chem. Rev. (Eng. Transl.)*, 1967, **36**, 284.

³ (a) R. E. Keay and G. A. Hamilton, *J. Am. Chem. Soc.*, 1976, **98**, 6578. (b) R. E. Keay and G. A. Hamilton, *J. Am. Chem. Soc.*, 1975, **97**, 6876.

⁴ A. A. Frimer, *Chem. Rev.*, 1979, **79**, 359.

⁵ W. Adam, *Chem.-Ztg.*, 1975, **99**, 142.

⁶ N. A. Porter and J. C. Mitchell, *Tetrahedron Lett.*, 1983, **24**, 543.

⁷ J. C. Mitchell, S. Heaton, and N. A. Porter, *Tetrahedron Lett.*, 1984, **25**, 3769.

⁸ A. J. Bloodworth, J. L. Courtneidge, and H. J. Eggelte, *J. Chem. Soc., Chem. Commun.*, 1983, 1267.

⁹ G. A. Hamilton, *J. Am. Chem. Soc.*, 1964, **86**, 3391.

¹⁰ G. A. Hamilton 'Molecular Mechanisms of Oxygen Activation', ed. O. Hayaishi, Academic Press, 1974, p. 405.

¹¹ O. L. Chapman and T. C. Hess, *J. Am. Chem. Soc.*, 1984, **106**, 1842.

zwitterions or peroxonium salts have been reported in the chemical literature. In the light of the availability of salts and ylides involving other heteroatoms, it is curious that the dioxygen analogues have proved so elusive¹²⁻¹⁹ (Table 1).

Table 1 Salts and ylides of nitrogen, oxygen, phosphorus, and sulphur

N	$\begin{array}{c} \text{R} \\ \\ \text{N}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{OR} \\ \\ \text{N}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{O} \quad \text{R} \\ \quad \\ \text{O}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{OR} \\ \\ \text{O}^+ \\ / \quad \backslash \end{array} \quad ?$
	$\begin{array}{c} \text{CH}_2^- \\ \\ \text{N}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{O}^- \\ \\ \text{N}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{CH}_2^- \\ \\ \text{O}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{O}^- \\ \\ \text{O}^+ \\ / \quad \backslash \end{array} \quad ?$
P	$\begin{array}{c} \text{R} \\ \\ \text{P}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{OR} \\ \\ \text{P}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{S} \quad \text{R} \\ \quad \\ \text{S}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{OR} \\ \\ \text{S}^+ \\ / \quad \backslash \end{array}$
	$\begin{array}{c} \text{CH}_2^- \\ \\ \text{P}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{O}^- \\ \\ \text{P}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{CH}_2^- \\ \\ \text{S}^+ \\ / \quad \backslash \end{array}$	$\begin{array}{c} \text{O}^- \\ \\ \text{S}^+ \\ / \quad \backslash \end{array}$

Reported methods of generation of these ions as intermediates in chemical reactions range from carbene trapping of oxygen,^{20,21} to the intramolecular alkylation of peroxides,^{6,8} and reactions of these species include oxidation of external nucleophiles,^{21,22} peroxy-migration, and elimination of carbocations.^{7,8}

This review will attempt to define and interrelate the chemistry of peroxides, dialkyl peroxonium ions, trialkyl peroxonium ions, dioxygen (oxo-oxonium) ylides, and carbonyl oxides.

2 Protonated Hydrogen Peroxide

Peroxonium ions can be most simply represented as the protonated ion H_3O_2^+ (5).

Protonation of hydrogen peroxide has been effected with sulphuric acid²³ and by mixtures of hydrogen fluoride and boron trifluoride.²⁴ This 'parent' peroxonium

¹² J. March, 'Advanced Organic Chemistry', McGraw-Hill Inc., 1977, pp. 337-378 and p. 1111.

¹³ A. R. Katritzky and J. M. Lagowski, 'Chemistry of the Heterocyclic N-Oxides', Academic Press, 1971, p. 142.

¹⁴ A. W. Johnson, 'Ylide Chemistry', Academic Press, 1966, pp. 7-131, 251-260, and 304-349.

¹⁵ H. Perst, 'Oxonium Ions in Organic Chemistry', Verlag Chemie GmbH, Weinheim/Bergstr., 1979.

¹⁶ R. A. Eades, P. G. Gassman, and D. A. Dixon, *J. Am. Chem. Soc.*, 1981, **103**, 1066.

¹⁷ B. J. Walker, 'Organophosphorus Chemistry', Penguin Books, Ltd., 1972, pp. 127-138.

¹⁸ S. G. Smith and S. Winstein, *Tetrahedron*, 1958, **3**, 317.

¹⁹ E. M. Arnett and V. M. DePalma, *J. Am. Chem. Soc.*, 1977, **99**, 5828.

²⁰ G. A. Bell and I. R. Dunkin, *J. Chem. Soc., Chem. Commun.*, 1983, 1213.

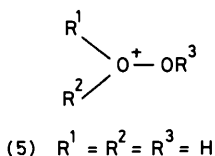
²¹ W. Ando, H. Miyazaki, and S. Kohmoto, *Tetrahedron Lett.*, 1979, **15**, 1317.

²² W. A. Pryor and C. K. Govindan, *J. Am. Chem. Soc.*, 1981, **103**, 7681.

²³ O. H. Derbyshire and W. A. Waters, *Nature*, 1950, **165**, 401.

²⁴ R. W. Alder and M. C. Whiting, *J. Chem. Soc.*, 1964, 908, 4707.

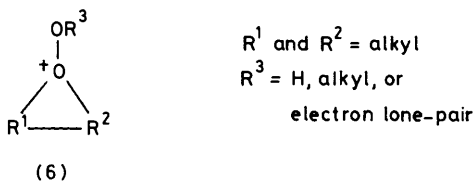
²⁵ G. A. Olah, A. L. Berrier, and G. K. Suryaprakash, *J. Am. Chem. Soc.*, 1982, **104**, 2373.



is reported to be a powerful but unselective oxidant, reacting with benzene and cyclohexane at room temperature.²⁴ The structure of this ion is supported in a recent account by Olah, who reports the protonation of hydrogen peroxide and describes the ^{17}O n.m.r. spectrum of this species.²⁵

3 Peroxides

In these systems the cationic oxygen is incorporated in a three-membered ring, with the exocyclic oxygen usually bearing a proton or electron lone pair [analogous to ions (2) and (4)]. Our laboratory has recently extended this class to include peroxides bearing alkyl groups on the exocyclic oxygen (6).



Peroxides have been postulated as intermediates in a variety of reactions, including singlet oxygenation of alkenes,⁴ basic cyclization of β -hydroperoxy bromides,²⁶ and implicated in the silver-mediated ring-closure of β -hydroperoxy bromides.²⁷

A. Singlet Oxygenation of Alkenes.—The existence of peroxonium intermediates in chemical reactions has been vigorously disputed in the scientific literature.^{26–32} Sharp²⁸ first proposed peroxide intermediates in singlet oxygen addition to isolated double bonds of alkenes (Scheme 1).

Estimates of the energetics of this peroxide intermediate (7) relative to the energies of other possible biradical (8) or zwitterionic (9) intermediates suggest that singlet oxygen addition occurs *via* a stepwise pathway^{33,34} involving either (8) or (9) rather than (7)³⁵ (see Table 2).

²⁶ K. R. Kopecky, W. A. Scott, P. A. Lockwood, and C. Mumford, *Can. J. Chem.*, 1978, **56**, 1114.

²⁷ K. R. Kopecky, J. E. Filby, C. Mumford, P. A. Lockwood, and J. Ding, *Can. J. Chem.*, 1975, **53**, 1103.

²⁸ D. B. Sharp, *Abstracts, 138th National Meeting, American Chemical Society*, 1960, p. 79.

²⁹ Sr. M. Bellarmine Grdina, M. Orfanopoulos, and L. M. Stephenson, *J. Am. Chem. Soc.*, 1979, **101**, 3111.

³⁰ M. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, 1975, **97**, 3978.

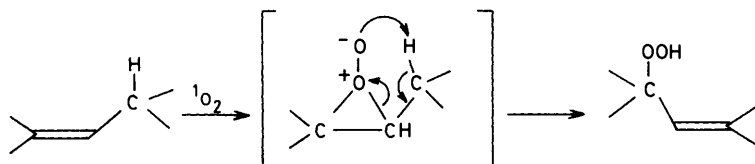
³¹ C. S. Foote, *Acc. Chem. Res.*, 1968, **1**, 104.

³² F. McCapra and I. Beheshti, *J. Chem. Soc., Chem. Commun.*, 1977, 517.

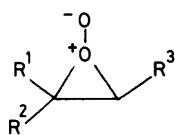
³³ L. B. Harding and W. A. Goddard, *J. Am. Chem. Soc.*, 1980, **102**, 439.

³⁴ L. B. Harding and W. A. Goddard, *J. Am. Chem. Soc.*, 1977, **99**, 4520.

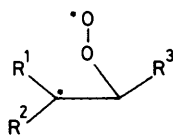
³⁵ Y. Yamaguchi, T. Fueno, I. Saito, T. Metsura, and K. N. Houk, *Tetrahedron*, 1981, **22**, 749.



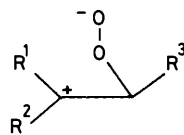
Scheme 1



(7)



(8)



(9)

Table 2 Energetics (kJ mol^{-1}) of addition of $^1\text{O}_2$ to alkyl-substituted olefins³³

Olefin	Zwitterion $\Delta H(a)$	Zwitterion $\Delta H(b)$	Perepoxide ΔH	Biradical $\Delta H(a)$	Biradical $\Delta H(b)$
		248	68	42	
	244	164	64	36	37
		134	58	26	
	235	76	59	31	34
	130	67	53	22	24

(a) more-substituted carbon; (b) less-substituted carbon

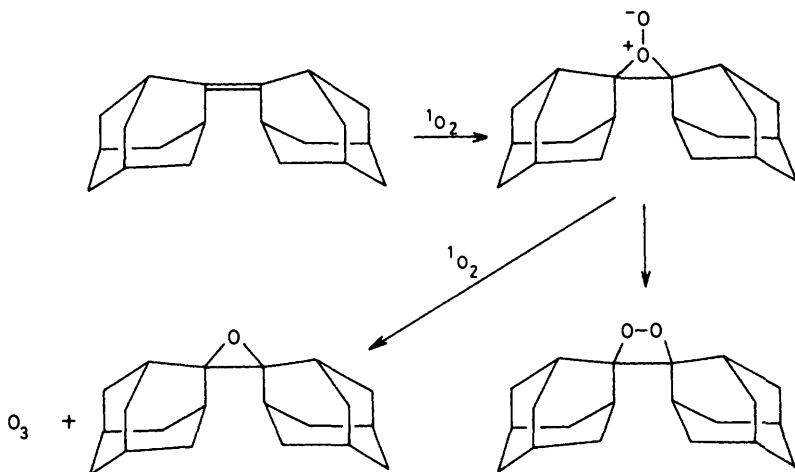
These energetics (Table 2) for singlet oxygen addition to alkyl-substituted ethylenes have been calculated by Goddard and Harding.³³ The calculations involve the combination of previous *ab initio* theoretical studies by the authors³⁴ with thermochemical methods for estimating substituent effects. This thermochemical method utilizes the group additivity method developed by Benson and

co-workers.³⁶ When the three proposed intermediates (7), (8), and (9) are considered by this technique, the one with the lowest energy is the peroxy biradical. The energy of the perepoxides averages 25–33 kJ mol⁻¹ above the biradical form while open zwitterions are higher by 40–200 kJ mol⁻¹. In the case of unsymmetrical olefins, zwitterion energetics appear to be dominated by the stability of the resultant carbonium ion. Simply, for zwitterionic intermediates, singlet oxygen addition should occur at the least substituted carbon. For biradical intermediates this regiochemistry of addition is reversed, with oxygen addition preferred to the more substituted carbon. In these cases the authors predict that the resultant less substituted radical would be of slightly lower energy.

If, indeed, the perepoxide is of the order of thirty kJ mol⁻¹ higher in energy than the acyclic isoelectronic biradical species in singlet oxygenation of alkenes (Table 2), surely the ring strain (*ca.* 115 kJ mol⁻¹ in oxirane)³⁷ must be a contributing factor to the higher energy of formation of this ylide.

Although theoretical examination of these reactions may cast doubt on the intermediate existence of perepoxides, experimental evidence for the intermediacy of the peroxonium species has been presented by both Bartlett and Stephenson.

When adamantylideneadamantane is reacted with singlet oxygen, dioxetane formation is always accompanied by epoxidation products as reported by Bartlett.³⁸ The production of epoxide occurs in all solvents utilized, with no evidence that any solvent is oxidized in the process. This product distribution is interpreted by Bartlett as involving a perepoxide intermediate (Scheme 2).



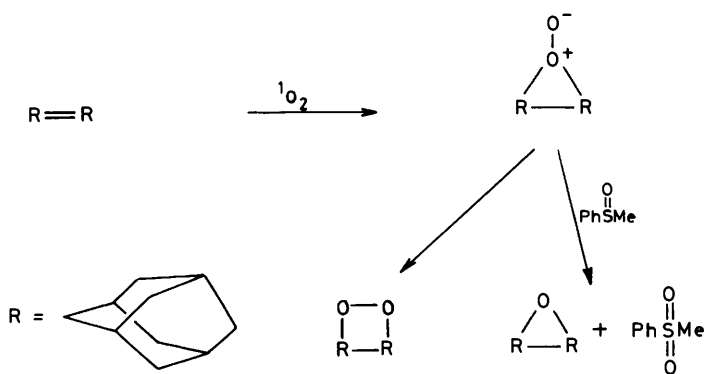
Scheme 2

³⁶ S. W. Benson, 'Thermochemical Kinetics', 2nd Edn., Wiley-Interscience, 1976.

³⁷ T. H. Lowry and K. S. Richardson, 'Mechanism and Theory in Organic Chemistry', Harper and Row, 1976, pp. 75–76.

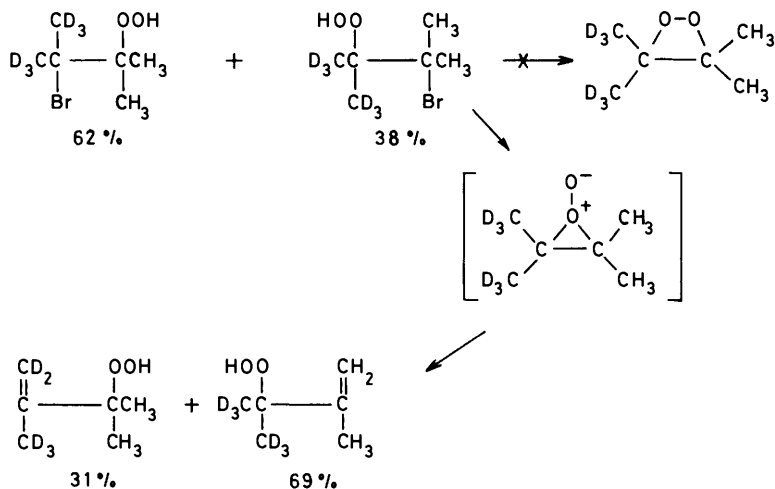
³⁸ P. D. Bartlett and M. E. Landis, 'Singlet Oxygen', ed. H. Wasserman, Academic Press, 1979.

photoreaction of oxygen with adamantylideneadamantane, the reaction was proposed to proceed *via* a dioxygen ylide that rearranges to cyclic peroxide or is trapped by sulphur to yield oxidized sulphone products and epoxide (Scheme 4).



Scheme 4

B. Reactions of β -Hydroperoxy Bromides.—Work in this area by Kopecky *et al.* involving the reactions of 1,2-bromohydroperoxides with methanolic sodium hydroxide resulted not in the production of dioxetane but gave products resulting from peroxy-migration and proton abstraction.²⁶ In these studies it was concluded that these reactions proceeded by way of perepoxide intermediates that collapsed to the observed 'ene' products (Scheme 5).



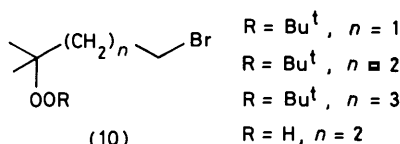
Scheme 5

Reaction of these systems with silver acetate in methylene chloride results in both hydroperoxy alkenes and cyclic peroxides.²⁷ This product distribution supports the formation of a cyclic intermediate that can rearrange to the familiar ene product or dioxetane.

4 Intramolecular Alkylation of Peroxides

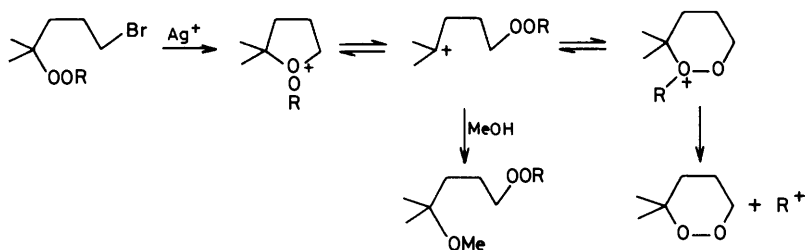
The intermediacy of peroxonium ions, analogous to ion (4), has been proposed and supported by investigation of the intramolecular alkylation of peroxides. To date, these reactions have taken three forms, electrophilic attack on alkylperoxy alkenes, the Lewis-acid-induced ring-closure of alkylperoxy bromides, and the base-induced ring-closure of hydroperoxy bromides. In the case of Lewis-acid-mediated reactions, a variety of silver salts as well as antimony halides have been investigated.⁴⁰

A. Ring Closures of Alkylperoxy Bromides.—We have investigated the reaction of a series of dialkylperoxy bromides with silver trifluoroacetate, silver tetrafluoroborate, and antimony pentachloride. Reaction products are dependent on both chain length and nucleophilic character of the reaction solvent (10).⁶



4-Bromo-2-methyl-2-(t-butylperoxy)butane (R = Bu^t, n = 1) reacts with silver tetrafluoroborate in methanol to produce 3,3-dimethyl-1,2-dioxolane and t-butyl methyl ether in quantitative yield. However, the reaction of 5-bromo-2-methyl-2-(t-butylperoxy)pentane (R = Bu^t, n = 2) with silver salt in methanol produces a peroxy-migration product, while reaction in methylene chloride produces 3,3-dimethyl-1,2-dioxane. The intermediacy of two different cyclic peroxonium ions has been enlisted to explain these results (Scheme 6).

Low-temperature n.m.r. investigation of this reaction in methylene chloride does



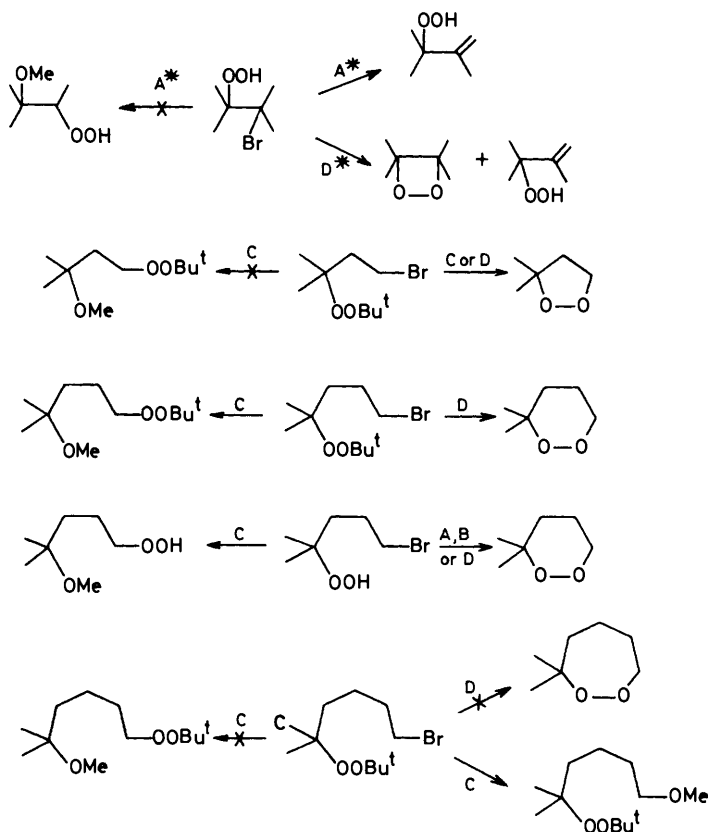
Scheme 6

⁴⁰ J. C. Mitchell and N. A. Porter, unpublished results.

indicate production of ionic intermediates as well as t-butyl cation⁷ (see Figure 2).

When 6-bromo-2-methyl-2-(t-butylperoxy)hexane ($R = \text{Bu}^t$, $n = 3$) was combined with silver salt under the same conditions as the 1,3- and 1,4-peroxy bromides, no reaction to produce any peroxonium intermediate was detected.⁶

This work, when considered in combination with the earlier work of Kopecky, necessitates a mechanistic consideration of enthalpic and entropic effects in these small-ring closures.^{41,42} In all cases a preference for 'kinetic' ring-closure to



Reagents

A - NaOMe in MeOH

A^* - NaOH in MeOH

B - NaH in pentane

C - AgBF₄ in MeOH

D - AgBF₄ in CH₂Cl₂

D^* - AgOCOMe in CH₂Cl₂

Scheme 7

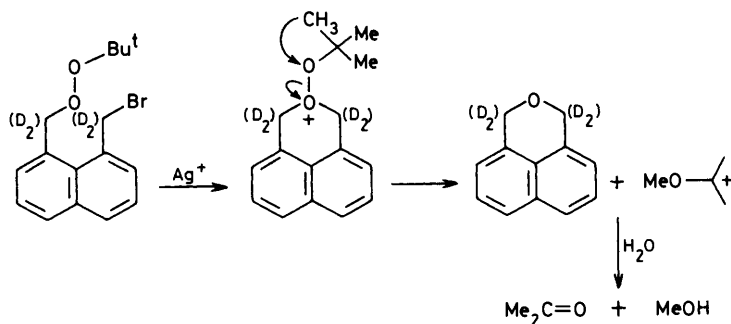
⁴¹ E. L. Eliel, 'Conformational Analysis', Interscience Publishers, 1965, pp. 189—197.

⁴² C. Galli, G. Illuminati, L. Mandolini, and P. Tamborra, *J. Am. Chem. Soc.*, 1977, **99**, 2591.

peroxonium ions is observed. That is, attack from the peroxy-oxygens will favour the formation of three- or five-membered rings, and products will result from these kinetic intermediates. As little difference in nucleophilicity between the two peroxy-oxygens can be expected,⁴³ this phenomenon can be exploited to generate products from peroxonium intermediates (with one oxygen exocyclic), or peroxides with both oxygens endocyclic (Scheme 7).

It is perhaps surprising that no peroxonium chemistry was observed for the reaction of our acyclic 1,5-peroxy bromide with silver salt, as a six-membered ring peroxonium intermediate appears accessible.⁴¹

In a related reaction, the silver-mediated ring-closure of 1-bromomethyl-8-(*t*-butylperoxy)methyl-naphthalene yields naphtho-pyran and trapped 2-methoxy-2-propyl cation.⁷ A mechanistic scheme involving the intermediacy of a peroxonium ion can be written to describe production of naphtho-1,8-pyran from the starting peroxy bromide (Scheme 8).



Scheme 8

Formation of both the intermediate peroxonium ion and 2-methoxy-2-propyl cation is strongly supported by low-temperature n.m.r. spectroscopy. When this peroxy bromide is reacted with silver tetrafluoroborate or antimony pentachloride at low temperature, low-field ¹H (or ²H from a deuterated precursor) resonances can be observed (Figure 3).

B. Electrophilic Attack on Alkylperoxy Alkenes.—Another example of this Baeyer-Villiger type O—O cleavage with 1,2-nucleophilic migration of a methyl group may be found in a recent report by Bloodworth *et al.*⁸ Here, intramolecular alkylation of dialkylperoxide was accomplished by electrophilic attack on alkylperoxy alkenes.

When 5-*t*-butylperoxycyclo-octene is reacted with *N*-bromosuccinimide or bromine in carbon tetrachloride, a mixture (3:1 ratio of A to B) of bicyclic ethers is produced (Scheme 9).

⁴³ R. Hiatt, 'Organic Peroxides', Wiley-Interscience, 1971, Vol. 1, Chap. IV.

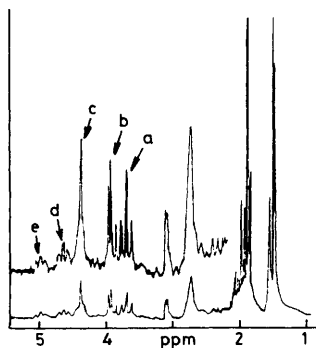


Figure 2 Low temperature ^1H n.m.r. of 5-bromo-2-methyl-2-(*t*-butylperoxy) pentane with antimony pentachloride in sulphuryl chlorofluoride (-60°C): (a) bromoperoxide, (b) *t*-butyl cation, (c) cyclic peroxide, (d,e) transient signals due to interconverting carbocation and peroxonium ion? (see Scheme 6)

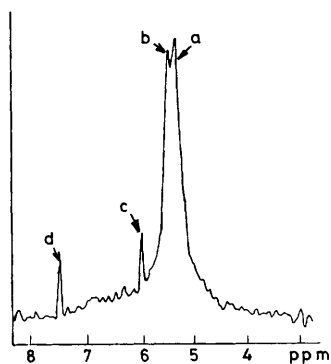
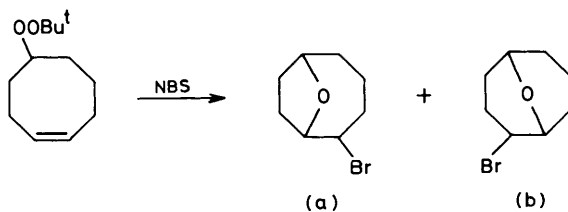
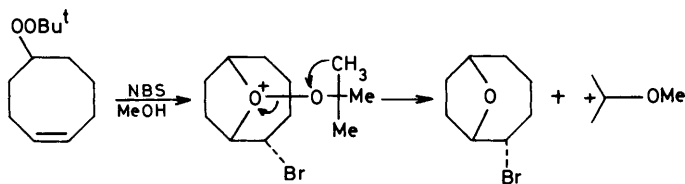


Figure 3 Low temperature ^2H n.m.r. of 1-bromomethyl-8-*t*-butylperoxy- $[\text{}^2\text{H}_4]$ methyl-naphthalene with antimony pentachloride in methylene chloride (-55°C): (a) naphtho-pyran, (b) peroxy bromide, (c) peroxonium ion? (d) CDCl_3 (see Scheme 8)



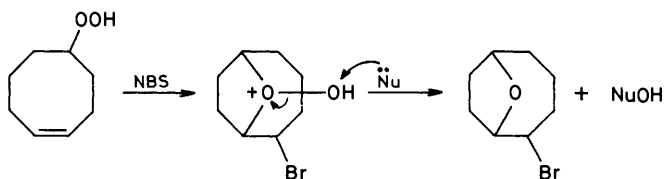
Scheme 9

The reaction mechanism is reported to be electrophilic attack on the double bond, followed by intramolecular alkylation of the peroxide, and subsequent methyl migration to produce the ether product and 2-methoxy-2-propyl cation (Scheme 10).



Scheme 10

Evidence that internal nucleophilic attack at oxygen (Scheme 10) is not a prerequisite for O–O cleavage in peroxonium ions is also presented by Bloodworth. When 5-hydroperoxycyclo-octene was treated with *N*-bromosuccinimide or bromine in carbon tetrachloride the same 3:1 ratio of bicyclic ethers was obtained as in the case of *t*-butylperoxycyclo-octene. Reactions of this type suggest that peroxonium ions from hydroperoxy precursors may be sources of electrophilic OH, which can be activated by suitable nucleophiles (Scheme 11).

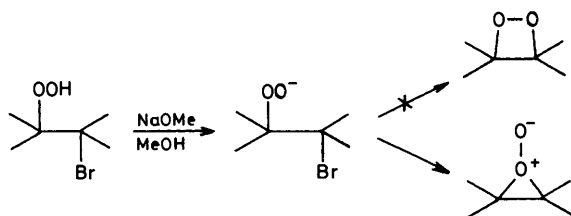


Scheme 11

C. Base-induced Ring-closure of Hydroperoxy Bromides.—Aside from electrophilic attack on hydroperoxy alkenes, the production of peroxonium ions from hydroperoxy precursors has been reported by base-induced ring-closures of hydroperoxy bromides.

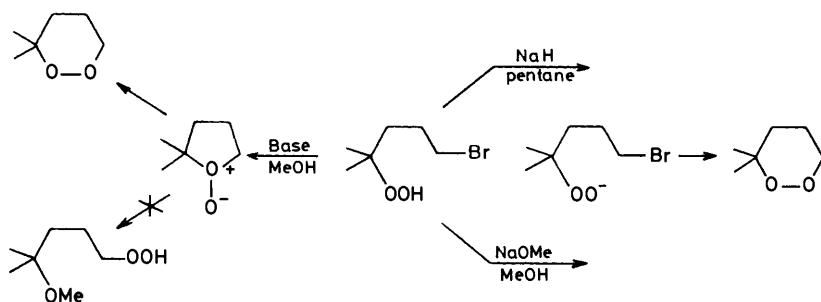
The previously discussed work of Kopecky *et al.*, on the reactions of β -hydroperoxy bromides to produce perepoxide intermediates, is of this type.^{26,27} Our curiosity with these reactions stems from the observation that ring-closure of these systems seems not to occur solely through attack by the 'outside' anionic oxygen (Scheme 12), to yield stable peroxides, but involves formation of dioxygen ylides.

To investigate further this phenomenon we have studied the reaction of 5-bromo-2-methyl-2-hydroperoxypentane with sodium hydride in pentane and with sodium methoxide in methanol. In both cases we isolated 3,3-dimethyl-1,2-dioxane. These reaction products indicate that upon reaction of this 1,4-hydroperoxy bromide



Scheme 12

with base, attack is made to displace bromide by the 'outside' anionic oxygen thus forming the six-membered dioxane. An alternative route, which we have no data to support, is the formation of the 'kinetic' five-membered ring peroxonium compound, followed by rapid peroxy-transfer and subsequent ring-closure (Scheme 13).



Scheme 13

5 Carbonyl Oxides

The ability of perepoxides and peroxonium ions to oxidize external nucleophiles is coincidental with some recently reported chemistry of carbonyl oxides. Carbonyl oxides have long been recognized as intermediates in the ozonolysis of olefins^{1,44} (Scheme 14).

These oxenoid intermediates have been reported to transfer oxygen atoms to alkanes,⁴⁵ olefins,^{3,46,47} sulphides,⁴⁸ sulphoxides,^{21,49} and aromatic rings.^{50,51} These species are also believed to be involved in the Baeyer–Villiger decomposition

⁴⁴ R. Criegee and G. Wenner, *Liebigs Ann. Chem.*, 1949, **9**, 564.

⁴⁵ G. A. Hamilton and J. R. Giacini, *J. Am. Chem. Soc.*, 1966, **88**, 1584.

⁴⁶ H. Kwart and D. H. Hoffman, *J. Org. Chem.*, 1966, **31**, 419.

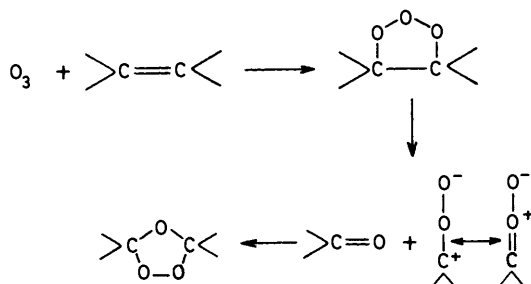
⁴⁷ T. A. Hinricks, V. Ramachandian, and R. W. Murray, *J. Am. Chem. Soc.*, 1979, **101**, 1282.

⁴⁸ Y. Sawaki, H. Kato, and Y. Ogata, *J. Am. Chem. Soc.*, 1981, **103**, 3832.

⁴⁹ W. Ando, S. Kohmoto, and K. Nishizawa, *J. Chem. Soc., Chem. Commun.*, 1978, 894.

⁵⁰ J. W. Jerina, D. M. Jerina, and B. Witkop, *Experientia*, 1972, **28**, 1129.

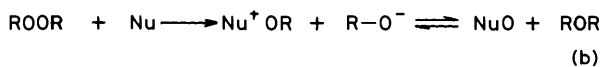
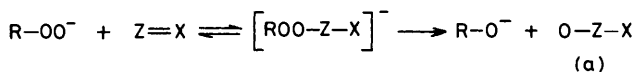
⁵¹ S. K. Chandhary, R. A. Hoyt, and R. W. Murray, *Tetrahedron Lett.*, 1976, 4235.



Scheme 14

of furan endoperoxides.⁵² Epoxidations of olefins by metal-ion co-ordinated carbonyl oxides have been reported,⁵³ as well as the observation that ozonolysis of olefins in the presence of tetracyanoethylene can result in the production of tetracyanoethylene oxides.⁵⁴ Ogata has concluded that nucleophilic oxygen transfer is a characteristic reaction of these species,⁴⁸ although electrophilic oxidation of sulphides has also been reported.⁵⁵

DiFuria and Modena⁵⁶ describe nucleophilic oxygen transfer as a two-step process which involves the addition of the peroxo compound to the substrate and subsequent cleavage of the peroxide intermediate (Scheme 15a). Electrophilic oxygen transfer is described in Scheme 15b.



Scheme 15

Ab initio and MINDO/3 molecular orbital (MO) calculations have been used to investigate the stabilities of carbonyl oxides and related isoelectronic structures, (11a–c) and (12).

Of the four isomers considered, dioxirane (12) has been determined to be 120–170 kJ mol⁻¹ more stable than carbonyl oxides (11).^{57–60} The parent dioxirane has

⁵² W. Adam and A. Rodriguez, *J. Am. Chem. Soc.*, 1980, **102**, 404.

⁵³ H. S. Ryang and C. S. Foote, *J. Am. Chem. Soc.*, 1980, **102**, 2129.

⁵⁴ P. S. Bailey, 'Ozonation in Organic Chemistry', Academic Press, 1978, Vol. 1.

⁵⁵ W. Ando, Y. Kabe, and H. Miyazaki, *Photochem. Photobiol.*, 1980, **31**, 191.

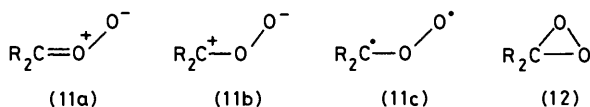
⁵⁶ F. DiFuria and G. Modena, *Pure Appl. Chem.*, 1982, **54**, 1853.

⁵⁷ W. R. Wadt and W. A. Goddard, *J. Am. Chem. Soc.*, 1975, **97**, 3004.

⁵⁸ L. B. Harding and W. A. Goddard, *J. Am. Chem. Soc.*, 1978, **100**, 7180.

⁵⁹ D. Cremer, *J. Am. Chem. Soc.*, 1979, **101**, 7199.

⁶⁰ K. Yamaguchi, S. Yabushita, T. Fueno, S. Kato, K. Morokuma, and S. Iwata, *Chem. Phys. Lett.*, 1980, **71**, 563.

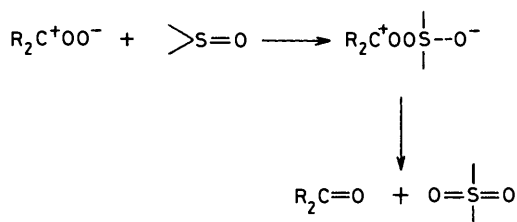


been synthesized *via* ozonolysis of ethylene, and has been characterized by mass and microwave spectrometry.^{61–63} Although the dioxirane was shown to be more stable, a MINDO/3 calculation has shown the energy barrier in the isomerization from (11) to (12) to be on the order of 105 kJ mol⁻¹.⁶⁴

When the stabilities of (11a–c) are considered, MINDO/3 analysis predicts the zwitterionic structure (11a) to be more stable than (11b) or (11c).⁴⁸ *Ab initio* calculation suggests, however, that the singlet diradical structure is more stable than (11a),⁵⁷ but relative stabilities may be changed by substituents or solvents.⁵⁸

If the orbital energies of (11a) *versus* (12) are considered, the ionization potential as well as the energy of the LUMO of the carbonyl oxide (11a) structure is lower than that for the dioxirane (12) structure. This suggests both that (11a) may be a much stronger nucleophile than (12), and that the electron affinity of the carbonyl oxide (11a) is also much higher.⁴⁸

Experimental support for this difference in reactivity and nucleophilicity of the two isomeric structures (11) and (12) has been recently provided by both Adam⁶⁵ and Murray.⁶⁶ Earlier work by Ogata had provided evidence for nucleophilic oxygen atom transfer from carbonyl oxides to sulphoxide (Scheme 16).



Scheme 16

Murray has reported O-atom transfer by dimethyl dioxiranes to a series of arenes in good yield, and suggests that the transfer reaction may be electrophilic in nature⁶⁶ (Scheme 17).

Adam has reported an attempt to differentiate between the electrophilic or nucleophilic character of these oxygen transfer agents by incorporation in his reaction mixtures of an oxidizable substrate, containing both nucleophilic sulphide

⁶¹ F. J. Lovas and R. D. Suenram, *Chem. Phys. Lett.*, 1977, **51**, 453.

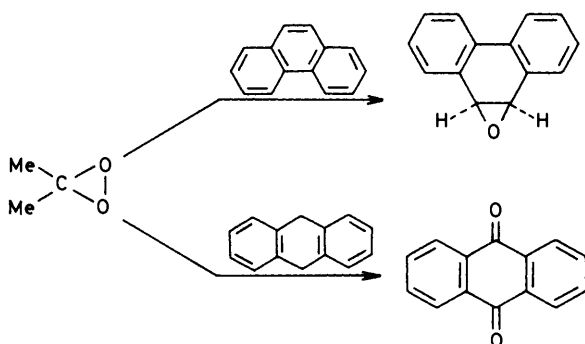
⁶² R. D. Suenram and F. J. Lovas, *J. Am. Chem. Soc.*, 1978, **100**, 5117.

⁶³ R. I. Martinez, R. E. Huie, and J. T. Herron, *Chem. Phys. Lett.*, 1977, **51**, 457.

⁶⁴ L. A. Hull, *J. Org. Chem.*, 1978, **43**, 2780.

⁶⁵ W. Adam, W. Haus, and G. Sieker, *J. Am. Chem. Soc.*, 1984, **106**, 5020.

⁶⁶ R. Jeyaraman and R. W. Murray, *J. Am. Chem. Soc.*, 1984, **106**, 2462.



Scheme 17

and electrophilic sulphoxide sites.⁶⁵ When carbonyl oxides and dioxiranes with the same substitution patterns were combined with thianthrene 5-oxide, the carbonyl oxides proved appreciably more nucleophilic than the dioxiranes. These same experimental conditions were also used to corroborate the fact that dioxiranes can epoxidize electron-poor substrates better than peroxy acids^{67,68} (i.e. *m*-chloroperbenzoic acid).

The formation of carbonyl oxides in ozonolysis reactions, as previously discussed, is well known but these systems are not appropriate for the study of reactivity because of the involvement of other peroxidic species.³ Ozone, 1,2,3-trioxolane, and carbonyl oxide are all potential oxygen atom transfer agents, and all three coexist under normal ozonolysis conditions.²² A clean and convenient method for the generation of carbonyl oxides is the reaction of diazo compounds with singlet oxygen.^{21,69,70} This method of generation of dioxygen ylides has been exploited both in studies of the mechanism of reaction of these ylides with heteroatom-centred substrates (see above), and in the spectroscopic investigation of the carbonyl oxides, themselves.^{11,20} Chapman has reported the generation, photochemistry, and spectroscopic observation of a carbonyl oxide isolated in an argon-oxygen matrix at 10 K.^{11,71} The carbonyl oxide is photochemically generated from a diazocyclopentadiene precursor, and infrared bands at 1395 cm^{-1} and 1385 cm^{-1} were tentatively assigned to the O-O stretch in the carbonyl oxide (Scheme 18).

This stretching frequency is approximately midway between carbon-oxygen double (*ca.* 1700 cm^{-1}) and single bonds (*ca.* 1150 cm^{-1}), with the corresponding band in ozone at 1110 cm^{-1} .^{11,72} This spectroscopic evidence in conjunction with

⁶⁷ J. O. Edwards, R. H. Pater, R. Curci, and F. DiFuria, *Photochem. Photobiol.*, 1979, **30**, 63.

⁶⁸ R. Curci, M. Fiorentino, L. Troisi, J. O. Edwards, and R. H. Pater, *J. Org. Chem.*, 1980, **45**, 4758.

⁶⁹ D. P. Higley and R. W. Murray, *J. Am. Chem. Soc.*, 1974, **96**, 3330.

⁷⁰ J. C. Scaiano, S. E. Sugamori, and H. L. Casal, *J. Am. Chem. Soc.*, 1984, **106**, 7623.

⁷¹ O. L. Chapman and C. L. McIntosh, *J. Chem. Soc. D.*, 1971, 770.

⁷² M. K. Wilson and R. M. Badger, *J. Chem. Phys.*, 1948, **16**, 741.

mechanism resulting in oxygen atom transfer.^{9,76} It has also been suggested that carbonyl oxides serve as models for mono-oxygenase enzymes in that they are capable of oxidizing hydrocarbons to alcohols or carbonyl compounds,^{4,5} and are capable of oxidizing pyrroles⁷⁷ and aromatic hydrocarbons.⁵¹ The flavin adenine dinucleotides (FAD, FADH₂) function as prosthetic groups of these oxidation-reduction enzymes, which are also known as flavoenzymes or flavoproteins (Figure 4). These enzymes catalyse the oxidation of a variety of substrates using molecular oxygen.⁷⁸

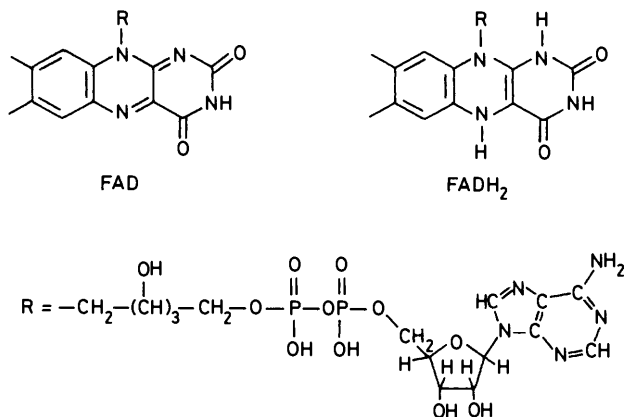


Figure 4

Reaction of aromatic compounds in non-enzymatic systems to produce hydroxylated aromatic compounds is known to occur when flavins are present. One mechanism for this hydroxylation is reported to involve a dioxygen ylide⁷⁶ (Scheme 21). Goddard, however, has suggested that, based on molecular orbital calculations, this oxidation results not from a carbonyl oxide like dioxygen ylide, but from a diradical isomer of the ylide.^{79a} Also, the recent work of Bruice *et al.* tends to show that ring-opening (and hence the formation of dioxygen ylides) is not involved in flavin-catalysed oxidation.^{79b,c}

The photo-reactions of porphyrins are also believed to involve dioxygen ylides. Both free base and metalloporphyrins are known to sensitize oxygen triplet- to singlet-state conversion in photo-oxidation processes.⁸⁰⁻⁸² Protoporphyrin IX,

⁷⁶ G. A. Hamilton, 'Progress in Bioorganic Chemistry', Wiley-Interscience, 1971, Vol. 1.

⁷⁷ H. H. Wasserman and A. H. Miller, *Chem. Commun.*, 1969, 199.

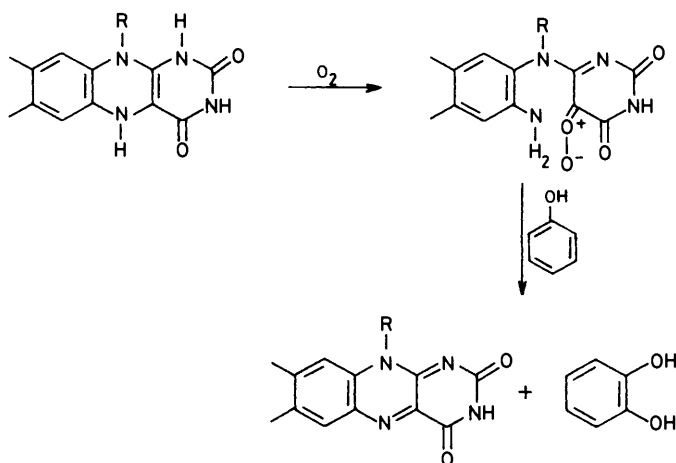
⁷⁸ A. L. Leninger, 'Biochemistry', 2nd Edn., Worth Publishers, 1975.

⁷⁹ (a) see: J. L. Fox, *Chem. Eng. News*, 1978, May 22, p. 28, (b) T. C. Bruice, J. B. Noar, S. S. Ball, U. V. Vankataram, *J. Am. Chem. Soc.*, 1983, **105**, 2452, (c) A. Wessiak and T. C. Bruice, *J. Am. Chem. Soc.*, 1983, **105**, 4809.

⁸⁰ G. Cauzzo, G. Gennari, G. Jori, and J. D. Spikes, *Photochem. Photobiol.*, 1977, **25**, 389.

⁸¹ S. Cannistraro, A. von de Vorst, and G. Jori, *Photochem. Photobiol.*, 1978, **28**, 257.

⁸² C. Emiliani and M. Delmelle, *Photochem. Photobiol.*, 1983, **37**, 487.



Scheme 21

hematoporphyrin IX, and bilirubin have all been implicated in this photochemical conversion.^{83,84} The process is known to result in oxidation of amino-acids and in photodynamic membrane damage.⁸⁵ Porphyrin-O₂ species have also been implicated in several photobiological disorders, such as erythropoietic protoporphyria and neonatal jaundice.

Although much research has been devoted to clinical studies of these disorders, little is known of the chemical interaction of the relevant porphyrins with oxygen or of the subsequent products. It has been reported that the reaction products of the self-sensitized photo-oxidation of protoporphyrin IX are medium dependent.^{86,87}

In organic (*i.e.* isotropic) media, products arise from attack of singlet oxygen on the porphyrins⁸⁷ (Scheme 22). In micelles or vesicles (*i.e.* organized media) more complex behaviour is observed, with a report of 'superoxide-like' character.⁸⁸

When photo-oxidation of protoporphyrin IX is carried out in human erythrocyte membranes, which contain saturated and unsaturated lipids as well as a variety of membrane proteins, disruption as well as cross-linking of the membrane is known to occur.^{85,89} If the amino-acids methionine, histidine, or tryptophan are included in aqueous microemulsions of the porphyrin, the oxidation of these amino-acids is concurrent with the formation of a porphyrin epoxide.⁸⁴

It is not clear whether the formation of epoxides results from direct reaction of the porphyrins with singlet oxygen, or results from attack on the porphyrins by an

⁸³ J. D. Spikes in 'Porphyrin Photosensitization', ed. D. Kessel and T. J. Dougherty, Plenum Press, New York, 1983.

⁸⁴ M. Krieg and D. G. Whitten, *J. Am. Chem. Soc.*, 1984, **106**, 2477.

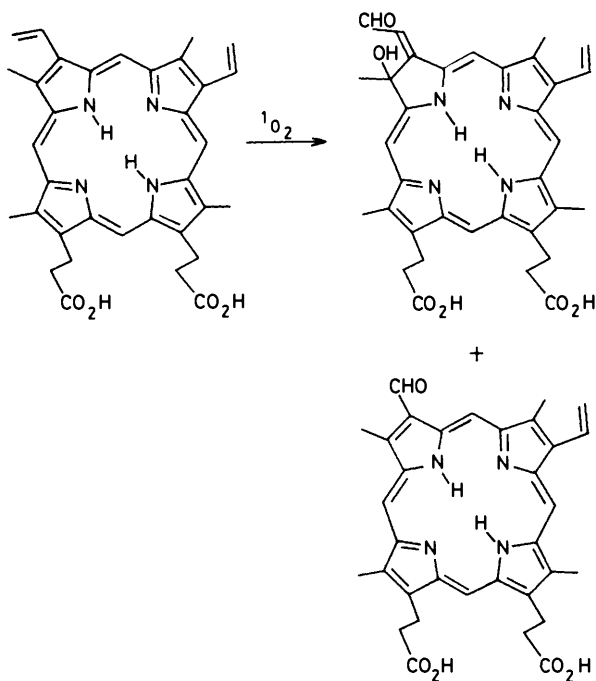
⁸⁵ A. W. Girotti, *Biochemistry*, 1975, **14**, 3377.

⁸⁶ G. Cox and D. G. Whitten, *J. Am. Chem. Soc.*, 1982, **104**, 516.

⁸⁷ H. H. Inhoffen, H. Brockmann, and K. Bliessner, *Liebigs Ann. Chem.*, 1969, **730**, 173.

⁸⁸ G. S. Cox, M. Krieg, and D. G. Whitten, *J. Am. Chem. Soc.*, 1982, **104**, 6930.

⁸⁹ A. W. Girotti, *Biochem. Biophys. Acta*, 1980, **602**, 42.



Scheme 22

intermediate oxygenated species. Since the thioether group is a well known substrate for singlet oxygen,⁷³ it has been suggested that sulphur-containing amino-acids (*i.e.* methionine) can be oxidized to persulphoxides ($R^1R^2S^+OO^-$) that degrade the photo-sensitizing porphyrins themselves.⁸⁴

The success of photo-therapy in the treatment of neonatal jaundice seems to depend in part on the photo-degradation of bilirubin. Both McDonagh⁹⁰ and Bonnett⁹¹ have suggested that bilirubin can sensitize oxygen triplet- to singlet-state conversion and that oxidation by singlet oxygen may be involved in the mechanism of photo-decomposition of bilirubin. Support for the formation of endoperoxides as intermediates in the photo-oxidation of bilirubin has been presented by Bonnett⁹² and Lightner.^{93,94} More recently, Lightner has considered the dye-sensitized photo-oxygenation of pyrroles as a model for the photo-decomposition of bilirubin. When *N*-methylpyrrole undergoes photo-reaction with singlet oxygen, the formation of an endoperoxide intermediate that can rearrange to a peroxirane

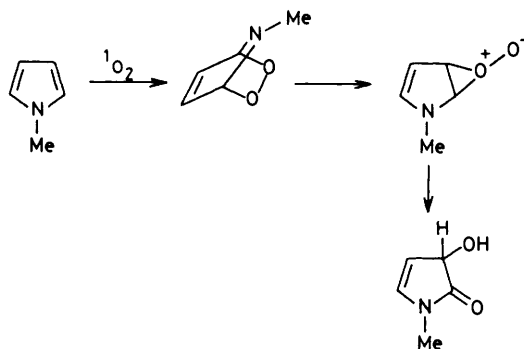
⁹⁰ A. F. McDonagh, *Biochem. Biophys. Res. Commun.*, 1971, **44**, 1306.

⁹¹ R. Bonnett and J. C. M. Stewart, *Biochem. J.*, 1972, **130**, 895.

⁹² R. Bonnett and J. C. M. Stewart, *J. Chem. Soc., Chem. Commun.*, 1972, 596.

⁹³ D. A. Lightner and D. C. Crandell, *Tetrahedron Lett.*, 1973, **12**, 953.

⁹⁴ D. A. Lightner and G. B. Quistad, *FEBS Lett.*, 1972, **25**, 94.



Scheme 23

is suggested.⁹⁵ This dioxygen ylide can then either internally rearrange or react hydrolytically to form the observed hydroxylactams (Scheme 23).

7 Conclusions

Clearly, the production of peroxonium ions and dioxygen ylides in chemical or biochemical systems is of increasing interest to chemical researchers. That formation of these intermediates can result in a wide range of reaction types, including peroxy-migration, peroxidation, epoxidation, formation of ethers, and production of carbocations, makes these ions and ylides a concern of synthetic chemists. Of equal concern to theoretical chemists is the exact nature of charge distribution in these species. The debate over the zwitterionic *versus* diradical structure of both perepoxides and carbonyl oxides suggests that further considerations of substituent effects and solvation need to be included in future molecular orbital calculations.

The intramolecular alkylation of peroxides, whether by reaction of peroxy bromides with silver salts, or by electrophilic attack on peroxy alkenes, appears to be under kinetic control in that a propensity for three- or five-membered ring formation exists. In the case of reaction of hydroperoxy bromides with base, however, although perepoxides appear to be formed *via* 1,2-hydroperoxy bromides at the expense of dioxetane formation, reaction of 1,4-hydroperoxy bromides appears to form products under thermodynamic control (*i.e.* dioxanes).

Of particular interest is the ability of some of these peroxonium ions and ylides to oxidize external substrates by oxygen atom transfer. This chemistry is similar to oxygen atom transfer reactions reported for carbonyl oxides and may have ramifications in the photochemistry of the biologically important flavins and porphyrins. The photo-degradation of these biological systems appears to involve an oxenoid mechanism, resulting in oxygen transfer. These photodynamic processes may be involved in the oxidation of amino-acids and unsaturated fats, as well as in cellular membrane disruption.

⁹⁵ D. A. Lightner, G. S. Bisacchi, and R. D. Norris, *J. Am. Chem. Soc.*, 1976, **98**, 803.