Organic Reactions involving Electrophilic Oxygen

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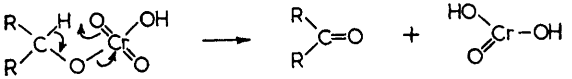
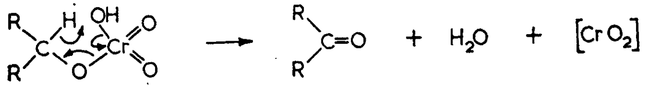
1 Introduction

In many of the more familiar reactions of organic compounds in which an oxygen atom is directly involved at the reaction centre, the oxygen atom behaves as a nucleophile. In such reactions as the solvolysis of alkyl halides, epoxides, esters, and amides by hydroxylic solvents,[1] and in the protonation of epoxides, aldehydes, etc.,[1,2] in cases of neighbouring-group participation by oxygenated groups,[3] the oxygen atom clearly forms bonds to other atoms with a pair of its own electrons. In some other cases, as for example in the breakdown of (postulated) chromate or vanadyl esters,[4] mechanisms may be drawn formally involving either nucleophilic (1) or electrophilic behaviour (2) (or even radical formation)



(1)



(2)

and considerable experimental work may be needed to establish the correct mechanism. At the other end of this 'spectrum' of behaviour are a number of reactions in which oxygen clearly behaves electrophilically, the second molecule involved (the nucleophile) donating a pair of electrons to the (at least incipiently) electron-deficient oxygen. Thus the Baeyer–Villiger conversion of ketones into esters[5] provides an early example of this type of behaviour, and it is now appreciated that electrophilic behaviour by an oxygen atom occurs commonly in a wide range of reactions.

One major group of reactions where such electrophilic behaviour is shown involves rearrangements of peroxy-compounds where a group (alkyl or aryl) migrates from carbon to oxygen (3) (X = OR). Apart from other heterolytic

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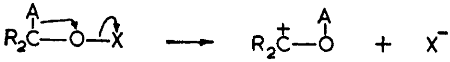
[1] *E.g.*, see C. A. Bunton 'Nucleophilic Substitution at a Saturated Carbon Atom', ed. E. D. Hughes, Elsevier, London, 1963.

[2] *E.g.*, J. N. Brönsted, M. Kilpatrick, and M. Kilpatrick, *J. Amer. Chem. Soc.*, 1929, **51**, 428; H. J. Lichtenstein and G. H. Twigg, *Trans. Faraday Soc.*, 1948, **44**, 905.

[3] *E.g.*, S. Winstein and R. Buckles, *J. Amer. Chem. Soc.*, 1942, **64**, 2780.

[4] *E.g.*, J. S. Littler and W. A. Waters, *J. Chem. Soc.*, 1959, 4046; W. A. Waters, *Quart. Rev.*, 1958, **12**, 277; *Helv. Chim. Acta*, 1962, **45**, 2554; L. Kaplan, *J. Amer. Chem. Soc.*, 1955, **77**, 5469.

[5] A. von Baeyer and V. Villiger, *Ber.*, 1899, **32**, 3625; 1900, **33**, 858.



$$R_2\overset{A}{C}-O-X \longrightarrow R_2\overset{+}{C}-\overset{A}{O} + X^-$$

(3)

peroxide reactions, the rearrangement of ozonides,[6] the breakdown of certain oxyesters,[7] and certain reactions of amine oxides and sulphoxides, for example, are among reactions of this type.

Consideration of the rearrangements occurring in peroxy-compounds has drawn attention[8] to features which these reactions and certain other rearrangements have in common. Compare, for example, the simplified equation* (4) for the Beckmann reaction[9] with the generalised equation* (3): whilst these are

$$R\overset{A}{C}=N-X \longrightarrow R\overset{+}{C}=\overset{A}{N}\ X^-$$

(4)

essentially *intra*molecular reactions, there are certain unifying aspects mechanistically in a series of both *inter-* and *intra*-molecular reactions, which we hope to underline in this Review, which revolve essentially around the generation of an electron-poor oxygen atom in the presence of some suitable nucleophilic group.

These reactions often take place in such a way as to avoid the generation of an atom (usually O, C, N) having only six outer valency electrons. It is not always possible to ascertain whether such an electron-deficient atom is ever formed completely, or whether concerted migration prevents its formation. In some cases intermediate discrete ionic species are formed, but this does not occur invariably.

In intermolecular reactions, by the term 'electrophilic oxygen' we imply a process which may be generalised as (5), where Y is a group capable of forming

$$X{:}\ \underset{Z}{O}-Y \longrightarrow \underset{(A)}{\overset{+}{X}}-\underset{Z}{O}\ Y^-$$

(5)

a stable ion (*e.g.*, acyl) and Z usually is hydrogen. Loss of a proton from (A) gives the stable neutral product, the conjugate base of (A).

Before discussing particular examples, it is worth noting the following characteristics one might expect most of these reactions to exhibit.[10] (*a*) The reaction will be of the second order; first order with respect to X: , first order with respect

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* The representation of charged intermediates in these equations is not to be taken to imply complete ion formation necessarily.

[6] J. E. Leffler, *Chem. Rev.*, 1949, **45**, 385.

[7] M. Anbar, I. Dostrovsky, D. Samuel, and A. D. Yoffe, *J. Chem. Soc.*, 1954, 3603.

[8] R. Criegee, *Annalen*, 1948, **560**, 127; G. Robertson and W. A. Waters, *J. Chem. Soc.*, 1948, 1574; see also W. A. Waters 'Mechanisms of Oxidation of Organic Compounds', Methuen, London, 1964, ch. 3.

[9] W. Z. Heldt and L. G. Donaruma, *Org. Reactions*, 1960, **11**, ch. 1.

[10] J. O. Edwards, 'Peroxide Reaction Mechanisms', Interscience, London, 1962, p. 69.

to YOZ. (*b*) Increased electron availability at the reacting centre of X: will accelerate rate of reaction; decreased electron availability will decelerate it. (*c*) Increased electron attraction by Y will accelerate the rate of reaction and *vice-versa*. (*d*) Where the atom in the radical Y next to the oxygen is capable of protonation, general or specific acid catalysis may be observed. (*e*) A salt effect may be observed. (*f*) Increased solvent polarity may increase the reaction rate. (*g*) The entropy of activation should be negative if an activated complex having a definite orientation is involved. (*h*) Energies of activation will be low (*e.g.*, 12–16 kcal./mole). High values would suggest homolytic bond cleavage leading to a radical-chain or other free-radical mechanism.[11]

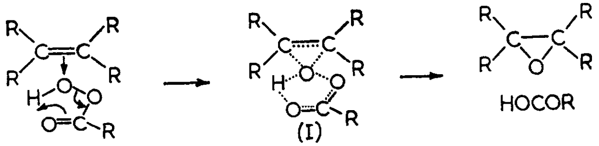
The precise mechanism of the reaction will determine to what extent each characteristic is found. In this Review reactions are considered under three headings; intermolecular, intramolecular, and other reactions.

2 Intermolecular Reactions Involving Electrophilic Oxygen

These reactions can be further classified by the nature of the nucleophile.

A. Olefins and Related Systems.—(i) *The Prileschajew reaction.*[12] Peroxy-acids react with olefinic double bonds to give epoxides.[13] The reaction involves an electrophilic attack by the peracid on the C=C bond. This is borne out by the observation that substituents on the bond which enhance its nucleophilic character (*e.g.*, alkyl) increase the reaction rate whereas electron-withdrawing groups (*e.g.*, -CO.X) considerably decrease reaction rate.[14] Further, the stronger the peracid the greater the rate; trifluoroperacetic acid is particularly effective.[15]

The reaction, which is of the second order (first order with respect to olefin and to peracid) is most easily effected in a non-ionising solvent such as benzene, and is not subject to a salt effect.[16]



This suggests a non-ionic transition state of the type (I)[17] where proton transfer occurs by a concerted intramolecular process. An alternative polar stepwise addition involving charge-separated intermediates (II, III) seems unlikely.

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[11] K. M. Ibne-Rasa and J. O. Edwards, *J. Amer. Chem. Soc.*, 1962, **84**, 767.

[12] N. Prileschajew, *Ber.*, 1909, **42**, 4811; *J. Russ. Phys. Chem. Soc.*, 1910, **42**, 1387; 1911, **43**, 609; 1912, **44**, 613.

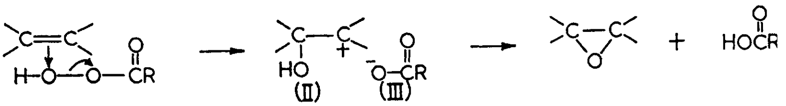
[13] (*a*) D. Swern, *Chem. Rev.*, 1949, **45**, 1; (*b*) D. Swern, *Org. Reactions*, 1953, **7**, 378.

[14] D. Swern, *J. Amer. Chem. Soc.*, 1947, **69**, 1692.

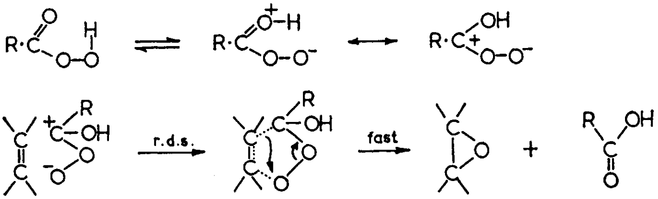
[15] W. D. Emmons, A. S. Pagano, and J. P. Freeman, *J. Amer. Chem. Soc.*, 1954, **76**, 3472; W. D. Emmons and A. S. Pagano, *ibid.*, 1955, **77**, 89.

[16] B. M. Lynch and K. H. Pausacker, *J. Chem. Soc.*, 1955, 1525.

[17] P. O. Bartlett, *Rec. Chem. Prog.*, 1950, **11**, 47.

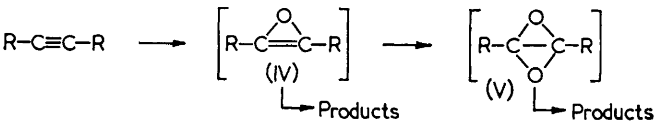


The stereochemistry of olefin epoxidation has recently been reviewed.[18] An interesting alternative mechanism[19] involving a 1,3-dipolar addition as the rate determining step has recently been proposed by Kwart *et al.*[19a] The mechanism



has received some criticism.[19b] Thus, for example, dipolar addition of nitrones is strongly accelerated by electron withdrawing groups attached to the double bond, whereas such groups drastically inhibit epoxidation.[19c] Further, substituent effects on the rate of epoxidation, *e.g.*, the additive effect of alkyl groups on either side of the double bond, suggest a fairly symmetrical transition state. In contrast, the dipolar addition mechanism would predict a heavily unsymmetrical transition state.[19c]

(ii) *Acetylenes.* Treatment of the acetylenic triple bond with peroxyacids gives a mixture of products.[20,21] Addition of peracid by a concerted mechanism (similar to the olefin case) has been postulated.[20,21] This produces the oxiren (IV) which can be further converted into the 1,3-dioxobicyclo [1,1,0]butane (V), both intermediates undergoing further reaction.



(iii) *αβ-Unsaturated ketones with hydrogen peroxide in alkali.* αβ-Unsaturated ketones form epoxides on treatment with alkaline hydrogen peroxide.[22] The mechanism[23] does not involve nucleophilic attack on the peroxide. The carbonyl group confers electrophilic character on the C=C bond, which is attacked by the $^-$OOH anion (VI).

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[18] H. B. Henbest, in *Chem. Soc. Special Publ.*, No. 19, 1965, p. 83; H. C. Stevens and A. J. Kaman, *J. Amer. Chem. Soc.*, 1965, **87**, 734.

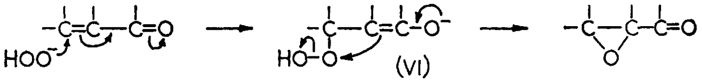
[19] (*a*) H. Kwart and D. M. Hoffman, *J. Org. Chem.*, 1966, **31**, 419; H. Kwart, P. S. Starcher, and S. W. Tinsley, *Chem. Comm.*, 1967, 335; (*b*) K. D. Bingham, G. D. Meakins, and G. H. Whitham, *Chem. Comm.*, 1966, 445; (*c*) G. H. Whitham, private communication.

[20] R. N. McDonald and P. A. Schwab, *J. Amer. Chem. Soc.*, 1964, **86**, 4866.

[21] J. K. Stille and D. D. Whitehurst, *J. Amer. Chem. Soc.*, 1964, **86**, 4871.

[22] Reviewed by C. H. Hassall, *Org. Reactions*, 1957, **9**, 73.

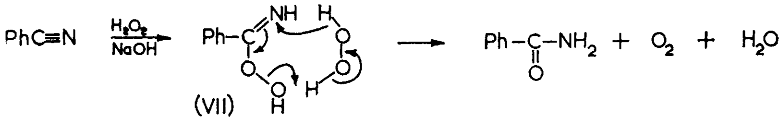
[23] C. A. Bunton and G. O. Minkoff, *J. Chem. Soc.*, 1949, 665.



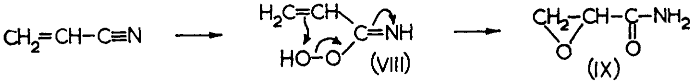
The peracid epoxidation of olefins is known to proceed stereospecifically; the configuration of the resulting epoxide is usually identical with that of the original olefin.[13a,14,24–26]

Under similar reaction conditions $\alpha\beta$-unsaturated aldehydes[27] and alkylidenemalonic esters[28] can be epoxidised.

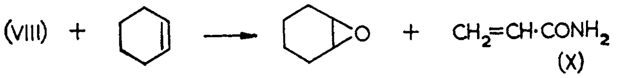
(iv) *Nitriles and $\alpha\beta$-unsaturated nitriles.* Nitriles are hydrolysed to amides by alkaline hydrogen peroxide.[29] The peroxycarboximidic acid (VII) formed initially decomposes *via* a concerted reaction which involves a further molecule of hydrogen peroxide.[30]



In the case of an $\alpha\beta$-unsaturated nitrile self-epoxidation occurs[31] (VIII) to give the epoxy-amide[31,32] (IX).



Addition of a competing olefin, cyclohexene, halves the yield of glycidamide (IX) with concomitant production of acrylamide (X), which is also obtained, but in very low yield, in the absence of cyclohexene.[31]



Good use of the intermediate (VIII) has been made in enabling added olefins to be oxidised under mildly alkaline conditions.[33,34] Keto-olefins have thus been epoxidised without formation of Baeyer–Villiger products, since the latter reaction is usually acid-catalysed.[35]

(v) *$\alpha\beta$-Unsaturated ketones with organic peracids.* Organic peracids react with

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[24] S. Winstein and R. B. Henderson, R. C. Elderfeld, 'Heterocyclic Compounds', vol. 1, John Wiley, New York, 1950, p. 1.

[25] H. O. House and R. S. Ro, *J. Amer. Chem. Soc.*, 1958, **80**, 2428.

[26] H. E. Zimmerman, L. Singer, and B. S. Thyagarajan, *J. Amer. Chem. Soc.*, 1959, **81**, 108.

[27] G. B. Payne, *J. Org. Chem.*, 1960, **25**, 275; *J. Amer. Chem. Soc.*, 1959, **81**, 4901.

[28] G. B. Payne, *J. Org. Chem.*, 1959, **24**, 2048.

[29] B. Radziszewski, *Ber.*, 1884, **17**, 1289.

[30] K. B. Wiberg, *J. Amer. Chem. Soc.*, 1953, **75**, 3961; 1955, **77**, 2519.

[31] G. B. Payne and P. H. Williams, *J. Org. Chem.*, 1961, **26**, 651.

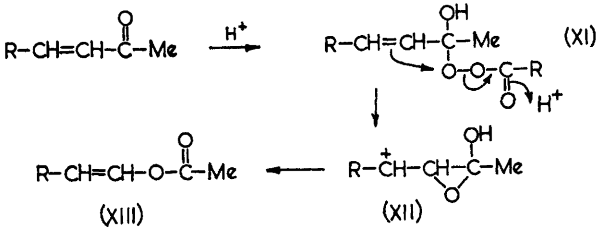
[32] G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, 1961, **26**, 659; G. B. Payne, *ibid.*, 1961, **26**, 663, 668; *Tetrahedron*, 1962, **18**, 763; Y. Ogata and Y. Sawaki, *ibid.*, 1964, **20**, 2065.

[33] G. B. Payne, P. H. Deming, and P. H. Williams, *J. Org. Chem.*, 1961, **26**, 659.

[34] Y. Ogata and Y. Sawaki, *Tetrahedron*, 1964, **20**, 2065.

[35] C. H. Hassall, *Org. Reactions*, 1957, **9**, 74.

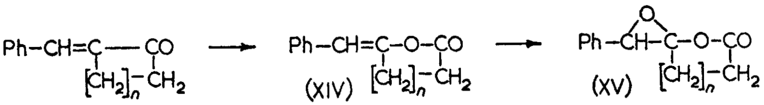
αβ-unsaturated ketones to give enol esters (XIII) or lactones. The mechanism[36] is a specific example of the Baeyer–Villiger oxidation.



The reaction is considered[37,38] to be acid-catalysed. The route *via* the carbonium-ion intermediate (XIII) is additionally favoured by a stabilising aryl group for R. Benzylideneacetophenone, for instance, gives exclusive formation of enol ester on oxidation with peracetic acid.[39]

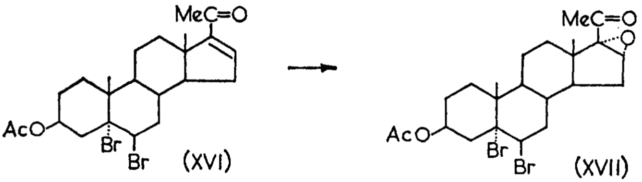
$$PhCH{=}CH{-}COMe \longrightarrow PhCH{=}CH{-}O{-}COMe$$

Similarly the benzylidene cycloalkanones give the lactones (XIV) which can be further oxidised to (XV).[40]



Where acid catalysts are absent and benzylidene-ketones are not involved, the use of organic peracids usually,[22] but not invariably,[36,41,42] leads to enol esters.

5,6-Dibromo-3-hydroxy-16-pregnen-20-one acetate (XVI) gives with perbenzoic acid not enol ester but the 16,17-epoxy-derivative (XVII);[41] since addition to carbonyl is often the rate-determining stage this suggests that attack at the carbonyl is more difficult in this case than at the 16,17-double bond. Parallel



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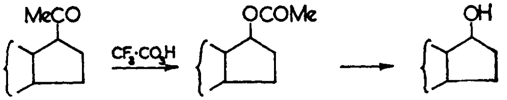
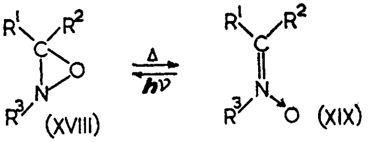
[36] E. Wenkert and M. Rubin, *Nature*, 1952, **170**, 708.
[37] P. Wieland and K. Miescher, *Helv. Chim. Acta*, 1949, **32**, 1768.
[38] L. H. Sarett, *J. Amer. Chem. Soc.*, 1947, **69**, 2899.
[39] J. Boeseken and A. L. Soesman, *Rec. Trav. chim.*, 1933, **52**, 874.
[40] H. M. Walton, *J. Org. Chem.*, 1957, **22**, 1161; C. R. Zanesco, *Helv. Chim. Acta*, 1966, **49**, 1002.
[41] P. L. Julian, E. W. Meyer, and I. Rydon, *J. Amer. Chem. Soc.*, 1950, **72**, 367.
[42] G. B. Payne and P. H. Williams, *J. Org. Chem.*, 1959, **24**, 284.

difficulty in carbonyl addition in saturated analogues has been noted.[43] However, with strong peracids carbonyl addition occurs,[44] thus providing a useful route for conversion of 17-acyl-steroids into the 17-hydroxy-analogues.

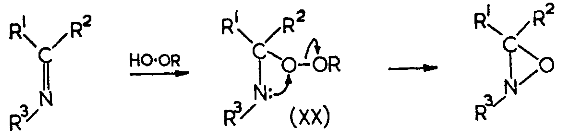


B. Peracid Oxidation of C=N and N=N Bonds.—(i) *Schiff bases.* Peracid oxidation of the C = N bond has been demonstrated with Schiff bases[45–48] and benzoylimines[49] (the nitrogen analogues of $\alpha\beta$-unsaturated ketones).

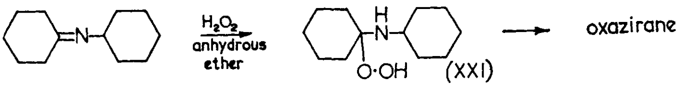
Schiff-base oxidation yields oxazirans (XVIII). Emmons[46b] has demonstrated clearly that the isomeric nitrone (XIX) is not formed. Irradiation converts (XIX) into (XVIII);[48,50] thermal isomerisation regenerates nitrone from oxaziran.[46b,48]



The available evidence suggests initial nucleophilic attack by peroxyacid on the positive carbon, followed by nucleophilic displacement of an acyl ion by the electron-rich nitrogen (XX).



This is supported by the isolation of the intermediate hydroperoxide (XXI) in certain conditions.[51]



A similar mechanism can be suggested for the related oxidations of *C*- and *N*-benzoylimines [Section **B.** (ii)]; contrast the mechanism with the two other possibilities (6) and (7), both involving *electrophilic* attack by peracid initially.

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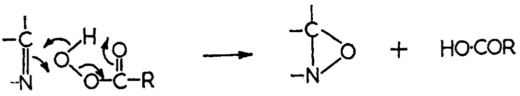
[43] J. L. Mateos, *J. Org. Chem.*, 1959, **24**, 2034; R. Cetina and J. L. Mateos, *ibid.*, 1960, **25**, 704.
[44] R. E. Marker, *J. Biol. Chem.*, 1940, **62**, 650.
[45] H. Krimm, *Chem. Ber.*, 1958, **91**, 1057.
[46] W. D. Emmons, *J. Amer. Chem. Soc.*, (*a*) 1956, **78**, 6208; (*b*) 1957, **79**, 5739.
[47] L. Horner and E. Jürgens, *Chem. Ber.*, 1957, **90**, 2184.
[48] E. Schmitz 'Advances in Heterocyclic Chemistry', ed. A. R. Katritsky, Academic Press, New York, 1963, vol. 2, p. 83.
[49] A. Padwa, *J. Amer. Chem. Soc.*, 1965, **87**, 4365.
[50] J. S. Splitter and M. Calvin, *J. Org. Chem.*, 1958, **23**, 651.
[51] E. Hoft and A. Rieche, *Angew. Chem. Internat. Edn.*, 1965, **4**, 525.



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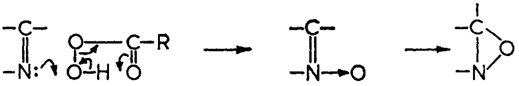
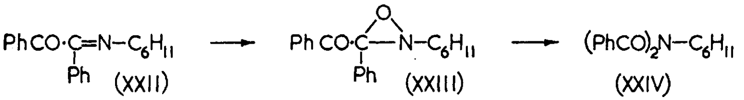


(7)

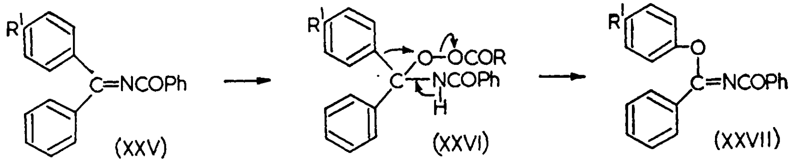
The analogous mechanism (6) to the Prileschajew reaction would in any case seem less favourable than direct attack by the more available nitrogen electron pair {cf. the peracid oxidation of azo-compounds and phenylhydrazones [Section **B.** (iii)]} (7), but the greater thermodynamic stability of nitrones[46,48] eliminates this mechanism as nitrones are not isolated.

(ii) C- *and* N-*Benzoylimines.* The action of organic peracids on *C*-benzoylimines produces oxazirans.[49] Monocyclohexyliminobenzil (XXII) yields, with *m*-chloroperbenzoic acid, 3-benzoyl-2-cyclohexyl-3-phenyl-oxaziran (XXIII), which rearranges to *NN*-dibenzoylcyclohexylamine (XXIV) on heating.



(XXII) (XXIII) (XXIV)

Peracid oxidation of the related *N*-benzoylimines (XXV) proceeds by a Baeyer–Villiger type of rearrangement of the peracid adduct (XXVI) first formed.



(XXV) (XXVI) (XXVII)

The product (XXVII) is usually hydrolysed in the work-up. The observed migratory aptitudes[49] in the rearrangement step (XXVI) → (XXVII) are consistent with migration to an electron-deficient atom.[52] An alternative rearrangement of an oxaziran intermediate[53] seems less plausible unless one postulates relief of steric strain as the driving force. The case differs from Schiff-base oxidation *via* intermediate (XX) where the Schiff-base nitrogen is considerably more nucleophilic.

(iii) *Phenylhydrazones and azo-compounds.* Phenylhydrazones[54–57] and azo-

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[52] P. A. S. Smith, 'Molecular Rearrangements', ed. P. de Mayo, John Wiley, New York, 1963, part 1, p. 585.

[53] Footnote 29 in ref. 49.

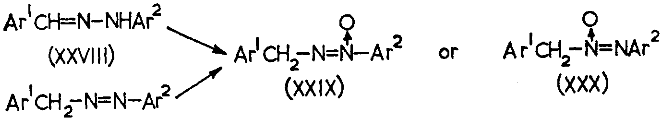
[54] K. H. Pausaker, *J. Chem. Soc.*, 1950, 3478; B. M. Lynch and K. H. Pausaker, *ibid.*, 1953, 2517; 1954, 3340.

[55] B. M. Lynch and K. H. Pausaker, *J. Chem. Soc.*, 1954, 1131.

[56] B. Witkop and H. M. Kissman, *J. Amer. Chem. Soc.*, 1953, 75, 1975.

[57] J. N. Brough, B. Lythgoe, and P. Waterhouse, *J. Chem. Soc.*, 1954, 4069.

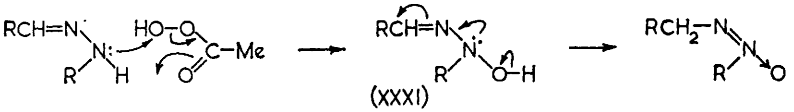
compounds[58] both give azoxy-compounds on oxidation with peracids, although the products differ structurally.[57]


(XXVIII) (XXIX) (XXX)

In the case of the aromatic aldehyde phenylhydrazones (XXVIII) the dispute concerning alternative structures (XXIX) and (XXX)[54–57,59] for the products has resolved in favour of the *cis*-form of (XXIX).[57] The reaction has been extended to the aromatic aldehyde alkylhydrazones.[60]

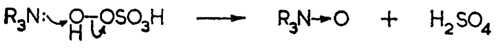
The isomeric azo-compounds give both (XXIX) and (XXX) the former predominating,[57] both however in the *trans* configuration.

The hydrazone–peracid reaction is of the second order, and has identical entropy of activation in polar and non-polar solvents.[55] Electrophilic molecular (non-ionic) attack by the peracid followed by rapid rearrangement of (XXXI) seems likely.


(XXXI)

Similar attack by the nitrogen lone pair (contrast the π-bond attack of olefins) can occur with azo-compounds.

C. Amines.—(i) *Oxidation with peracids.* Tertiary amines yield amine oxides with organic peracids.[61] Slower reaction occurs with hydrogen peroxide.[61,62,63] Caro's acid has been used.[63,64]


$$R_3N{:}\;\underset{H}{O}{-}OSO_3H \longrightarrow R_3N{\rightarrow}O + H_2SO_4$$

Ogata and Tabushi[64] observed second-order rate constants with Caro's acid and *p*-substituted *NN*-dimethylaniline; substituent effects were consistent with the amine's behaving nucleophilically. Ross[65] had earlier found second-order kinetics in the hydrogen peroxide–triethylamine reaction.[66,67] In contrast, primary and secondary amines give mixed products on oxidation; initially a

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[58] D. Swern, *Chem. Rev.*, 1949, **45**, 1.

[59] M. Bergmann, R. Ulpto, and C. Witte, *Ber.*, 1923, **56**, 679.

[60] B. T. Gillis and K. F. Schimmel, *J. Org. Chem.*, 1962, **27**, 413.

[61] D. Swern, *Chem. Rev.*, 1949, **45**, 6.

[62] W. R. Dunstan and E. Goulding, *J. Chem. Soc.*, 1899, **75**, 1004.

[63] A. C. Cope and E. R. Trumbull, *Org. Reactions*, 1960, **11**, 317.

[64] Y. Ogata and I. Tabushi, *Bull. Chem. Soc. Japan*, 1958, **31**, 969.

[65] S. D. Ross, *J. Amer. Chem. Soc.*, 1946, **68**, 1484.

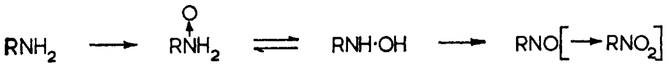
[66] A. A. Oswald and D. L. Quertin, *J. Org. Chem.*, 1963, **28**, 651.

[67] H. Wieland, *Ber.*, 1921, **54**, 2353.

hydroxylamine forms; nitrones (from secondary amines) or nitroso- and nitro-compounds (from primary amines) are later products. Condensation reactions give rise to by-products.[68,69,70]

Detailed studies[71,72] of the oxidation of anilines with peracetic acid show slow formation of phenylhydroxylamines preceding rapid conversion into nitroso-compounds.[71] Kinetic results are consistent with bimolecular nucleophilic attack by amine on the peroxide oxygen.

Overall oxidation proceeds according to (8).



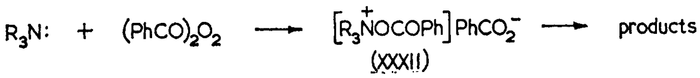
$$RNH_2 \longrightarrow R\overset{O}{\overset{\uparrow}{N}}H_2 \rightleftharpoons RNH{\cdot}OH \longrightarrow RNO[\longrightarrow RNO_2]$$

(8)

Edwards *et al.*[72] showed that the oxidation of nitroso- to nitro-benzene gave similar kinetic results, indicating a similar nucleophilic attack by the nitrogen on peroxy-oxygen. This is in conflict with Bunton's suggestion[73] that the reactants behave in a reverse manner, *i.e.*, that the peroxyacid behaves nucleophilically.

Direct oxidation of primary arylamines to nitro-compounds is most easily achieved by use of trifluoroperacetic acid.[74]

(ii) *Oxidation with acyl peroxides.* The reaction of tertiary amines with benzoyl peroxide initially gives a quaternary derivative (XXXII) by nucleophilic attack on the peroxide.[75–81] Evidence includes substituent effects;[75] electron-donating



$$R_3N: + (PhCO)_2O_2 \longrightarrow \underset{(XXXII)}{[R_3\overset{+}{N}OCOPh]PhCO_2^-} \longrightarrow \text{products}$$

groups accelerate, electron-withdrawing retard reaction when substituted in the amine,[75] but act conversely when substituted in the peroxide.[76] It is suggested[82] that decomposition of (XXXII) is a radical process. Dimethylaniline *N*-oxide also gives an intermediate similar to (XXXII), with acetic anhydride.[83] Secondary amines with benzoyl peroxide give *O*-benzoylhydroxylamines or

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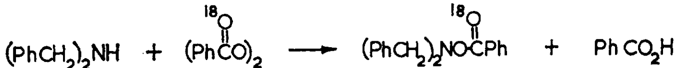
[68] E. Baumberger and T. Scheutz, *Ber.*, 1901, **34**, 2262.
[69] J. D'Ans and A. Kneip, *Ber.*, 1915, **48**, 1136.
[70] I. P. Gragerov and A. F. Levit, *Zhur. obshchei Khim*, 1960, **30**, 372.
[71] K. M. Ibne-Rasa and J. O. Edwards, *J. Amer. Chem. Soc.*, 1962, **84**, 763.
[72] K. M. Ibne-Rasa, C. G. Lauro, and J. O. Edwards, *J. Amer. Chem. Soc.*, 1963, **85**, 1165.
[73] C. A. Bunton, 'Peroxide Reaction Mechanisms', ed. J. O. Edwards, Interscience, New York, 1962, p. 21.
[74] W. D. Emmons, *J. Amer. Chem. Soc.*, 1954, **76**, 3470; 1957, **79**, 5528.
[75] L. Horner and K. Scherf, *Annalen*, 1951, **573**, 35.
[76] L. Horner and W. Kirmse, *Annalen*, 1955, **597**, 48.
[77] L. Horner and H. Junkermann, *Annalen*, 1955, **591**, 53.
[78] M. Imoto and S. Choe, *J. Polymer Sci.*, 1955, **15**, 485.
[79] C. Walling and N. Indictor, *J. Amer. Chem. Soc.*, 1958, **80**, 5814.
[80] D. Buckley, S. Dunstan, and H. B. Henbest, *J. Chem. Soc.*, 1957, 4901.
[81] W. B. Geiger, *J. Org. Chem.*, 1958, **23**, 298.
[82] For a summary, see C. Walling, 'Free radicals in solution', Wiley, New York, 1957, p. 590.
[83] V. Boekelheide and D. C. Harrington, *Chem. and Ind.*, 1955, 1423.

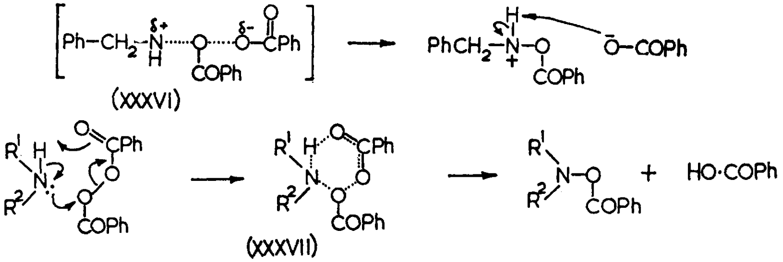
their rearrangement products. There is evidence for participation of free radicals in some instances[84,85] but a non-radical mechanism has also been suggested.[86,87] Using benzoyl peroxide labelled with oxygen-18 in the carbonyl positions (XXXIV) Denney and Denney[86] showed that dibenzylamine (XXXIII) and diphenylamine react by nucleophilic displacement on an oxygen of the peroxide link to give (XXXV).



$$(PhCH_2)_2NH + (Ph\overset{^{18}O}{\overset{\|}{C}}O)_2 \longrightarrow (PhCH_2)_2NO\overset{^{18}O}{\overset{\|}{C}}Ph + PhCO_2H$$

(XXXIII) (XXXIV) (XXXV)

The suggestion[82,86] that the transition state (XXXVI) decomposes *via* ions with subsequent proton transfer, is not supported by the observation[87] that solvent polarity has little effect on reaction rate. More likely is a concerted proton transfer through a cyclic intermediate (XXXVII).



(XXXVI)

(XXXVII)

D. Peroxidation of Sulphur Compounds.—The peroxidation of sulphides[88] involves two steps. A sulphoxide is first formed and further converted at a slower rate into a sulphone:

$$R_2S \xrightarrow{[O]} R_2SO \xrightarrow{[O]} R_2SO_2$$

The mechanism has been shown clearly to involve electrophilic peroxide attack on sulphur. Thus when bis-(*p*-chlorobenzyl) sulphide is oxidised by substituted benzoic acids[89] the reaction is accelerated by electron-attracting substituents, and *vice versa*, with a Hammett reaction constant of $\rho = +1{\cdot}05$. The rate, which is of the first order in peroxide and sulphide (or sulphone), is

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[84] Kh. S. Bagdasaryan and R. I. Milyutinskaya, *Zhur. fiz. Khim.*, 1953, **27**, 420.

[85] D. A. Chaltykyan, E. N. Anatasyan, N. M. Beileryan, and G. A. Marmaryan, *Russ. J. Phys. Chem.*, 1959, **33**, 36.

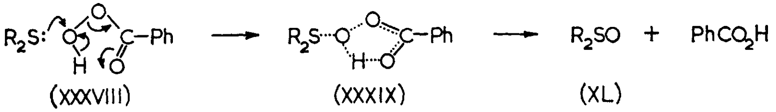
[86] D. B. Denney and D. Z. Denney, *J. Amer. Chem. Soc.*, 1960, **82**, 1389.

[87] Ya. K. Syrkin and I. I. Moiseev, *Russ. Chem. Revs.*, 1960, **29**, 193.

[88] D. Barnard, L. Bateman, and J. I. Cunneen, 'Organic Sulphur Compounds', ed. N. Kharasch, Pergamon, London, 1961, p. 229.

[89] C. G. Overburger and R. W. Cummins, *J. Amer. Chem. Soc.*, 1953, **75**, 4250.

not subject to a salt effect, and is faster in toluene than isopropyl alcohol, suggesting[89] an intramolecular hydrogen-transfer (XXXVIII—XL).



The increased rate in toluene which accompanies lower energy and entropy of activation could, however, be due to the strong hydrogen bonding possible in isopropyl alcohol hindering proton transfer.

Peracid oxidation of sulphoxide has similarly been shown to involve electrophilic attack by the peracid.[90,91]

When hydrogen peroxide[92,93] or hydroperoxides[94–96] are the oxidants the medium can have marked effects on the kinetics and solvent may participate in the transition state.

Addition of acetic acid to the ethanethiol–t-butyl hydroperoxide reaction system produces a sharp change in rate when amounts added are large, the acid thus behaving more like a solvent. Acid catalysis seems to be specific rather than general,[96] which is also the case for the oxidation by hydrogen peroxide of other systems.[97–99] General acid catalysis has been observed in the oxidation of sulphite ion by hydrogen peroxide.[100]

E. Peroxidation of Phosphorus Compounds.—(i) *With diaroyl and diacyl peroxide* Laible *et al.*[101] report that dibenzoyl peroxide reacts with trialkyl phosphites to give benzoic anhydride and phosphate ester. The reaction with phosphines has been studied in greater detail, and is probably ionic.[102]

(ii) *With hydrogen peroxide and hydroperoxides.* Hydroperoxides react readily with both tertiary phosphines and tertiary phosphites,[103] and since analogous products are obtained it seems reasonable to assume that analogous mechanisms are involved. Primary phosphines also react vigorously to give, initially, primary

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[90] G. Modena, *Gazzetta*, 1959, **89,** 843; 1960, **90,** 3, 11.

[91] G. Kreeze, W. Schramm, and G. Gleve, *Chem. Ber.*, 1961, **94,** 2060.

[92] C. G. Overburger and R. W. Cummins, *J. Amer. Chem. Soc.*, 1953, **75,** 4783.

[93] S. D. Ross, *J. Amer. Chem. Soc.*, 1946, **68,** 1484.

[94] L. Bateman and K. R. Hargrave, *Proc. Roy. Soc.*, 1954, *A*, **224,** 389.

[95] L. Bateman and K. R. Hargrave, *Proc. Roy. Soc.*, 1954, *A*, **224,** 399.

[96] J. O. Edwards and D. H. Fortnum, *J. Org. Chem.*, 1962, **27,** 407.

[97] I. R. Wilson and G. M. Harris, *J. Amer. Chem. Soc.*, 1960, **82,** 4515; 1961, **83,** 286.

[98] H. A. Liebhafsky and A. Mohammed, *J. Amer. Chem. Soc.*, 1933, **55,** 3977; 1934, **56,** 1680.

[99] E. Abel, *Monatsh.*, 1907, **28,** 1239; K. Sandred and J. B. Hotte, *Chem. Abs.*, 1939, **33,** 4856.

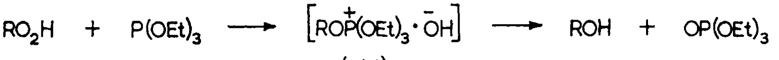
[100] P. M. Mader, *J. Amer. Chem. Soc.*, 1958, **80,** 2634.

[101] R. C. Laible, R. M. Esteve, and J. D. Morgerum, *J. Appl. Polymer Sci.*, 1959, **1,** 376; *Chem. Abs.*, 1960, **54,** 10827.

[102] L. Horner and W. J. Jurgeleit, *Ann. Chem.*, 1955, **591,** 138; M. A. Greenbaum, D. B. Denney, and A. K. Hoffman, *J. Amer. Chem. Soc.*, 1956, **78,** 2563; D. B. Denney and M. A. Greenbaum, *ibid.*, 1957, **79,** 979.

[103] (*a*) M. A. Greenbaum, D. B. Denney, and B. Goldstein, *J. Amer. Chem. Soc.*, 1960, **82,** 1396; (*b*) C. Walling and R. Rabinowitz, *ibid.*, 1957, **79,** 5326; (*c*) I. S. Bengelsdorf, Ph.D. Thesis, Univ. of Chicago, 1951.

phosphine oxides[104] which rapidly decompose at room temperature. Bengelsdorf's original suggestions[105] were confirmed by later workers[106] who suggested that an intermediate quasi-phosphonium compound was produced (XLI).

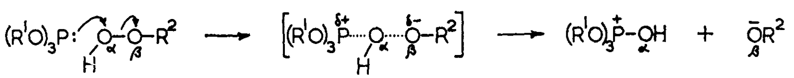


$$RO_2H + P(OEt)_3 \longrightarrow [RO\overset{+}{P}(OEt)_3 \cdot \overset{-}{O}H] \longrightarrow ROH + OP(OEt)_3$$

(XLI)

However, in an examination[107] of the reaction of triphenylphosphine with *trans*-9-decalyl hydroperoxide, retention of configuration, and a lack of exchange of labelled oxygen with either product when labelled water was added, was found.

In formation and breakdown of an intermediate of type (XLI) one would most reasonably suggest *either* inversion *or* racemisation of the group R as likely to occur, and lack of exchange of labelled oxygen would require (XLI) to decompose much more quickly than equilibration of OH^- and water.

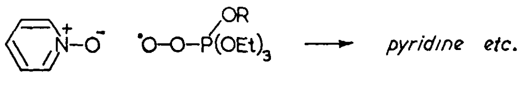


A simpler explanation is to assume a mechanism in common with other heterolytic peroxide oxidations.

The reaction should show similar characteristics to other reactions of this type, *e.g.*, protonation of O should accelerate reaction. However, although the reaction has been applied synthetically,[108] no kinetic study has been made. Denney *et al.*[109] examined the oxidation of optically active phosphines with various oxidising agents, and assumed that t-butyl hydroperoxide reacted without inversion, but no direct evidence is available on this point.

(iii) *With dialkyl peroxides.* Walling and Rabinowitz[103b] considered that the reaction of di-t-butyl peroxide with phosphites was a radical process (this may be a steric effect; see footnote 11 in ref. 110).

The interesting observation[111] that peroxides, but not hydroperoxides, reduce pyridine *N*-oxide in the presence of triethyl phosphite, led Rees and Emerson to postulate a radical process.



The reaction has certain analogies with the reduction of *N*-oxides by H_2O_2 in acetic acid,[110] which would imply nucleophilic attack by the *N*-oxide upon peroxide.

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[104] S. A. Buckler and M. Epstein, *Tetrahedron*, 1962, **18**, 1221.

[105] I. S. Bengelsdorf, Ph.D. Thesis, Univ. of Chicago, 1951.

[106] D. B. Denney, M. A. Greenbaum, and B. Goldstein, *J. Amer. Chem. Soc.*, 1960, **82**, 1396.

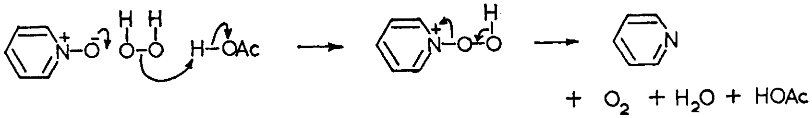
[107] D. B. Denney, W. F. Goodyear, and B. Goldstein, *J. Amer. Chem. Soc.*, 1960, **82**, 1393.

[108] T. Tanaka, *Yakugaku Zasshi*, 1960, **80**, 439; (*Chem. Abs.* 1960, **54**, 19470).

[109] D. B. Denney and J. W. Hanifin, *Tetrahedron Letters*, 1963, No. 30, 2177; cf. D. B. Denney *et al.*, *J. Amer. Chem. Soc.*, 1960, **82**, 1393; 1961, **83**, 1726; 1962, **84**, 4737; 1956, **78**, 2563.

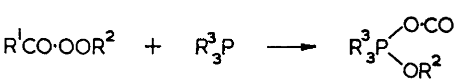
[110] I. J. Pachter and M. C. Kloetzel, *J. Amer. Chem. Soc.*, 1951, **73**, 4958.

[111] T. R. Emerson and C. W. Rees, *Proc. Chem. Soc.*, 1960, 418.



These authors found[111] that an electron-donating (*e.g.*, *p*-OMe) substituent accelerated reaction, while an electron-attracting substituent slowed reaction, which would fit a heterolytic mechanism, but the evidence is too slight to permit a clear decision.

(iv) *With peresters.* In a detailed study[112] of the oxidation of tertiary phosphines with peresters, isotopic and stereochemical results indicated clearly that a quinquecovalent phosphorus compound resulted from attack by phosphorus on peroxy-oxygen atoms.

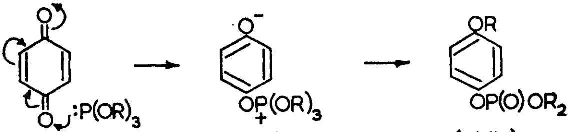


$$R^1CO\cdot OOR^2 + R^3_3P \longrightarrow R^3_3P\begin{matrix} \diagup O\cdot COR^1 \\ \diagdown OR^2 \end{matrix}$$

(XLII)

Since only slight rate enhancement occurs with increased solvent polarity (contrast the reaction of triphenylphosphine with sulphur,[113] for example) a relatively small separation of charge in the transition state is indicated. The entropy of activation observed[114] is in line with this. Tertiary phosphites behave similarly.[115]

(v) *Oxygen other than peroxy-oxygen.* Apart from peroxide systems, attack by phosphorus on oxygen is claimed to occur in a number of cases. For example, triethyl phosphite with benzoquinones reacts mainly to give the products of 1,6-addition (XLIV).[116,117]



(XLIII) (XLIV)

Consideration of other results[118,119] suggests an alternative mechanism.

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[112] D. B. Denney, W. F. Goodyear, and B. Goldstein, *J. Amer. Chem. Soc.*, 1961, **83**, 1726.

[113] P. D. Bartlett and G. Meguerian, *J. Amer. Chem. Soc.*, 1956, **78**, 3710.

[114] A. A. Frost and R. G. Pearson, 'Kinetics and Mechanism', Wiley, New York, 1953, ch. 7.

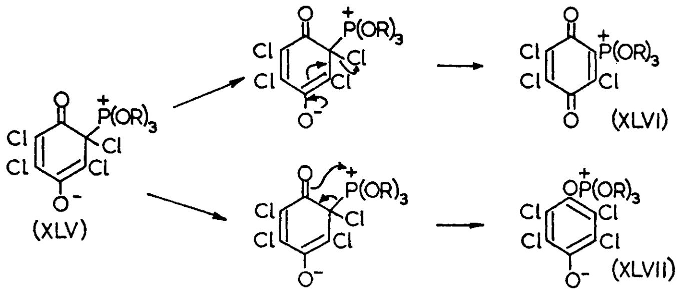
[115] J. B. Lee, unpublished observations.

[116] F. Ramirez, E. H. Chen, and S. Derschowitz, *J. Amer. Chem. Soc.*, 1959, **81**, 4338; F. Ramirez and S. Derschowitz, *ibid.*, 1959, **81**, 587; *J. Org. Chem.*, 1957, **22**, 856; 1958, **23**, 778.

[117] V. A. Kukhtin and K. M. Orekhova, *Proc. Acad. Sci. U.S.S.R., Chem. Sect.*, 1959, 73; (*Chem. Abs.*, 1961, **55**, 1567); V. A. Kukhtin, K. M. Orekhova, and N. S. Garifyanov, *J. Gen. Chem. U.S.S.R.*, 1961, **31**, 1070.

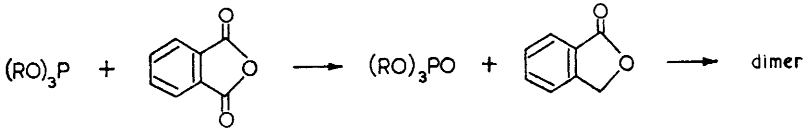
[118] T. Reetz, U.S. Patent, 2,935,518/1960; (*Chem. Abs.*, 1960, **54**, 19598); Abs. of papers of the 134th meeting, A.C.S., Chicago, Ill., 1958, p. 86-P.

[119] R. G. Harvey, E. G. de Sombre, and E. V. Jensen, Abs. of papers of the 135th meeting, A.C.S., Boston, Mass., 1959, p. 69-O; R. G. Harvey and E. V. Jensen, Abs. of papers of the 144th meeting, A.C.S., Los Angeles, Calif., 1961, p. 44-O; G. Kamai and V. A. Kukhtin, *J. Gen. Chem. U.S.S.R.*, 1958, **28**, 913; (*Chem. Abs.*, 1958, **52**, 17162); *Proc. Akad. Sci. U.S.S.R., Chem. Sect.*, 1957, 129; (*Chem. Abs.*, 1957, **51**, 13742); *Zhur. obshchei Khim.*, 1957, **27**, 2376; (*Chem. Abs.*, 1958, **52**, 7127).



Although electrophilic attack by phosphite esters upon episulphide sulphur is easy, reaction with epoxides involves attack upon carbon.[120] Similarly, attack on nitrogen seems more likely than direct attack on oxygen in the deoxygenation (with phosphines and/or phosphites) of pyridine *N*-oxides,[121] and some related reactions.[122–4]

Attack upon carbonyl carbon is the usual mode of reaction of phosphites with aldehydes and anhydrides but in the unique case of phthalic anhydride in reaction with trialkyl phosphites attack upon oxygen to give phosphate and a carbene has been reported.[125]



F. Peroxidation of Boron Compounds.—The recent extensive use of hydroboration with ensuing oxidation, to hydrate double bonds, involves hydrogen peroxide oxidation of intermediate boranes, probably involving attack on electron-deficient oxygen.

Hydrogen peroxide oxidation of phenyl boronic acid was suggested to involve attack upon the boron by hydroperoxide anion,[126] followed by migration of the (phenyl) group in the hydroperoxide and expulsion of a hydroxyl ion with production of phenyl borate.

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[120] C. B. Scott, *J. Org. Chem.*, 1957, **71**, 578; N. P. Neureister and F. G. Bordwell, *J. Amer. Chem. Soc.*, 1959, **81**, 578.

[121] F. Ramirez and A. Aguiar, Abs. of papers of 134th A.C.S. meeting, Chicago, Ill., 1958, 42-N. M. Haman, *J. Pharm. Soc. Japan*, 1955, **75**, 139; T. Emerson and C. Rees, *Proc. Chem. Soc.*, 1960, 418.

[122] P. Bunyan and J. I. G. Cadogan, *Proc. Chem. Soc.*, 1962, 78; T. Mukaiyama, H. Nambu, and M. Okamato, *J. Org. Chem.*, 1962, **27**, 3651.

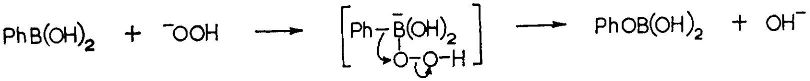
[123] J. I. G. Cadogan and M. Cameron-Wood, *Proc. Chem. Soc.*, 1962, 361.

[124] T. Mukaiyama, H. Nambu, and M. Okamato, *J. Org. Chem.*, 1962, **27**, 3651.

[125] P. Bunyan and J. I. G. Cadogan, *Proc. Chem. Soc.*, 1962, 78; cf. T. T. Mukaiyama, H. Nambu, and M. Okamato, *J. Org. Chem.*, 1962, **27**, 3651; J. H. Boyer and S. Ellzey, *ibid.*, 1961, **26**, 4684.

[126] H. G. Kuivila, *J. Amer. Chem. Soc.*, 1954, **76**, 870; 1955, **77**, 4014, 4830; 1957, **79**, 5659.

$$H_2O_2 + {}^{-}OH \rightleftharpoons HOO^{-} + H_2O$$



$$PhB(OH)_2 + {}^{-}OOH \longrightarrow \left[Ph-\bar{B}(OH)_2 \atop O-O-H\right] \longrightarrow PhOB(OH)_2 + OH^{-}$$

So far no detailed kinetic study of oxidation of trialkylboranes has been reported. The first significant observation was probably that of Johnson and Van Campen,[127] who demonstrated the rapid, quantitative low-temperature reaction of tri-n-butylborane with perbenzoic acid. Their observation on the similar action of alkaline hydrogen peroxide was later developed into an analytical technique.[128] Other workers[129] found the reaction proceeded rapidly at low temperature.

The absence of free radicals is indicated[130] and the lack of any rearrangement of the migrating group is well established,[130] the migrating group retaining its optical structure unchanged.[115,131]

G. Peroxidation of Silicon Compounds.—Triorganosilyl peroxides (XLVII) and silanes (XLIX) have been prepared by a variety of methods,[132–4] most involving nucleophilic attack by peroxy-oxygen.

$R_3Si-O-O-SiR_3$ (XLVIII) $\qquad$ $R_3Si-O-O-CR_3$ (XLIX)

Breakdown of the peroxides (XLVIII) on distillation possibly involves a rearrangement (XLVIII → L).

(XLVIII)

(L)

$$R_2Si(Me)-O-O-SiR_3 \longrightarrow R_2Si(OMe)OSiR_3$$

The occurrence of rearrangement in the peroxysilanes (XLIX) is not well established, and attempts to prepare triorganosilyl peroxyesters (LI) led directly to rearranged products, but under similar conditions trialkylperoxysilanes did not rearrange.[133] Rearrangement of the silyl perbenzoates seems to occur much more readily than for the analogous carbon compounds.[115] Since silicon shows

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[127] J. R. Johnson and M. G. Van Campen, *J. Amer. Chem. Soc.*, 1938, **60**, 121.

[128] R. Belcher, *Mikrochim. Acta*, 1952, **40**, 76.

[129] H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1956, **78**, 5694; A. A. Carotti and P. F. Winternitz, *ibid.*, 1960, **82**, 2430.

[130] *Inter al.*, H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 1959, **81**, 247; W. J. Wechter, *Chem. and Ind.*, 1959, 294; R. Koster, G. Griansnow, W. Larbig, and P. Binger, *Annalen*, 1964, **672**, 1; H. C. Brown, N. R. Ayyanger, and G. Zweifel, *J. Amer. Chem. Soc.*, 1964, **86**, 397; D. K. Shumway and J. D. Barnhurst, *J. Org. Chem.*, 1964, **29**, 2320; M. Nussin, Y. Mazur, and F. Sondheimer, *ibid.*, 1964, **29**, 1120, 1131.

[131] H. C. Brown and G. Zweifel, *J. Amer. Chem. Soc.*, 1964, **86**, 393; F. R. Jensen, *ibid.*, 1960, **82**, 148, 246.

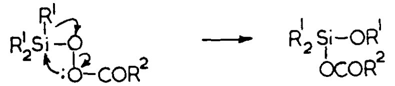
[132] W. Hahn and L. Metzinger, *Makromol. Chem.*, 1956, **21**, 113.

[133] E. Buncel and A. G. Davies, *Chem. and Ind.*, 1956, 1052; *J. Chem. Soc.*, 1958, 1550.

[134] R. A. Pike and L. A. Shaffer, *Chem. and Ind.*, 1957, 1294; *Chem. Abs.*, 1955, **49**, 13290.

a great ease of front-side attack in displacement reactions[135a] a synchronous mechanism of the type (LI → LII) should proceed rapidly.

(LI)



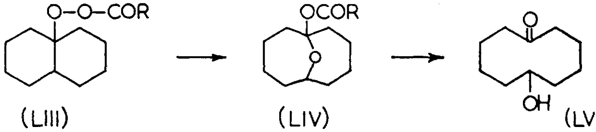
(LII)

Further evidence of this process is desirable. Since phenyl migrates in preference to methyl, and acid catalysis is shown, one may assume that reaction occurs as in the carbon case.[115]

A comprehensive review of the chemistry of organometalloid and organometallic peroxides is recently available.[135b]

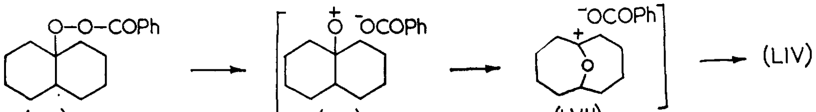
3 Intramolecular Rearrangements Involving Electrophilic Oxygen

A. Peroxyesters.—In 1944 Criegee noted[136] that acetate and benzoate esters of *trans*-9-decalyl hydroperoxide (LIII) rearranged on standing to give isomeric esters of type (LIV); subsequent hydrolysis gave 6-hydroxycyclodecanone (LV) (R= Me or Ph).



(LIII) (LIV) (LV)

Kinetic studies showed that the rate increased with more polar solvent and also with increased electron-withdrawing character of R (in LIII, LIV).[137] Criegee and Kasper[137] pointed out the analogy in this respect with carbonium-ion rearrangements of the Wagner–Meerwein, pinacol–pinacolone, and Beckmann types. They suggested that heterolytic fission of the peroxide-bond occurred, but that the benzoate ion was never free, *i.e.*, that an ion-pair mechanism was involved.



(LIII) (LVI) (LVII) (LIV)

Further study showed that the reaction was of the first order,[138,139] subject to slight acid catalysis, and that the rates of rearrangement of *para*-substituted benzoate esters fitted the Hammett equation ($\rho = +1{\cdot}34$).[138] Furthermore, in

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[135] (*a*) L. H. Sommer and O. F. Bennett, *J. Amer. Chem. Soc.*, 1957, **79**, 3295; 1959, **81**, 251; (*b*) G. Sosnovsky and J. H. Brown, *Chem. Rev.*, 1966, **66**, 529.

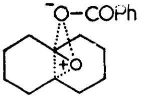
[136] R. Criegee, *Ber.*, 1944, **77**, 722.

[137] R. Criegee and R. Kaspar, *Annalen*, 1948, **560**, 127.

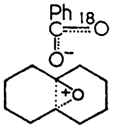
[138] P. D. Bartlett and J. L. Kice, *J. Amer. Chem. Soc.*, 1953, **75**, 5591.

[139] H. L. Goering and A. C. Olsen, *J. Amer. Chem. Soc.*, 1953, **75**, 5853.

the presence of added *para*-substituted benzoate ions there is no interchange between these and the benzoate ions of the decalyl perbenzoate.[138,139] A number of mechanisms have been proposed[138–141] and it seems likely that an intermediate of the type (LVIII) or (LIX) is involved.[141,142]

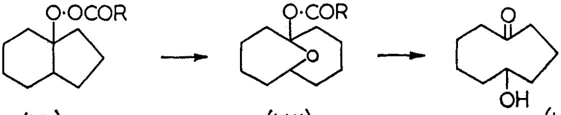


(LVIII)



(LIX)

The Criegee rearrangement has been further demonstrated[142] in hydrindanyl peroxy-esters (LX), leading to the cyclononanone system (LXII).



(LX) (LXI) (LXII)

B. Hydroperoxides.—Industrially important preparations of phenols have been based upon the rearrangement of certain hydroperoxides. Thus, condensation of propene and benzene followed by oxidation and rearrangement yields phenol and acetone.[144] Probably the 'prototype' of this reaction was the *p*-cymene hydroperoxide rearrangement.[145] In these cases the migration of an aryl group occurs to the exclusion of the alternative alkyl migration.

One of the earliest examples[146,147] established the ionic nature of the acid-catalysed rearrangement of triphenylmethyl hydroperoxide (R = Ph).

$$R_3C{-}O{-}O{-}H \xrightarrow{H^+} R_2CO + ROH$$

Later work[148] developed a one-stage conversion of triarylmethanols into ketone and phenol. Initial observations[145,148,149] established the relative 'migratory aptitude' of the aryl groups: an electron-releasing substituent increases, an

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[140] D. B. Denney, *J. Amer. Chem. Soc.*, 1955, **77**, 1706.

[141] D. B. Denney and D. G. Denney, *J. Amer. Chem. Soc.*, 1957, **79**, 4806.

[142] S. Winstein and G. C. Robinson, *J. Amer. Chem. Soc.*, 1958, **80**, 169.

[143] R. Criegee and H. Zogel, *Chem. Ber.*, 1951, **84**, 215.

[144] *E.g.*, P. W. Sherwood, *Ind. Chemist*, 1954, **30**, 25, 71.

[145] H. Hock and S. Lang, *Ber.*, 1944, **77**, 257.

[146] Cf. L. H. Cone and M. Gomberg, *Ber.*, 1904, **37**, 3538.

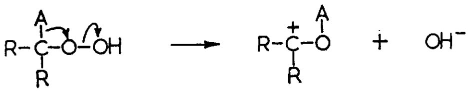
[147] H. Wieland and J. Maier, *Ber.*, 1931, **64**, 1205.

[148] W. Dilthey, F. Quint, and H. Dierichs, *J. prakt. Chem.*, 1938, **151**, 25.

[149] P. D. Bartlett and J. D. Cotman, *J. Amer. Chem. Soc.*, 1950, **72**, 3095; cf., however, Y. Ishii, A. Furuno, and S. Sumi, *Kogyo Kagaku Zasshi*, 1961, **64**, 472.

electron-attracting decreases, the tendency to migrate. Study of competitive migrations established[150] that the migratory aptitude increased as the ability to stabilise a positive centre increased; both protonic and Lewis acids strongly accelerated the reaction.

In secondary benzylic hydroperoxides aryl groups migrate almost to the complete exclusion of alkyl groups, except vinylic groups which are similar in mobility to phenyl. A similar series of migratory aptitude is shown, for example, in the pinacol–pinacolone rearrangement.[151] While the latter reaction shows a very marked steric effect with *ortho* substitution, this effect is much less marked[152] in the peroxide rearrangement, reflecting lower steric crowding at the reaction terminus in this case. (There will also be some effect here from interference in the orientation of the benzene ring, but this is obviously small.)



For alkyl groups, the order tertiary > secondary > primary > methyl holds. The position of hydrogen in the series is more doubtful.[153,154]

Kinetic studies[152,155–158] with isotopic[159] and other evidence[160] give strong support for a rate-determining concerted rearrangement of a protonated form of the hydroperoxide (LXIII).

Reaction is of the second order overall; first order in peroxide, first order in acid, pseudo-first order at a given acid concentration. Specific, rather than

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[150] M. S. Kharasch, A. Fono, and W. Nudenberg, *J. Org. Chem.*, 1950, **15**, 748; M. S. Kharasch, A. Fono, W. Nudenberg, and A. C. Pushkus, *ibid.*, 1950, **15**, 775; M. S. Kharasch and J. G. Burt, *ibid.*, 1951, **16**, 150; M. S. Kharasch, A. Fono, W. Nudenberg, and B. Bischof, *ibid.*, 1952, **17**, 207.

[151] C. K. Ingold, 'Structure and Mechanism in Organic Chemistry', Bell, London, 1953, p. 477.

[152] A. W. de Ruyter van Steveninck and E. C. Kooyman, *Rec. Trav. chim.*, 1960, **79**, 413.

[153] *E.g.*, W. Pritzkow and K. A. Müller, *Ber.*, 1956, **89**, 2312.

[154] *E.g.*, Cf. M. S. Kharasch and J. G. Burt, *J. Org. Chem.*, 1951, **16**, 13, 128; N. Kornblum and H. E. De La Mare, *J. Amer. Chem. Soc.*, 1951, **73**, 851; A. M. White, Thesis, Univ. of London, 1953; W. J. Farrisey, *J. Org. Chem.*, 1962, **27**, 3065; *J. Amer. Chem. Soc.*, 1962, **84**, 1002; H. B. van Leeuwen, J. P. Wibaut, I. F. Bickel, and E. C. Kooyman, *Rec. Trav. chim.*, 1959, **78**, 667; A. D. Boggs, Thesis, Ohio State Univ., 1954.

[155] F. H. Seubold and W. E. Vaughan, *J. Amer. Chem. Soc.*, 1953, **75**, 3790.

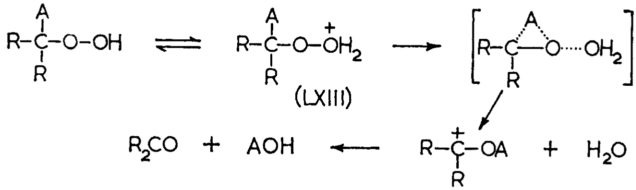
[156] O. Wichterle and P. Cefelin, *Coll. Czech. Chem. Comm.*, 1957, **22**, 1083.

[157] A. W. de Ruyter van Steveninck, *J. Chem. Soc.*, 1958, 2066.

[158] Yu A. Shiyapnikov, *Kinetika i Kataliz*, 1960, **1**, 365; V. A. Shushunov and Yu. A. Shiyapnikov, 'Works on Chemistry and Chemical Technology', Gorkii, 1958, p. 50, 1959, p. 102; V. A. Shushanov and Yu. A. Shiyapnikov, *Doklady Akad. Nauk S.S.S.R.*, 1959, **128**, 341.

[159] M. Bussey, C. A. Bunton, A. G. Davies, T. A. Lewis, and D. R. Llewellyn, *J. Chem. Soc.*, 1955, 2471.

[160] A. G. Davies and R. Feld, *J. Chem. Soc.*, 1958, 4637.

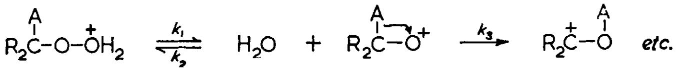

(LXIII)

general, acid catalysis is involved.[155] Activation energies suggest an ionic rather than a free-radical reaction.[152,157] The effects of *para*-substituents on aryl migration fit[152] the Hammett σ^+ (rather than σ) relationship, with a large reaction constant of $-4{\cdot}57$ supporting a concerted rearrangement of the protonated material (LXIII).

^{18}O-Labelled methanols gave hydroperoxide free from label.[159]

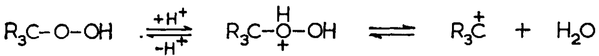
$$R_3C^{18}OH \xrightarrow[H^+]{H_2O_2} R_3CO{-}OH + H_2{}^{18}O$$

Since some rearrangement occurs in these conditions, there cannot have been an equilibrium involving R–O$^+$; rearrangement is either concerted therefore (*via* LXIII), or occurs immediately upon formation of R–O$^+$ (*i.e.*, $k_3 \gg k_2$) thus:



The easy decomposition of 1-phenylethylhydroperoxide as compared with t-butyl hydroperoxide, suggests a synartetic process. The mechanism varies with structure.[160]

The overall reaction is somewhat more complex than this.[161] Protonation to form two distinct conjugate acids is possible (LXIII, LXIV), and whilst rearrangement of (LXIV) will not occur, a reversible breakdown to hydrogen peroxide and a carbonium ion is to be expected, particularly with triarylmethyl hydroperoxides.



$$R_3C{-}O{-}OH \underset{-H^+}{\overset{+H^+}{\rightleftharpoons}} R_3C{-}\overset{H}{\underset{+}{O}}{-}OH \rightleftharpoons R_3\overset{+}{C} + H_2O$$

(LXIV)

In the presence of a second methanol, equilibration between water, methanol, hydroperoxide, and hydrogen peroxide occurs at a rate comparable with the rate of rearrangement.[161]

Information on hydroperoxide rearrangement in groups other than aralkyl hydroperoxides is relatively sparse.

In nitrogen heterocycles the -C=N.R group migrates to the exclusion of

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[161] D. E. Blissing, C. A. Mutuszak, and W. E. McEwen, *Tetrahedron Letters*, 1962, No. 17, 763; *J. Amer. Chem. Soc.*, 1964, **86**, 3824.

phenyl, alkyl, or -N(Aryl)$_2$ migration[162–165] and one may assume that the oxidative breakdown of tryptophan to formylkynurenine[166,167] can be explained by a similar migration in a hydroperoxide intermediate.

The rearrangement of metal alkyls to alkoxides is likely to involve an ionic rearrangement *via* hydroperoxide.[168]

In certain other cases, where isomerisation of hydroperoxides occurs, no evidence is available to permit distinction between electrophilic or nucleophilic oxygen.[169] The electrophilic attack by olefin upon hydroperoxide has been discussed above.[170] A number of reviews have appeared on hydroperoxides.[171–173]

C. The Baeyer–Villiger Reaction.—The oxidation of ketones by peracids proceeds *via* a peroxy-intermediate, with subsequent carbon to oxygen migration leading to an ester or lactone. Since its discovery[174] the reaction has been very widely applied.[175]

$$R^1{\cdot}CO{\cdot}R^2 \xrightarrow{R^3OOH} R^1{\cdot}CO{\cdot}OR^2 + R^3OH$$

Use of acids other than Caro's acid[174] has led to improvements.[173,176]

Mechanistic studies[177] led to the formulation of the reaction as initial nucleophilic addition of peracid to the protonated carbonyl group, followed by migration of an electron-pair bearing group, in the hydroxyperoxide produced, to an electrophilic oxygen.

A summary of this evidence is as follows. Rearrangement of [^{18}O]benzophenone gives phenyl benzoate with the same carbonyl oxygen isotope content

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[162] C. W. Bird, *J. Chem. Soc.*, 1965, 3490.

[163] D. M. White, *J. Amer. Chem. Soc.*, 1964, **86,** 5685.

[164] E. H. White and M. J. C. Harding, *J. Amer. Chem. Soc.*, 1964, **86,** 5687.

[165] L. A. Cohen and B. Witkop, *J. Amer. Chem. Soc.*, 1955, **77,** 6595.

[166] A. Ek, H. M. Kissman, J. B. Patrick, and B. Witkop, *Experientia*, 1952, **8,** 38.

[167] A. A. Haakim and K. A. Thiele, *Biochem. Biophys. Res. Comm.*, 1960, **2,** 242.

[168] *E.g.*, H. Hock, H. Kropf, and F. Ernst, *Angew. Chem.*, 1959, **71,** 541; cf. A. G. Davies, 'Organic Peroxides', Butterworths, London, 1961, pp. 120–126, 155–160.

[169] *E.g.*, G. O. Schenk, O. A. Neumuller, and W. Eisfed, *Angew. Chem.*, 1960, **70,** 595.

[170] W. F. Brill and N. Indictor, *J. Org. Chem.*, 1965, **30,** 2074; 1964, **29,** 710; *J. Amer. Chem. Soc.*, 1963, **85,** 141.

[171] P. D. Bartlett, *Rec. Chem. Progr.*, 1950, **11,** 47.

[172] J. E. Leffler, *Chem. Rev.*, 1949, **45,** 385.

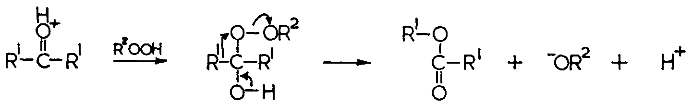
[173] E. Testa, 'Oxydationen durch Wasserstoff peroxyd. und persauren die zur spaltung von C-C Bindungen fuhren', Juris Verlag, Zurich, 1950.

[174] A. von Baeyer and V. Villiger, *Ber.*, 1899, **32,** 3625.

[175] *E.g.*, L. Ruzicka and E. Stoll, *Helv. Chim. Acta*, 1928, **11,** 1159; V. Burkhardt and T. Reichstein, *ibid.*, 1942, **25,** 821, 1435; H. Heuser, A. Segre, and A. Plattner, *ibid.*, 1948, **31,** 1183; V. Prelog, L. Ruzicka, P. Meister, and P. Wieland, *ibid.*, 1945, **28,** 618, 1651; R. E. Marker, *J. Biol. Chem.*, 1940, **62,** 650.

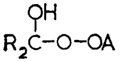
[176] J. E. Leffler, *Chem. Rev.*, 1949, **45,** 385; C. H. Hassall, *Org. Reactions*, 1957, **9,** 74.

[177] R. Criegee, *Annalen*, 1948, **560,** 127; S. L. Friess and N. Farnham, *J. Amer. Chem. Soc.*, 1950, **72,** 5518; W. E. Doering and L. Speers, *ibid.*, 1950, **72,** 5515; W. E. Doering and E. Dorfmann, *ibid.*, 1953, **75,** 5595; J. L. Mateos and H. Mechata, *J. Org. Chem.*, 1964, **29,** 2026. See ref. 19*a* in contrast.



(LXV) (LXVI) (LXVII)

as the initial ketone.[178] The most likely intermediate is (LXVIII) or one of its *O*-protonated conjugate acids.[179]



$R_2C(OH){-}O{-}OA$

(LXVIII)

The actual rearrangement is clearly intramolecular; several groups of workers[180–183] have reported complete retention of configuration in migrating centres.

The relative 'migratory aptitude' of groups in unsymmetrical ketones has been extensively examined.[184,185] *para*-Substitution in a phenyl group influences migratory aptitude in proportion to electron-releasing effect[186] suggesting a concerted rearrangement. *ortho*-Substitution reduces mobility *vis-à-vis para.*[186] In general, the group best able to sustain a positive charge migrates most readily, but this electronic effect is not the sole factor.

Sauers[187] confirmed the observation[174] that the only lactone isolable from the action of Caro's acid on camphor was the 'abnormal' α-campholide: but showed, in agreement with other work,[188] that the 'normal' lactone (that is, the product of migration of a tertiary group) was further decomposed in these conditions. Further, the 'normal' lactone only was obtained on oxidation of camphor with buffered peracetic acid.[187] The expected bridgehead migration occurs with norcamphor.[189] Epicamphor and 1-methylnorcamphor[190] differ sharply, with exclusive methylene migration in the former case, while fenchone gives mixed products.

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[178] W. E. Doering and E. Dorfmann, *J. Amer. Chem. Soc.*, 1953, **75**, 5595; cf. C. A. Bunton, *Chem. and Ind.*, 1954, 191.

[179] Originally suggested by R. Criegee and R. Kaspar, *Annalen*, 1948, **560**, 127.

[180] T. F. Gallagher and T. H. Kritchevsky, *J. Amer. Chem. Soc.*, 1950, **72**, 882; R. B. Turner, *ibid.*, 1950, **72**, 878; L. H. Sarrett, *ibid.*, 1957, **69**, 2899; R. E. Marker, *ibid.*, 1940, **62**, 2543; V. Burkhardt and T. Reichstein, *Helv. Chim. Acta*, 1942, **25**, 1434.

[181] K. Mislow and J. Bremner, *J. Amer. Chem. Soc.*, 1953, **75**, 2319.

[182] J. W. Wilt and A. Danielzadeh, *J. Org. Chem.*, 1958, **23**, 920; J. A. Berson and S. Suzuki, *J. Amer. Chem Soc.*, 1959, **81**, 4088.

[183] R. B. Turner, *J. Amer. Chem. Soc.*, 1950, **72**, 879.

[184] M. F. Hawthorne, W. D. Emmons, and K. S. McCallum, *J. Amer. Chem. Soc.*, 1958, **80**, 6393; R. R. Sauers and R. W. Ubersax, *J. Org. Chem.*, 1965, **30**, 3939; J. R. Owen and W. H. Saunders, *J. Amer. Chem. Soc.*, 1966, **88**, 5809, 5816.

[185] Y. Yukawa and T. Yokoyama, *Mem. Inst. Sci. Ind. Res., Osaka Univ.*, 1956, **13**, 171; (*Chem. Abs.*, 1957, **51**, 2633); S. L. Friess and R. Pinson, *J. Amer. Chem. Soc.*, 1952, **74**, 1302.

[186] (*a*) W. H. Saunders, *J. Amer. Chem. Soc.*, 1955, **77**, 4679; (*b*) W. E. Doering and L. Speers, *ibid.*, 1950, **72**, 5515.

[187] R. R. Sauers, *J. Amer. Chem. Soc.*, 1959, **81**, 925.

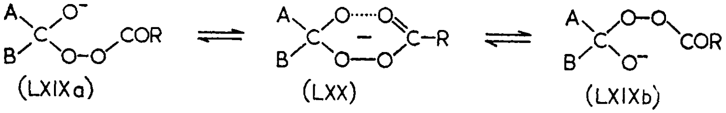
[188] J. D. Connolly and K. H. Overton, *Proc. Chem. Soc.*, 1959, 188.

[189] J. Meinwald and E. Frauenglass, *J. Amer. Chem. Soc.*, 1960, **82**, 5235.

[190] R. R. Sauers and G. P. Ahearn, *J. Amer. Chem. Soc.*, 1961, **83**, 2759; cf. J. T. Edward and P. F. Morand, *Canad. J. Chem.*, 1960, **38**, 1325.

A steric effect of addition to the carbonyl, was suggested,[191] but since the relative migration tendency for the methylene and bridgehead carbons in these cases is somewhat dependent upon the reagent used, we suggest that an additional factor may be the nature of the leaving group. Thus, in the case of camphor two alternatives are *either* (i) that the addition reaction is rate-limiting with one reagent (Caro's acid) but rearrangement is rate-limiting with another, *or* (ii) that the relative energies in the transition states in the rearrangement are greatly different. The sulphate ion is a better leaving group than acetate, which should accelerate the rearrangement step and give less selectivity;[187–190] similar differences have been reported with other peracids.[192] Likewise the change in size of the acid group should alter the relative stabilities of the various transition states leading directly to altered product ratios.

A complicating factor may be the rapid interconversion[193] of epimeric adducts (LXIX) *via* a cyclic intermediate (LXX) although this seems at variance with the results of the isotopic labelling experiments.



Some workers[194] suggest that a further factor is relief of Pitzer strain, since where electronic factors are approximately equal (*e.g.*, fenchone) oxidation proceeds mainly as forecast for maximum strain release.

While saturated groups migrate without rearrangement,[182] isomerisation may occur with unsaturated compounds.[189,195]

Kinetic studies have been made.[196–199] In certain cases reaction is of the second order overall;[196] first order in ketone, first order in oxidant: the addition to the carbonyl group is slow and rate-determining. Steric hindrance to addition is shown in alicyclic ketones. 4-Substituted cyclohexanones show acceleration in the order H $<$ Me $<$ t-butyl, the authors suggesting a non-classical carbonium ion giving 1,4-stabilisation[196] (LXXI) since analogous 1,4-effects are known.[197] However, all the latter examples involve 4-halogeno- or 4-oxy-containing groups. α-Halogeno-ketones also show reduced reaction rates.[196]

[191] M. F. Murray, B. A. Johnson, R. L. Pederson, and A. C. Off, *J. Amer. Chem. Soc.*, 1956, **78,** 981; cf. D. Y. Curtin, *Rec. Chem. Progr.*, 1954, **15,** 111 and also ref. 189.

[192] R. W. White and W. D. Emmons, *Tetrahedron*, 1962, **17,** 31.

[193] A. Rassat and G. Ourisson, *Bull. Soc. chim. France*, 1959, 1133.

[194] R. R. Sauers and J. A. Beisler, *J. Org. Chem.*, 1964, **29,** 210.

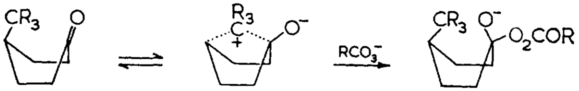
[195] J. Meinwald, M. C. Seidel, and B. C. Cadoff, *J. Amer. Chem. Soc.*, 1958, **80,** 6303; G. Buchi and I. M. Goldman, *ibid.*, 1957, **79,** 4741.

[196] J. L. Mateos and H. Mechaca, *J. Org. Chem.*, 1964, **29,** 2026.

[197] *E.g.*, L. Owen, *J. Chem. Soc.*, 1949, 320; E. L. Bennett, *J. Amer. Chem. Soc.*, 1952, **74,** 5076; H. L. Goering, *ibid.*, 1957, **79,** 6270; D. S. Noyce, *ibid.*, 1957, **79,** 755; 1960, **82,** 885, 1246.

[198] S. L. Friess and P. E. Frankenburg, *J. Amer. Chem. Soc.*, 1952, **74,** 2679; S. L. Friess and R. Pinson, *ibid.*, 1952, **74,** 1302; S. L. Friess and A. H. Soloway, *ibid.*, 1951, **73,** 3968; 1949, **71,** 2571; 1950, **72,** 5518.

[199] M. F. Hawthorne and W. D. Emmons, *J. Amer. Chem. Soc.*, 1958, **80,** 6398.



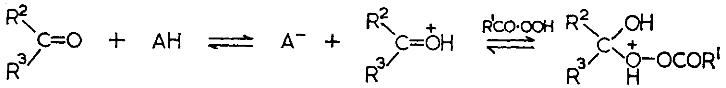
(LXXI)

Rates for different ring sizes in alicyclic and cycloalkyl methyl ketones were compared.[198] A rough correlation with Hammett's equation obtains for substituted acetophenones. Since the rates[198] were of the first order with electron-attracting substituents, and intermediate for acetophenone, a change in rate-controlling step is obviously occurring.

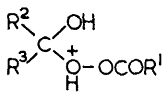
In contrast, other workers[199] conclude that the acid-catalysed decomposition of the peracid–ketone complex is rate-controlling.

Distinct acid catalysis, suggestive of general acid catalysis, is observed even with weak peracids, and catalysis by strong acids is marked.[186b] Increased solvent polarity accelerates the reaction.

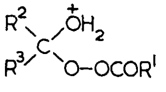
It seems that the most reproducible reagent is trifluoroperoxyacetic acid[199–201] and with this third-order (sometimes pseudo-first or -second order) kinetics are observed. This implies that the intermediate species is derived from all three reagents (that is, ketone, peracid, and acid).



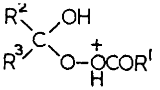
(LXXII)



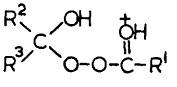
(LXXII)



(LXXIII)

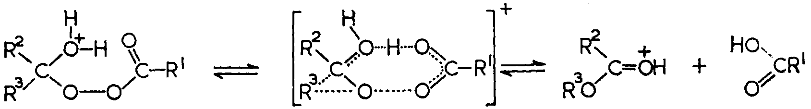


(LXXIV)



(LXXV)

Hawthorne and Emmons[199] confirm this adduct formation. The protonated intermediate (LXXII) will be in rapid equilibrium with three further forms (LXXIII, LXXIV, LXXV) and of these two (LXXIV, LXXV) appear most favourable to rearrangement since both would give rise directly to neutral acid and protonated ester.[199] However, in view of the strength of trifluoroacetic acid,[202] protonation to give (LXXIV) or (LXXV) seem rather unfavourable, and a cyclic intermediate would seem to us more likely, namely (LXXVI).



(LXXVI)

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[200] W. D. Emmons and G. B. Lucas, *J. Amer. Chem., Soc.*, 1955, **77**, 2287.

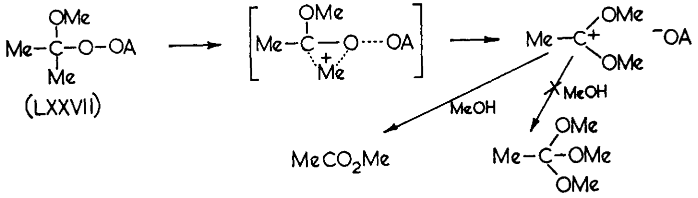
[201] W. F. Sagar and A. Duckworth, *J. Amer. Chem. Soc.*, 1955, **77**, 188.

[202] Cf. M. Ussanovitch and V. Tartakovskaya, *Zhur. obshchei Khim.*, 1946, **16**, 1987; T. Sumarokova and Z. Grishken, *ibid.*, p. 1991; L. P. Hammett and A. J. Deyrup, *J. Amer. Chem. Soc.*, 1933, **55**, 1900.

Although the measured Hammett reaction constants gave negative values, these are the result of composite effects, and cannot be held to confirm conclusively a concerted process.[203]

Catalysis by trifluoroacetic acid of the cyclohexanone reaction with peracetic and trifluoroperacetic acids respectively, proceeded much less rapidly in the former case, in keeping with a rate-determining rearrangement.

In a slightly different context, Winstein[204] examined analogues of the postulated Baeyer–Villiger intermediate (LXXII), namely (LXXVII).



Alcoholysis of (LXXVII) unexpectedly gave acetate esters.[204]

While the Baeyer–Villiger reaction is essentially acid-catalysed, some study has been made[205] of the use of alkaline hydrogen peroxide.

Enolisable *β*-diketones do not undergo a normal Baeyer–Villiger oxidation,[206] and the peroxide attack on benzils proceeds also by a different route.[207]

D. The Elbs Persulphate Oxidation.[208]—Treatment of a phenol in alkaline solution, with persulphate, followed by acidification, gives mainly *para* hydroxylation, although *ortho* products (catechols) are formed as secondary products. The reaction has been used fairly extensively by several groups of workers.[208–213]

Application to anilines gives predominantly *ortho* substitution,[214] although 2-aminobenzaldehyde gives the Dakin reaction product, *viz.*, 2-aminophenol.[215] It may be noted that benzoyl peroxide converts *N*-alkylanilines into 2-benzamido-phenols.[216] Baker and his co-workers[210] suggest a radical mechanism,

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[203] R. Stuart and K. Yates, *J. Amer. Chem. Soc.*, 1958, **80**, 6355.

[204] S. Winstein, *Tetrahedron Letters*, 1962, No. 13, 567.

[205] H. O. House and R. L. Wasson, *J. Org. Chem.*, 1957, **22**, 1157.

[206] H. O. House and W. F. Gannon, *J. Org. Chem.*, 1958, **23**, 879.

[207] H. Kwart and N. J. Wegemer, *J. Amer. Chem. Soc.*, 1961, **83**, 2746.

[208] K. Elbs, *J. prakt. Chem.*, 1893, **48**, 179.

[209] T. R. Seshadri, *Experientia*, Suppl. 2, 14th International Congress of Chemistry, Zürich 1955, p. 258; T. R. Seshadri and P. S. Rao, *Proc. Indian Acad. Sci.*, 1943, *A*, **18**, 222.

[210] W. Baker and N. C. Brown, *J. Chem. Soc.*, 1948, 2303; W. Baker and R. I. Savage, *ibid.*, 1938, 1602; 1941, 662.

[211] J. Forrest and V. Petrow, *J. Chem. Soc.*, 1950, 2340.

[212] F. E. King, T. J. King, and L. C. Manning, *J. Chem. Soc.*, 1957, 563; E. J. Behrman and B. M. Pitt, *J. Amer. Chem. Soc.*, 1958, **80**, 3717.

[213] K. C. Roberts, *J. Chem. Soc.*, 1960, 785.

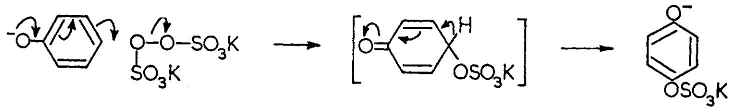
[214] E. Boyland, D. Manson, and P. Sims, *J. Chem. Soc.*, 1953, 3613; E. Boyland and P. Sims, *ibid.*, 1954, 980.

[215] E. Bamberger, *Ber.*, 1903, **36**, 2042.

[216] J. T. Edward, *J. Chem. Soc.*, 1954, 1464.

largely on the basis of free-radical formation in persulphate decomposition.[217] Support for this is the finding of some coupling products.[218]

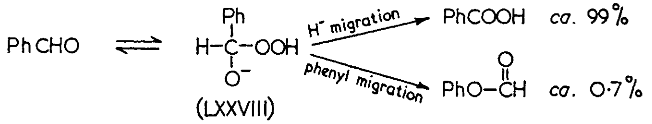
Behrman and Walker[219] investigated the reaction kinetically. They confirmed that phenoxide ion is involved, which is further supported by the variation of this effect with phenol structure.[219,220] Addition of cupric or ferrous ions equally has no effect: since electron-releasing substituents in the phenol accelerate the reaction,[219] a nucleophilic attack on persulphate seems likely as first step.

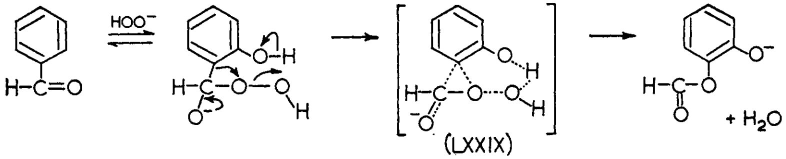


E. The Dakin Reaction.—Alkaline hydrogen peroxide oxidises *o*- and *p*-hydroxybenzaldehydes[221] and -acetophenones[222] to catechols and quinols.

In mechanism it is closely parallel to the Baeyer-Villiger reaction. It is not surprising therefore to find that electron-releasing groups facilitate reaction.[223] For benzaldehyde itself hydride migration is the main reaction, only traces of phenol being formed.[223,224]

Salicylaldehyde gives catechol almost quantitatively,[225] presumably *via* a cyclic intermediate (LXXIX).





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[217] For a review see S. M. Sethna, *Chem. Rev.*, 1951, **49**, 91; see also K. B. Wiberg, *J. Amer. Chem. Soc.*, 1959, **81**, 252; 1953, **75**, 1439; E. Ben Zvai and T. L. Allen, *ibid.*, 1961, **83**, 4352; D. L. Ball, M. M. Crutchfield, and J. O. Edwards, *J. Org. Chem.*, 1960, **25**, 1599.

[218] I. M. Kolthoff and I. K. Miller, *J. Amer. Chem. Soc.*, 1951, **73**, 3055; R. G. R. Bacon, R. Grime, and D. J. Munro, *J. Chem. Soc.*, 1954, 2275.

[219] E. J. Behrman and P. R. Walker, *J. Amer. Chem. Soc.*, 1962, **84**, 3454. cf. also S. M. Sethna, ref. 217.

[220] I. M. Kolthoff, *Rec. Trav. chim.*, 1923, **42**, 969.

[221] H. D. Dakin, *Amer. Chem. J.*, 1909, **42**, 477.

[222] W. Baker, E. H. T. Jukes, and C. A. Subrahmanyam, *J. Chem. Soc.*, 1934, 1681; W. Brown, H. F. Brady, J. Gumb, and D. Miles, *ibid.*, 1953, 1615.

[223] E. Spath, M. Pailer, and G. Gergeley, *Ber.*, 1940, **73**, 935.

[224] J. D'Ans and A. Kneip, *Ber.*, 1915, **48**, 1143; J. Hawkins, *J. Chem. Soc.*, 1950, 2169.

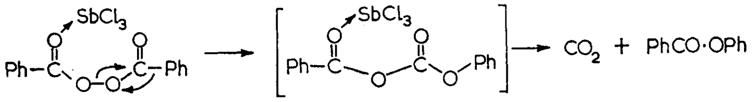
[225] A. Wacek and H. O. Eppinger, *Ber.*, 1940, **73**, 644; A. Wacek and A. V. Bezard, *ibid.*, 1941, **74**, 845.

Labelling of the carbonyl group in *p*-methoxyacetophenone followed by oxidation led to products in which all label was retained in the acetate carbonyl.[178]

4 Other Reactions in which Oxygen behaves Electrophilically

A. Ozonolysis.—This is a topic large enough to warrant separate review. There is a considerable volume of literature available[226] including some reviews[227] and it is not proposed to discuss this further.

B. Peracid Rearrangements under the Influence of Lewis Acids.—The rearrangement of peracids under the influence of Lewis acids has been discussed and probably involves[228] a concerted carbon-to-oxygen migration with simultaneous attack on carbonyl carbon by the second peroxy-oxygen (LXXX).



(LXXX)

Using labelled oxygen compounds, Denney *et al.*[229] showed direct attack by carbanion on peroxides in their reactions, and reviewed work already done on Grignard reagents and a number of active-methylene compounds.

The Friedel–Crafts hydroxylation of aromatic compounds by peracids was examined *inter alia* by Waring and Hart,[230] who originally postulated attack by HO^+, but an alternative of nucleophilic attack by the aromatic compound upon a peracid–Lewis acid complex is also possible (LXXXI).

(LXXXI)

In agreement, electron-releasing substituents facilitate reaction.[230] Aromatic oxygenation can be achieved with aryl peroxides and with peroxydicarbonates

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[226] *E.g.*, D. G. M. Diaper and D. L. Mitchell, *Canad. J. Chem.*, 1965, **43**, 319; P. S. Bailey, *J. Amer. Chem. Soc.*, 1956, **78**, 3811; *J. Org. Chem.*, 1958, **23**, 1089; 1962, **27**, 1192, 1198; R. H. Callaghan *et al.*, *ibid.*, 1961, **26**, 1379; J. Pasero *et al.*, *Bull. Soc. chim. France*, 1960, 1717; D. G. M. Diaper and D. L. Mitchell, *Canad. J. Chem.*, 1962, **40**, 1189; K. A. Pollart and R. E. Miller, *J. Org. Chem.*, 1962, **27**, 2392; D. G. M. Diaper and D. L. Mitchell, *Canad. J. Chem.*, 1960, **38**, 1976; P. S. Bailey and S. S. Bath, *J. Amer. Chem. Soc.*, 1951, **73**, 3120; 1960, **83**, 6136; G. Riezebos, J. G. Grimelikhysen, and D. A. van Dorp, *Rec. Trav. chim.*, 1963, **82**, 1234; P. R. Story, R. W. Murray, and R. D. Youssefyeh, *J. Amer. Chem. Soc.*, 1966, **88**, 3143, 3144; F. L. Greenwood, *ibid.*, 1966, **88**, 3146.

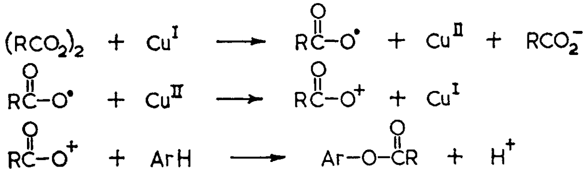
[227] R. Criegee, *Rec. Chem. Progr.*, *Kresger-Hooker Sci. Lib.*, 1957, **18**, 111; *Annalen*, 1948, **560**, 127; P. S. Bailey, *Chem. Rev.*, 1958, **58**, 925.

[228] D. Z. Denney, T. M. Valega, and D. B. Denney, *J. Amer. Chem. Soc.*, 1964, **86**, 46.

[229] D. Z. Denney, S. O. Lawesson, C. Frisell, and D. B. Denney, *Tetrahedron*, 1963, **19**, 1299.

[230] (*a*) A. J. Waring and H. Hart, *J. Amer. Chem. Soc.*, 1963, **85**, 2177; 1964, **86**, 1454. (*b*) P. Kovacic, *ibid.*, 1965, **87**, 1566, 4811. *J. Org. Chem.*, 1966, **31**, 2011. (*c*) P. Kovacic and M. E. Kurz, *J. Amer. Chem. Soc.*, 1966, **88**, 2068; *Chem. Comm.*, 1966, 321; *Tetrahedron Letters*, 1966, 2689.

using cupric or ferric chloride catalysts. Although a purely radical mechanism can be invoked, Kovacic and Kurz[230c] have pointed out that some evidence, notably isomer distribution, supports possible involvement of an oxonium ion resulting from oxidation of an oxyradical, as shown.



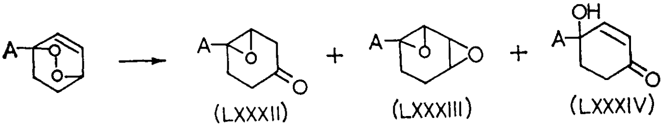
$$(RCO_2)_2 + Cu^{I} \longrightarrow R\overset{O}{\overset{\|}{C}}{-}O^{\bullet} + Cu^{II} + RCO_2^-$$
$$R\overset{O}{\overset{\|}{C}}{-}O^{\bullet} + Cu^{II} \longrightarrow R\overset{O}{\overset{\|}{C}}{-}O^{+} + Cu^{I}$$
$$R\overset{O}{\overset{\|}{C}}{-}O^{+} + ArH \longrightarrow Ar{-}O{-}\overset{O}{\overset{\|}{C}}R + H^{+}$$

R = aryl or O-alkyl

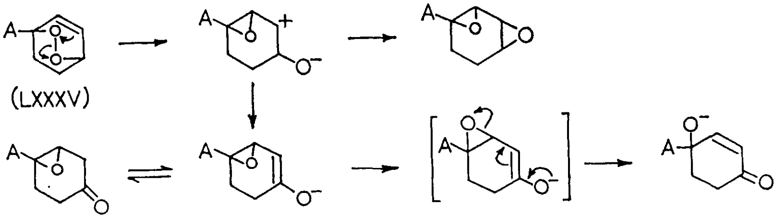
C. Electrophilic Behaviour involving Hypohalites.—Formation of acetyl hypoiodite from iodine and peracid is postulated[231] in the iodination of aryl compounds with these reagents but the mechanism is not clear.

In an anomalous Hunsdieker reaction observed by Pandit and Dirk[232] a possible mechanism involves also nucleophilic attack by aromatic electrons upon oxygen (in this case an acyl hypobromite).

D. Rearrangement of Diepoxides.—Rearrangement of 1,4-diepoxide rings to epoxy-ketones or diepoxide occurs, together with formation of allylic ketol, (LXXXII) → (LXXXIV), in many steroidal,[233] and some other[234] systems. Although usually stated to be base-catalysed[235] rearrangements, these could possibly involve electrophilic behaviour of oxygen (LXXXV).



(LXXXII) (LXXXIII) (LXXXIV)



(LXXXV)

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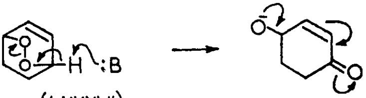
[231] Y. Ogata and K. Nakajima, *Tetrahedron*, 1964, **20**, 43, 2751; Y. Ogata and K. Aoki, *J. Org. Chem.*, 1966, **31**, 1625.

[232] U. K. Pandit and I. P. Dirk, *Tetrahedron Letters*, 1963, 891; cf. J. W. Wilt and D. D. Oathaudt, *J. Org. Chem.*, 1958, **23**, 218; J. W. Wilt and J. L. Finnerty, *ibid.*, 1961, **26**, 2173.

[233] R. J. Conca and W. Bergman, *J. Org. Chem.*, 1953, **18**, 1104; E. L. Skau and W. Bergman, *ibid.*, 1939, **3**, 166; W. Bergman, F. Hirschman, and E. L. Skau, *ibid.*, 1940, **4**, 29; M. Matic and D. A. Sutton, *J. Chem. Soc.*, 1953, 349; R. B. Woodward and R. H. Eastman, *J. Amer. Chem. Soc.*, 1950, **72**, 399; T. G. Halsall, W. J. Rodewald, and D. Willis, *Proc. Chem. Soc.*, 1958, 231; A. Windaus and G. Brunkin, *Annalen*, 1928, **460**, 225.

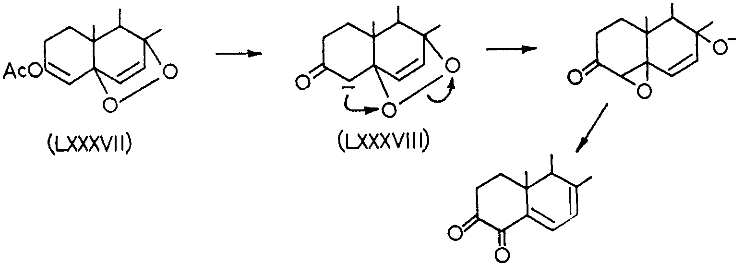
[234] *E.g.*, D. C. De Luca, *Diss. Abs.*, 1965, **25**, 2225.

[235] E. J. Agnello, R. Pinson, and G. D. Laubach, *J. Amer. Chem. Soc.*, 1956, **78**, 4756.



(LXXXVI)

The alternative mechanism, which postulates initial proton removal (LXXXVI) is definitely not possible in certain cases (*e.g.*, ergosteryl diepoxides)[236] where the oxygen atoms are attached to tertiary carbons, and it is difficult to explain diepoxide formation by this mechanism.[237] Bladon[238] reports a similar rearrangement of a diepoxide (LXXXVII) which almost certainly involves electrophilic oxygen (LXXXVIII).



(LXXXVII) (LXXXVIII)

The rearrangement of steroid hydroperoxides may go by a similar pathway.[239]

We are grateful to Professor Wesley Cocker of Dublin for his assistance.

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[236] *E.g.*, A. Windaus and J. Brunkin, *Annalen*, 1928, **460**, 225.

[237] Cf. also W. Bergman and M. B. Myers, *Annalen*, 1959, **620**, 46; *J. Org. Chem.*, 1960, **25**, 1451; D. J. Giancola, Dissertation, Yale Univ., 1956.

[238] P. Bladon and T. Sleigh, *Proc. Chem. Soc.*, 1962, 183.

[239] G. O. Schenk, O. A. Neumuller, and W. Eisfeld, *Angew. Chem.*, 1960, **70**, 595.