PROGRESS IN ORGANIC CHEMISTRY

5

Joint Editors

J. W. COOK, D.Sc., F.R.S.
Vice-Chancellor
University of Exeter
Fellow of University College
London

and

W. CARRUTHERS, Ph.D.
M.R.C. Carcinogenic Substances Research Unit
Washington Singer Laboratories
Exeter

LONDON
BUTTERWORTHS
1961

FOREWORD

THE growing volume of original research publications makes it increasingly difficult for the student of organic chemistry to keep himself informed about the important developments which are taking place in his subject. In many fields of research it is not easy for those who are actively contributing to be sure that they are fully acquainted with recent progress even in their own fields. It has become almost impossible for them to keep abreast, from the original literature, with developments in other fields as well. Hence short surveys of selected topics such as are given in the chapters of the volumes of this series are providing an increasingly important service for all who are interested in organic chemistry. Advanced university students, research workers and those whose interests are more general, are all indebted to the authors of these surveys, whose labours do much to facilitate the assimilation of knowledge of recent progress.

The chapters by Dr. Waters and Dr. Loudon are complementary. Dr. Waters gives an up-to-date account of oxidation reactions involving free radicals as intermediaries. His orderly and systematic treatment of the subject serves to emphasize the extent to which it is now possible to provide rational interpretations of a large variety of miscellaneous oxidation processes. Dr. Loudon's chapter deals more exhaustively with a limited aspect of the subject, and he gives a succinct and fascinating account of methods by which additional hydroxyl groups can be introduced into the aromatic nucleus of phenols.

Carbohydrate chemistry continues to attract the attention of many organic chemists, both for its intrinsic interest and also because of the important part which substances of this group play in Nature and in natural processes. Dr. Ricketts has given a valuable review of recent work on the chemistry and biochemistry, including the biosynthesis, of dextran, a medicinally important carbohydrate produced by some of the lower organisms.

To the natural products chemist the chapter on the higher terpenoids will have outstanding appeal. From the earliest days of structural organic chemistry the terpenes and their derivatives have had a fascination of their own which has progressively increased as their ramifications and their inter-relationships have been steadily unfolded. Dr. Barltrop and Dr. Rogers have confined their treatment of recent chemical progress very largely to the diterpenoids, the knowledge of which has been impressively advanced in recent years. Not the least important achievement has been the elucidation of the stereochemical configuration of many members of this group, revealing a beautiful simplicity of pattern; but the most exciting part of this chapter is the final section dealing with terpene biogenesis. The problem of how the complex polycyclic structures present in the higher terpenoids and in the steroids have been elaborated from simple units seems to have been largely solved, thanks mainly to the use of isotopic tracers. The relationship between the higher terpenoids and the steroids, long suspected but difficult to reconcile wholly with their structural differences, has been placed on a firm experimental basis.

Among the quasi-aromatic compounds having non-benzenoid structures those related to cycloheptatrienone are the most extensively investigated and probably the most important. Fifteen years ago they represented an unknown field of organic chemistry, now they have found a permanent place in the classification of organic compounds, and some forty of them have been found in Nature. Professor Nozoe, himself a prolific worker in this field, gives in the last chapter of this book a lucid and systematic survey of the properties, structural relationships and methods of synthesis of tropylium salts, tropolones and related compounds.

I am greatly indebted to the authors for their co-operation in the preparation of these authoritative essays of topical chemical interest, and I wish also to express my appreciation of the collaboration of Dr. W. Carruthers who has rendered invaluable assistance as Joint Editor of this volume.

J. W. COOK

CONTENTS

PAGE

FOREWORD *vii*

1 HOMOLYTIC OXIDATION PROCESSES 1
W. A. WATERS, M.A., Ph.D., Sc.D., F.R.I.C., F.R.S., Reader in Physical-Organic Chemistry, University of Oxford

2 DEVELOPMENTS IN HYDROXYLATION OF PHENOLS 46
J. D. LOUDON, Ph.D., D.Sc., Lecturer in Chemistry, University of Glasgow

3 THE CHEMISTRY OF DEXTRAN 73
C. R. RICKETTS, D.Sc., Scientific Staff, Medical Research Council

4 THE CHEMISTRY OF THE HIGHER TERPONOIDS 96
J. A. BARLTROP, M.A., Ph.D. (Oxon.), University Demonstrator and Fellow of Brasenose College, Oxford
N. A. J. ROGERS, M.A., Ph.D. (Oxon.), Lecturer in Chemistry, University of Birmingham

5 TROPYLIUM AND RELATED COMPOUNDS 132
T. NOZOE, D.Sc., Professor of Organic Chemistry, Tohku University, Sendai, Japan

SUBJECT INDEX 166

1

HOMOLYTIC OXIDATION PROCESSES

W. A. Waters

THE ELECTRONIC THEORY OF OXIDATION 1

HOMOLYTIC OXIDATIONS INVOLVING HYDROGEN ABSTRACTION 3
- Homolytic halogenation 3
- Oxidation by oxy-radicals, R—O· 7
  - (*a*) Hydroxyl radicals 7
  - (*b*) Alkyloxy radicals 9
  - (*c*) Acyloxy radicals 13
  - (*d*) Alkylperoxy radicals 15

AUTOXIDATION 17
- Kinetic features 19
- The chemical reactions of inhibitors 20
- The catalysis of *autoxidation* 23

ONE-ELECTRON OXIDATIONS BY IONS CONTAINING TRANSITION METALS 26
- General features 26
- Oxidation of aldehydes and ketones 29
- Oxidation of alcohols and glycols 32
- Oxidation of phenols 35

THE ELECTRONIC THEORY OF OXIDATION

INORGANIC chemists are accustomed to use the terms *oxidation* and *reduction* for reactions whereby electrons are removed from, or added to, molecules or ions; *e.g.*

$$Fe^{2+} \underset{Reduction}{\overset{Oxidation}{\rightleftarrows}} Fe^{3+} + e$$

and, since they frequently deal with rapid reversible reactions, they often compare oxidizing agents in terms of their redox potentials, E_0, measured with reference to the normal hydrogen electrode. Biochemical oxidations involving enzyme catalysts, again being thermodynamically reversible, are often treated in a similar way though the appropriate potential (E_0'), for obvious convenience, refers to reactions in neutral solution.

To organic chemists, however, this potentiometric classification of oxidizing agents is seldom of obvious value, since few oxidations of organic compounds are reversible reactions.

In general, organic molecules have a carbon skeleton surrounded by a hydrogen skin attached by very strong covalences (the C—H bond strength is about 95 kcal) and have more weakly bound electrons available for removal only at the π-electron sites of olefins, or at atoms, such as oxygen, nitrogen or sulphur near which unshared pairs may be localized. It is at, or near, these groups which have accessible electrons that oxidations of organic molecules most easily occur. Wieland's generalization[1] of over 40 years ago to the effect that in organic chemistry ' oxidation ' and ' reduction ' were equivalent to *hydrogen removal* and *hydrogen addition*, respectively, is a tacit recognition of this difficulty of abstraction of electrons from organic molecules and is still a valuable dictum, provided that it is recognized that the oxidative removal of hydrogen from an organic molecule requires the abstraction of both a hydrogen nucleus and an electron, e.g.

$$CH_3\text{—}CH_2\text{—}OH \longrightarrow CH_3\text{—}CH\text{=}O + 2H^+ + 2e$$

and not that of the hydrogen nucleus alone, as in an ionization:

$$CH_3\text{—}CH_2\text{—}O\text{—}H \longrightarrow (CH_3\text{—}CH_2\text{—}O\!:)^- + H^+$$

Oxidations of organic molecules, like all other reactions of covalent molecules, involve electron-pair-bond rupture, and this may be effected either by heterolyses in which two electrons are removed in a single process, or by homolyses in which single electrons are removed in each of two consecutive reactions.

Nearly all heterolytic oxidation processes are recognizable additions or eliminations involving polar electrophilic reagents, while homolytic oxidations, since they sever electron pairs, necessarily involve the transient production of free radicals which can often be detected.

Homolytic oxidation can be effected either by hydrogen atom removal, e.g.

$$CH_3\text{—}CH_2\text{—}OH + \cdot OH \longrightarrow CH_3\cdot\dot{C}H\text{—}OH + H\text{—}OH$$

or merely by electron removal, e.g.

$$(Me\text{—}C_6H_4\text{—}O\!:)^- + \{Fe(CN)_6\}^{3-} \longrightarrow Me\text{—}C_6H_4\text{—}O\cdot + \{Fe(CN)_6\}^{4-}$$

and can be divided into two groups, according to whether the oxidant is a hydrogen-atom-abstracting agent or merely an electron abstractor. Active free atoms, such as chlorine, and active free radicals, such as $\cdot OH$, $\cdot C_6H_5$ or $\cdot CH_3$, together with the molecules from which they may be generated (e.g. benzoyl peroxide), fall into the first group, while ions of the higher valence states of many transition elements, e.g. Co^{3+}, Mn^{3+}, Fe^{3+}, Ce^{4+}, are oxidants of the second group. However, many oxidations of organic compounds now appear to be concerted electron removal processes in which it may be difficult to decide whether the bond fissions are of heterolytic or homolytic type. Some reagents, such as the halogens and the organic peroxides, can act both in heterolytic and in homolytic fashion according to the chemical nature of the solvents involved, and again there are complex inorganic oxidants, such as chromic acid and potassium permanganate, which may act consecutively in both heterolytic and homolytic manner. So, in the following pages, all that can be done is to illustrate the more typical features of homolytic electron removal.

HOMOLYTIC OXIDATIONS INVOLVING HYDROGEN ABSTRACTION

Homolytic Halogenation

The atomic chlorination of an organic compound

(1) $$R{-}CH_3 + \cdot Cl \longrightarrow R{-}CH_2\cdot + H{-}Cl$$

(2) $$R{-}CH_2\cdot + Cl_2 \longrightarrow R{-}CH_2{-}Cl + \cdot Cl$$

may be regarded as an oxidation since it leads, by subsequent hydrolysis,

(3) $$R{-}CH_2{-}Cl + NaOH \longrightarrow R{-}CH_2{-}OH + NaCl$$

to the formation of an oxidized derivative of the original compound. This is of technical importance for the side-chain oxidation of toluene but is of little general applicability, for the following reason. Reaction (1) is exothermic even for methane, and consequently reagents that can supply chlorine atoms, as for example chlorine gas activated by light, or sulphuryl chloride activated by free radicals produced thermally from benzoyl peroxide or, better, $\alpha\alpha'$-azobis-isobutyronitrile[2], effect chlorination of all positions in the higher paraffins, giving mixtures which have been regarded as intractable prior to the elaboration of methods of vapour-phase chromatography.

Now, however, it is clear that atomic chlorination does show some degree of *relative* selectivity[3]. Thus for attack on C—H groups of paraffins the relative orders of reactivity, at room temperature, are approximately *tertiary: secondary: primary* = 5:4:1 but they become more alike as the temperature of reaction increases[3,4]. For dichlorination there is a marked tendency for the second chlorine atom to attack either another hydrogen atom on the carbon which already has been halogenated or a C—H bond remote from the chlorine atom previously introduced. Again, in the chlorination of butyric acid the relative percentages of attack are

$$\begin{array}{cccc} CH_3— & CH_2— & CH_2— & CO_2H \\ 45 & 45 & 10 & \end{array}$$ with sulphuryl chloride[5]

$$\begin{array}{cccc} CH_3— & CH_2— & CH_2— & CO_2H \\ 31 & 64 & 5 & \end{array}$$ with irradiated chlorine[6].

Reaction (1) above involves the formation of a strongly dipolar molecule, H—Cl, and in the course of the C—H bond fission there is, consequently, an electron displacement away from the carbon centre. Hence groups, R, which are electrophilic should tend to decrease the ease of homolytic chlorination, and vice versa. Brown[7] has arranged substituents R, in $R—CH_2—$, in the following order in respect to their influence on the relative rates of atomic chlorination of the $—CH_2—$ group

$$CH_3 > H > ClCH_2 > Cl_2CH > HO{\cdot}CO > Cl_3C > F_3C$$

and comments that the order indicates a control of the reactivity by an inductive effect.

Recently, it has been shown by Russell that homolytic chlorination becomes a more selective reaction if it is carried out in an aromatic solvent such as benzene[8], and still more selective if carbon disulphide is used.

Table I indicates the magnitude of this solvent effect.
He suggests that the aromatic solvent forms a π-complex with the atomic chlorine, with the consequence that the thermochemistry of a liquid phase reaction (1) is no longer the same as that for the gas phase reaction, but involves a chlorine atom with lower intrinsic energy and leads to the production of a solvated organic radical[9].

Table I. Relative Reactivities of C—H *bonds towards Chlorine Atoms at* 40°C
(By courtesy of the American Chemical Society[8])

Hydrocarbon	*Hydrogen in*	'*Free* Cl·'	Cl· *in benzene*	Cl· *in* CS_2
2:3-*Dimethylpentane*	CH_3	1*	1*	1*
	CH	3·9	16	200
Cyclopentane	CH_2	2·8	5·2	23
Cyclohexane	CH_2	2·7	5·2	20
Chloroform	CH	0·005	—	0·033
Toluene	CH_3	1·1	2·1	11

* Assumed as the standard

In contrast to chlorination, photochemical bromination is highly selective[3] and is an excellent method for the preparation of tertiary bromides from appropriate paraffins. RUSSELL and BROWN[10] have found that, at 80°C, toluene is 60 times as reactive as cyclohexane towards bromine atoms, whereas towards chlorine atoms cyclohexane is 11 times as reactive as toluene. They ascribe this marked change to the difference in degree of bond breaking which is needed in reaching the transition states (*a*) and (*b*) in which the colliding particles have gained enough activation energy for hydrogen transfer to occur.

$$(a)\quad R''CH \cdots\cdots H \cdots\cdots Cl \qquad (b)\quad R''CH \cdots\cdots H \cdots\cdots Br$$

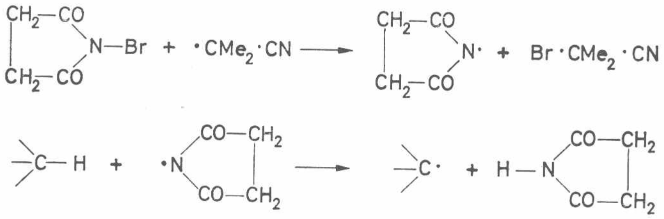
Homolytic chlorination (equation 1) is so exothermic that the degree of bond extension in reaching the energy peak (*a*) from the original molecule, R″CH—H, need not be large before the progressive energy gain in forming the final molecule, H—Cl·, helps the reaction forward. Consequently the chemical structure of molecule R″CH—H is not very important in controlling the energy level of transition state (*a*). The bond strength of H—Br, however, is so much less than that of H—Cl that, in arriving at transition state (*b*), a much greater degree of stretching of the C—H bond is needed than in case (*a*), and hence the energy level of (*b*) will depend to a considerable extent upon the energy difference between the structures of the molecule R″CH—H and of the eventual carbon radical R″CH·. Thus while, in the main, the course of homolytic chlorination of aliphatic molecules is controlled by inductive effects, for homolytic bromination the major controlling factor is the degree of resonance stabilization of the resulting organic free radical. In consequence, homolytic bromination shows sufficient selectivity to be applicable as a route for the specific oxidation of complex molecules at desired points.

With alkylbenzenes the attack is exclusively upon α—C—H groups since resonance-stabilized benzyl radicals then result. With allylic systems the reaction (4)

$$(4)\quad \mathrm{Br}\cdot + \mathrm{A{—}CH_2{—}CH{=}CH{—}B} \longrightarrow$$

$$\mathrm{HBr} + \mathrm{A{—}\dot{C}H{—}CH{=}CH{—}B} \longleftrightarrow \mathrm{A{—}CH{=}CH{—}\dot{C}H{—}B}$$

is exothermic and irreversible, while the thermochemistry of bromine atom addition to the C=C bond is so evenly balanced that the reaction is reversible, the ease of the addition or the dissociation of the bromine atom depending upon whether the *cis* or the *trans* isomer of the olefin is involved[11]. Molecular bromine, however, can easily effect heterolytic addition to olefins and consequently, to effect allylic bromination of a compound A—CH_2—CH=CH—B, bromine *atoms* should slowly be supplied at very low concentration so that reaction (4) can be the rate-controlling process. This can be done by adding bromine very slowly to a hot, irradiated solution of the olefin in a non-ionizing solvent[12] or by using a suspension of N-bromosuccinimide in a similar solvent together with a radical-producing catalyst, such as $\alpha\alpha'$-azobisisobutyronitrile, which has no undesired oxidizing action itself[13]. Under the latter conditions the real dehydrogenating agent is the succinimido radical (I).



I

To effect allylic bromination with N-bromo succinimide, care must be taken not to use an acidic solvent or catalyst, for the cation (II) reacts heterolytically, transferring a bromine cation to the double bond of an olefin or substituting bromine into an activated aromatic nucleus.

II

Oxidation by Oxy-radicals, R—O·

(*a*) *Free hydroxyl*—Since the energy needed to remove the first hydrogen atom from a molecule of water is about 140 kcal/mole, free hydroxyl radicals are the most powerful of known oxidizing agents. They can easily be produced in water by one-electron abstraction from hydrogen peroxide, e.g.

$$\mathrm{Fe^{2+} + HO{-}OH \longrightarrow (Fe{-}OH)^{2+} + {\cdot}OH} \tag{5}$$

by rupture of water molecules by ionizing radiations such as X-rays, γ-rays or neutrons

$$\mathrm{H_2O} \rightsquigarrow \mathrm{(H_2O)^+} + e \ : \ \mathrm{(H_2O)^+ \longrightarrow H^+ + {\cdot}OH} \tag{6}$$

or from ions of some transition metals by photochemical excitation, using radiation of wavelengths corresponding to charge-transfer absorption bands[14], e.g.

$$\mathrm{(Fe{-}OH)^{2+}} + h\nu \longrightarrow \mathrm{Fe^{2+} + {\cdot}OH} \tag{7}$$

However generated, free hydroxyl radicals are dehydrogenators with little selectivity towards C—H bonds, for they attack alcohols, ethers, esters and even saturated aliphatic acids, though the ensuing reactions of the resulting organic free radicals differ to a wide degree.

For example, hydroxyl radicals generated by Fenton's reagent (hydrogen peroxide together with a ferrous salt) as in equation (5) react with primary or secondary alcohols to produce organic radicals which are strong reducing agents, capable[15] of converting $\mathrm{Fe^{3+}}$ to $\mathrm{Fe^{2+}}$ or $\mathrm{Hg^{2+}}$ to $\mathrm{Hg^{+}}$. Consequently the sequence of reactions (5), (8) and (9) is a reaction chain whereby alcohol can be oxidized to aldehyde with little net consumption of $\mathrm{Fe^{2+}}$

$$\mathrm{HO{\cdot} + CH_3{-}CH_2{-}OH \longrightarrow HO{-}H + CH_3{-}\dot{C}H{-}OH} \tag{8}$$

$$\mathrm{CH_3{-}\dot{C}H{-}OH + Fe^{3+} \longrightarrow CH_3{-}CH{=}O + H^+ + Fe^{2+}} \tag{9}$$

though reaction (9) can be eliminated by adding a suitable complexing agent, such as fluoride, to remove the secondary oxidant, Fe^{3+}, from the solution[15,16]. Reactions such as (8) and (9) are used to advantage in many technical recipes for effecting the emulsion polymerization of olefins. In this type of polymerization, active radicals are generated from the olefins by the addition of hydroxyl radicals or of $\cdot SO_4H$ radicals generated similarly from sodium persulphate, and it is advisable to keep the concentration of Fe^{3+} to a low value, since one-electron oxidations, such as (11), are effective chain-terminating reactions[17].

$$(10)\quad HO\cdot + CH_2{=}CH{\cdot}R \longrightarrow HO{-}CH_2{-}\dot{C}H{-}R$$

$$(11)\quad HO{-}(CH_2{-}CHR)_n{-}CH_2{-}\dot{C}HR + Fe^{3+} \longrightarrow$$
$$HO{-}(CH_2{-}CHR)_n{-}CH{=}CHR + H^+ + Fe^{2+}$$

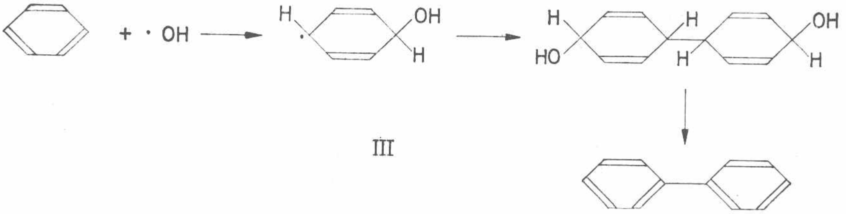
The induction of olefin polymerization (reaction 10) and the secondary reduction of a weak oxidizer during the progress of another oxidation reaction (reactions 9 or 12)

$$(12)\quad CH_3{-}\dot{C}H{-}OH + Hg^{2+} \longrightarrow CH_3{-}CH{=}O + Hg^+ + H^+$$

can both be used as diagnostic tests of homolytic oxidation.

There are, however, many organic free radicals which are too weak as reducing agents to react[16] with Fe^{3+} or Hg^{2+} and a very few free radicals, e.g. $\cdot CH(CO_2H)_2$, which even seem to be oxidizing agents[18].

For instance, the oxidations of aliphatic acids and esters are not chain reactions[15] and, under most conditions, neither is the reaction with benzene[19]. In this case it is probable that the primary reaction of free hydroxyl is an addition



III

to give a radical (III) which then dimerizes and loses water to form diphenyl, but if Fe^{3+} is present in very high concentration some phenol is formed

(13)


while with high concentrations of Fe^{2+} some benzene is regenerated[20].

(14) $$(\cdot C_6H_6\text{—}OH) + Fe^{2+} \longrightarrow C_6H_6 + (HO:)^- + Fe^{3+}$$

Complications due to the concurrent presence of different oxidizing and reducing agents also beset the oxidation of organic compounds that can be induced in water by ionizing radiations. While unstable $(H_2O)^+$ cations break to give hydroxyl radicals (equation 6), electrons can disrupt water molecules to yield hydrogen atoms

(15) $$e + H_2O \longrightarrow (H_2O)^- \longrightarrow H\cdot + (:OH)^-$$

and if the water contains dissolved air, this then reacts to give peroxy radicals.

(16) $$H\cdot + O{=}O \longrightarrow H\text{—}O\text{—}O\cdot$$

Since even hydrogen atoms can sometimes act as oxidizing agents[21]

(17) $$R\text{—}H + \cdot H \longrightarrow R\cdot + H_2$$

it is not surprising that radiochemical decompositions of aqueous solutions of organic compounds are, on the whole, oxidations of quite a complex character. The biochemical implications of such reactions are important, for electron transfer processes such as those of equations (6) and (15) can be effected within living cells.

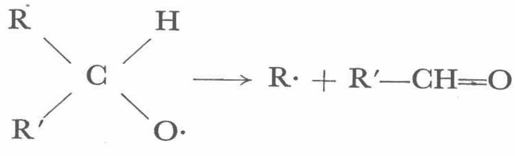
(*b*) *Alkyloxy radicals*—Reducing ions, such as Fe^{2+} and Co^{2+}, also split alkyl hydroperoxides, R—O—O—H, homolytically, but invariably give alkyloxy radicals, R—O·, and not hydroxyl, i.e.

(18) $$R\text{—}O\text{—}O\text{—}H + Fe^{2+} \longrightarrow R\text{—}O\cdot + (Fe\text{—}OH)^{2+}$$

Alkyloxy radicals, though they have a sufficiently long free life to be detected as end-groups of polymers formed by additions to olefins, tend to break down on heating to carbonyl derivatives and alkyl radicals:

(19) $$R\text{—}CH_2\text{—}O\cdot \longrightarrow R\cdot + CH_2{=}O$$

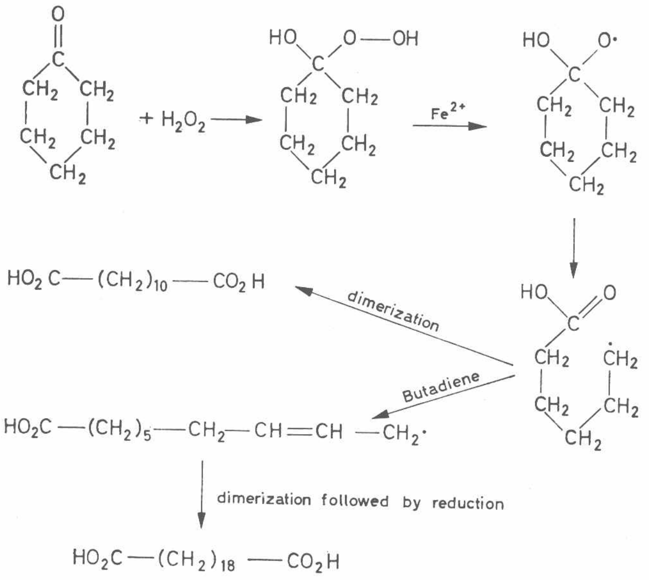
(20)



$$RR'C(H)\text{—}O\cdot \longrightarrow R\cdot + R'\text{—}CH{=}O$$

(21) $$R_3C\text{—}O\cdot \longrightarrow R\cdot + R_2C{=}O$$

This thermal degradation has a very important role in the gas phase oxidation of hydrocarbons[22,23]. The following reactions exemplify the synthetic potentialities of oxidations of this type[24].



Alkyloxy radicals are also generated by the thermal decomposition of dialkyl peroxides, alkyl hypochlorites, alkyl nitrites or alkyl nitrates, e.g.

(22) $(CH_3)_3C{-}O{-}O{-}C(CH_3)_3 \longrightarrow 2(CH_3)_3C{-}O\cdot$

(23) $C_8H_{17}{-}O{-}N{=}O \longrightarrow C_8H_{17}{-}O\cdot + \cdot N{=}O$

(24) $C_2H_5{-}O{-}NO_2 \longrightarrow C_2H_5{-}O\cdot + \cdot NO_2$

(25) $(CH_3)_3C{-}O{-}Cl \longrightarrow (CH_3)_3C{-}O\cdot + \cdot Cl$

and the chemistry of these decompositions has been reviewed by GRAY and WILLIAMS[23]. Since the subsequent decompositions (reactions 19 and 20) of primary and secondary alkyloxy radicals occur very easily indeed, these thermal decompositions are reactions which are highly exothermic and often of explosive character. For instance, a homolysis like (24) probably initiates the detonation of nitroglycerol. Again, t-butyl hypochlorite is a controllable homolytic chlorinating agent[25].

$$\left.\begin{array}{lll}(26) & (CH_3)_3C{-}O\cdot + H{-}R \longrightarrow & (CH_3)_3C{-}OH + R\cdot \\ (27) & R\cdot + (CH_3)_3COCl \longrightarrow & RCl + (CH_3)_3CO\cdot\end{array}\right\}$$

The thermal decomposition of ditertiary butyl peroxide (22), however, occurs controllably at 110–150° when the peroxide is refluxed in suitable solvents of this boiling range. Since both t-butoxy radicals, $(CH_3)_3C{-}O\cdot$ and the methyl radicals generated from them by the decomposition (21), are dehydrogenating agents, this peroxide is a valuable homolytic oxidant. For instance, the decomposition of di-t-butyl peroxide in boiling toluene generates benzyl radicals almost quantitatively. Though these rapidly combine to form dibenzyl, the reacting toluene solution can be used to benzylate active polycyclic aromatic or heterocyclic compounds such as anthracene or acridine[26]. The removal of α-hydrogen atoms from aromatic side chains in this way has been studied quantitatively by JOHNSTON and WILLIAMS[27]. By carrying out the dehydrogenations

$$(26)\quad (CH_3)_3C{-}O\cdot + CH_3{-}Ar \longrightarrow (CH_3)_3C{-}OH + \cdot CH_2{-}Ar$$

$$(28)\quad Ar{-}CH_2\cdot + \cdot CH_2{-}Ar' \longrightarrow Ar{-}CH_2{-}CH_2{-}Ar'$$

in a mixture of two solvents, $CH_3{-}Ar$ and $CH_3{-}C_5H_4N$ (γ-picoline), and analysing the resulting mixture of dimers they have shown that hydrogen abstraction by alkyloxy radicals, like hydrogen abstraction by chlorine atoms (see p. 5), does involve some degree of polarization in the transition state. Similar conclusions have been reached by HUANG[28] from studies of dehydrogenations by t-butoxy radicals of unsymmetrical benzyl ethers, $Ar\cdot CH_2{-}O{-}CH_2\cdot Ar'$, though in these molecules the main deciding factor is the degree of resonance stabilization of the resulting free radical.

t-Butoxy radicals react in a similar way with aliphatic amines; these are dehydrogenated at C—H groups adjacent to their nitrogen atoms[29].

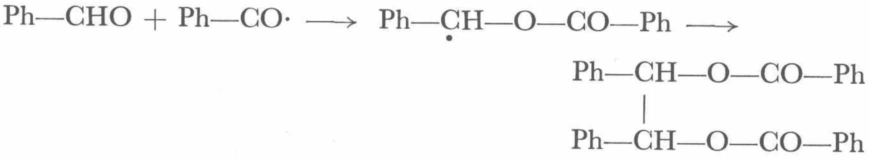
Dehydrogenations of aldehydes are of interest, as the radicals formed from aliphatic aldehydes lose carbon monoxide at temperatures over

100°, and there is then set up a reaction chain[30] which may be further catalysed by the addition of a small amount of a thiol[31].

$$(26) \qquad \mathrm{Me_3C{-}O\cdot + R{-}CHO \longrightarrow Me_3C{-}OH + R{-}CO\cdot}$$

$$(29) \quad \left\{ \begin{array}{l} \mathrm{R{-}CO\cdot \longrightarrow R\cdot + CO} \\ \\ \mathrm{R\cdot + R{-}CHO \longrightarrow R{-}H + R{-}CO\cdot} \end{array} \right.$$

Benzaldehyde, however, gives the resonance-stabilized radical Ph—CO· which adds on to the oxygen atom of another benzaldehyde molecule[32].



$$\mathrm{Ph{-}CHO + Ph{-}CO\cdot \longrightarrow Ph{-}\underset{\bullet}{C}H{-}O{-}CO{-}Ph \longrightarrow \begin{array}{c} \mathrm{Ph{-}CH{-}O{-}CO{-}Ph} \\ | \\ \mathrm{Ph{-}CH{-}O{-}CO{-}Ph} \end{array}}$$

Alkyloxy radicals can be formed by metallic-ion-catalysed reactions of per-esters as well as of hydroperoxides. t-Butyl-perbenzoate has recently been used together with a trace of a copper or cobalt salt to attack C—H groups adjacent to olefinic bonds without causing any rearrangement of the olefinic system[33]. The reaction with octene-1 has been represented as follows

$$(30) \quad \mathrm{Ph{\cdot}CO{\cdot}O{-}O{\cdot}CMe_3 + Cu^+ \longrightarrow (Ph{\cdot}CO{\cdot}O\ Cu)^+ + {\cdot}OCMe_3}$$

$$(26) \quad \mathrm{Me_3C{-}O\cdot + H{-}R \longrightarrow Me_3C{-}OH + R\cdot}$$

$$(31) \quad \mathrm{R\cdot + (Ph{\cdot}CO{-}O\ Cu)^+ \longrightarrow Ph{\cdot}CO{\cdot}O{-}R + Cu^+}$$

where processes (26) and (31) are thought to be concerted. However, $\mathrm{(Ph{\cdot}CO{\cdot}O\ Cu)^+}$ is really an ion pair, i.e. $\mathrm{(Ph{-}CO{\cdot}O{:})^-}$, $\mathrm{Cu^{2+}}$ and equation (31) may well comprise the reactions below (see p. 7)

$$\left. \begin{array}{l} \mathrm{R\cdot + Cu^{2+} \longrightarrow R^+ + Cu^+} \\ \\ \mathrm{R^+ + (Ph{\cdot}CO{\cdot}O{:})^- \longrightarrow Ph{\cdot}CO{-}O{-}R} \end{array} \right\}$$

though the complete absence of primary allylic benzoates from reactions of terminal olefins shows that neither *free* radical, (R·), nor *free* carbonium ion, (R+), intermediates can be liberated in catalysed oxidations of this type.

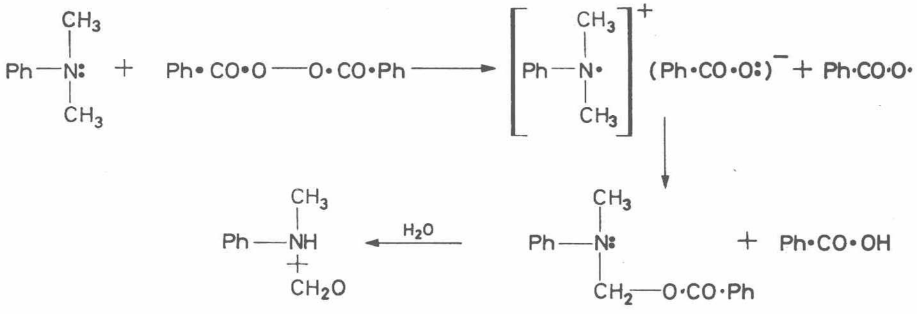
(*c*) *Acyloxy radicals*, $\mathrm{R{\cdot}CO{\cdot}O{\cdot}}$—The thermal decomposition of diacyl peroxides, such as benzoyl peroxide, is the best known method for generating free radicals, but the decomposition is, in part, a chain reaction[34]

(32) $\mathrm{Ph{\cdot}CO{\cdot}O{-}O{\cdot}CO{\cdot}Ph \rightleftharpoons 2\,Ph{\cdot}CO{\cdot}O{\cdot}}$

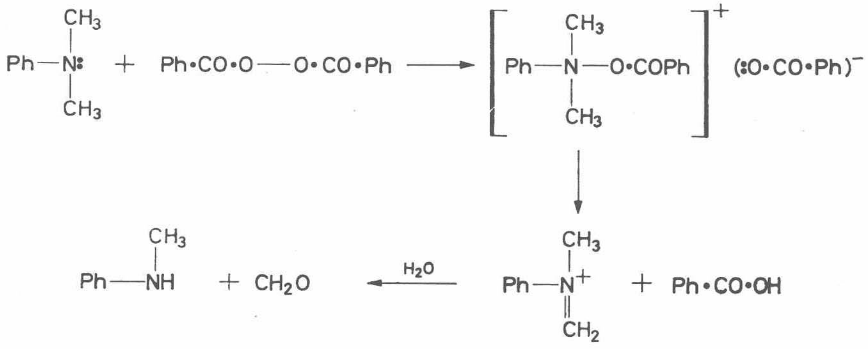
(33) $\mathrm{Ph{\cdot}CO{\cdot}O{\cdot} \longrightarrow Ph{\cdot} + CO_2}$

(34) $\mathrm{Ph{\cdot} + Ph{\cdot}CO{\cdot}O{-}O{\cdot}CO{\cdot}Ph \longrightarrow Ph{\cdot}O{\cdot}CO{\cdot}Ph + Ph{\cdot}CO{\cdot}O{\cdot}}$

and also may, in polar solvents, or under the influence of strong acid or base catalysts, take a heterolytic course[35]. For the latter reason it is now considered that a number of oxidations effected by benzoyl peroxide, and once thought to be homolytic processes, e.g. the oxidations of certain phenols[36] and arylamines, may not involve free radicals. For instance, the reaction between dimethylaniline and benzoyl peroxide can be interpreted in both the following ways[37].



Homolytic Reactions



Heterolytic Reactions of the Amine-oxide.