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Oxidation of Ketones by Molecular Oxygen

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The results of fundamental studies on different methods of oxidising aldehydes and ketones by oxygen are presented; the purely thermal oxidation, the photochemical oxidation, as well as the low-temperature oxidation in alkaline media are considered. The general postulates of the reaction mechanisms are described and specific instances involving aliphatic, alicyclic, saturated, and aromatic ketones as well as the mechanisms of the decomposition of the hydroperoxides of α-ketones are surveyed.
The bibliography includes 101 references.

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I. INTRODUCTION

The present author's two previous papers were devoted to various methods of oxidising alcohols[1] and phenols[2]; it is logical to examine also carbonyl compounds from this point of view. Indeed they are intermediates in the oxidation of hydrocarbons and are formed when animal or plant lipids are subjected to aerobic heat treatment. It is known that alcohols and carbonyl compounds (aldehydes or ketones depending on the structure of the hydrocarbons) are formed simultaneously in the oxidation of hydrocarbons via intermediate hydroperoxides; more carbonyl compounds are formed in the subsequent oxidation of the alcohols.

The mechanism of the formation of carbonyl compounds in the oxidation of hydrocarbons has been described in detail in reviews[1-3].

The main products of the oxidation of carbonyl compounds are carboxylic acids formed via chain dissociation or without such dissociation, depending on the initial compound—ketone or aldehyde. Different methods for the oxidation of carbonyl compounds are not only of theoretical but also of considerable practical interest for the synthesis of carboxylic acids and their derivatives by the oxidation of hydrocarbons, particularly for the synthesis of dibasic acids from alicyclic hydrocarbons.

The formation of mono- and poly-functional saturated and unsaturated carbonyl compounds from derivatives of oleic, linolenic, and linoleic acids has been described in detail in review articles[4-6]. Furthermore, numerous carbonyl compounds form part of the composition of natural products and are an important raw material for various branches of the manufacture of chemical products—solvents, pharmaceuticals, perfumes, dyes, and plastics.

It is noteworthy that methods for the oxidation of aldehydes in the liquid or vapour phase have now been described in fair detail (the latest review was published in 1976). Thus the liquid-phase oxidation of aldehydes has been described[7]; a review devoted to the mechanism and kinetics of the oxidation of aldehydes in the liquid and vapour phases has been published[8]. The photochemical oxidation of aldehydes in the liquid or vapour phase has been considered by Niclause and Lemaire[9], Maslov and Blyumberg[10] discussed in detail the liquid-phase oxidation of aldehydes and their joint oxidation with olefins. Elkik[11] described the mechanism of the oxidation of aldehydes in alkaline media.

Apart from the reviews listed above, the results of individual investigations during the last 26 years have been the subject of very detailed publications and in many instances noteworthy conclusions concerning the kinetics of the processes are presented.

Thus Combe et al.[12] published two papers on the oxidation of acetaldehyde and propionaldehyde in the vapour phase (certain considerations concerning the kinetics are presented and the experimental methods are described in detail). Lemaire[13] investigated the photochemical oxidation of C_7 aldehydes by infrared spectroscopy and Deglise[14] studied the photochemical oxidation of crotonaldehyde. The paper of Franck et al.[15], devoted to the liquid-phase oxidation of benzaldehyde, presents conclusions concerning the process kinetics and critical comments on previous studies. The autoxidation of furfural has been examined by Isacescu et al.[16], whose paper also contains an extensive historical review and a critical examination of early investigations.

Extensive review articles devoted to the oxidation of aldehydes of different types in volume VII of Grignard's collection[17-20] are noteworthy; they also deal with the oxidation reactions of aliphatic[17], alicyclic[18], aromatic[19], and unsaturated (mono- and poly-olefinic and acetylenic)[20] aldehydes.

Thus, since the methods for the oxidation of aldehydes have been described and discussed in a whole series of reviews (most of which were published in 1976) and original publications, the author believes that there is no need to consider them within the framework of the present survey.

The literature on the oxidation of ketones differs appreciably from that on aldehydes. As far as the present author is aware, there are only two reviews on the purely thermal[21] and vapour-phase[22] oxidations; the latter paper deals with various photochemical reactions in the vapour phase and with general postulates concerning the photochemical oxidation mechanism. However, the above reviews[21,22] do not deal either with the purely thermal liquid-phase oxidation of ketones in the presence of various catalysts or in their absence (there are only short sections in the general reviews on organic peroxides[23-25] with references up to 1960) or with their oxidation in an alkaline medium at a low temperature, which has been the subject of numerous detailed investigations in the last decade. The low-temperature oxidation in an alkaline medium proved to be highly effective, since it makes it possible not only to synthesise and isolate various

α-keto-t-hydroperoxides but also to investigate their properties, in particular their radical (in the liquid and vapour phases) and ionic decompositions catalysed by alkali.

It is noteworthy that individual ketones form part of the composition of many natural essential oils, sex hormones, and wood tar. It is known that methyl ketones CH_3COR (R represents an odd number of carbon atoms ranging from C_3 to C_{11}) are formed when saturated lipids become rancid and by the action of certain moulds on saturated aliphatic acids, their ammonium salts, and triglycerides, and also that ketones and aldehydes of various types are produced in the course of the thermal oxidation of lipids[4-6].

Data on the industrial applications of methyl ketones have been described by Miller[26].

A review article[27] on ketones and an article in volume VII of Grignard's collection[28-31], which deals with the synthesis and reactions of saturated aliphatic[29], ethylenic[30], and acetylenic[31] ketones are noteworthy. Turro's paper[32] is devoted solely to cyclopropanone and its derivatives and that of Srinivasan[33] deals with the photochemistry of cyclic ketones.

Various chemical and physical aspects of the ketone oxidation reactions are fairly interesting, particularly the studies of the last decade; therefore, from our point of view, it is appropriate to survey the literature data on the methods of oxidising ketones in addition to the information about the reactions of these compounds already available.

II. GENERAL POSTULATES

1. Thermal Oxidation under the Influence of O_2 in a Neutral Medium

Jenkins[34] claims that many ketones having the general formula $XC_6H_4-CH_2-COR$ acquire the smell of an aldehyde on simple storage at room temperature in the presence of atmospheric oxygen or in sunlight. He was unable to obtain *o*-chlorobenzoic acid and benzaldehyde from benzyl *o*-chlorophenyl ketone.

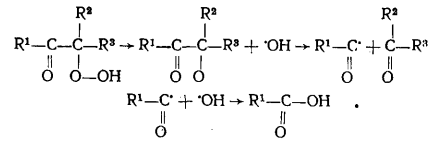
Scharp et al.[35] isolated butyric acid and propionaldehyde in the thermal autoxidation of dipropyl ketone at 110–120 °C. Furthermore, the authors noted the formation of a peroxide, whose content increases (primarily as a function of reaction time), passes through a maximum, and then falls (as in the oxidation of hydrocarbons of various types and other organic compounds); this is not observed for the extent of conversion to aldehyde and acid, which increases continuously. The same workers[36] isolated acetone and isobutyric acid after the thermal autoxidation of di-isopropyl ketone at 100° and 110 °C. It is of interest to note that in the first instance (in the presence of a secondary carbon atom conjugated with C=O) a small amount of water is formed and part of the aldehyde is converted into the corresponding acid.

It has been shown[37] that in the thermal autoxidation of certain alicyclic ketones (cyclohexanone and α- and β-tetralinones) at temperatures from 75° to 100 °C peroxide is formed initially and then, as a consequence of ring rupture, the corresponding aldehydoacids.

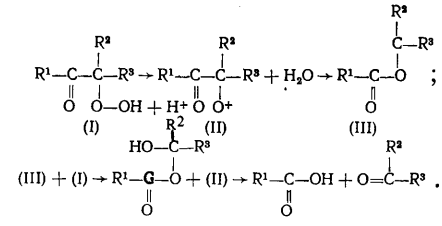
The experimental results obtained for several aliphatic, benzyl, and alicyclic ketones have shown that molecular oxygen initially acts (at least to a large extent) on the carbon atom in the α-position relative to the C=O group, which leads to the formation of the ketohydroperoxide $R^1C(=O)C.[(OOH)(R^2)(R^3)]$, which then decomposes into an aldehyde and carboxylic acid with dissociation of the O–O and C–C bonds in the C–C=O group.

As in the general case of hydrocarbons of various types, the rate of oxidation and stability of the hydroperoxides increase on passing from a secondary to a tertiary carbon atom.

The decomposition of the hydroperoxide proceeds mainly via a radical mechanism:



and then via an ionic mechanism, the process being catalysed by the acid formed:



Indeed it has been shown[38] that in the case of cyclohexanone the rate of decomposition of the hydroperoxide formed greatly increases after the introduction of acetic acid. The formation of acid is then clearly autocatalytic, as for dipropyl ketone at 120 °C; the acid content is low during the first 5 h after the start of reaction and then it reaches 0.022 and 0.080 mole per mole of the ketone after 8 and 12 h respectively[39].

Table 1. The autoxidation of ketones.

Ketone	*t*, °C	Time, h	Content of oxidation products, moles per mole of initial ketone		τ*, h	Refs.
			peroxide	acid		
Di-isopropyl ketone	85	8	0.022	0.0148	—	[40]
Di-isopropyl ketone	100	36	0.05	0.05	6	[36]
Di-isopropyl ketone	110	16	0.040	0.040	0	[36]
Dipropyl ketone	110	24	0.005	0.05	8	[35]
Dipropyl ketone	120	6	0.01	0.02	—	[35]
Ethyl methyl ketone	120	10	0 003	0.003	—	[39]

*τ is the induction period in the formation of the acid.

Table 1 presents quantitative data for the formation of hydroperoxides and acids from three ketones at different temperatures.

The method of acid-catalysed ionic decomposition of hydroperoxides was first developed[40] in relation to the decomposition of decalinyl hydroperoxide in the presence of H_2SO_4; the decomposition of cumenyl-hydroperoxide to phenol and acetone proceeds via the same mechanism[41], which has been discussed in detail by Tobolsky and Mesrobian[42].

We may note that, apart from the main pathway involving the rupture of the bond in the α-position relative to the C=O group, there is also a possibility (to a much lesser extent) of the dissociation of the bond in the β-position, particularly if the group in the β-position relative to C=O is an H atom (the formation of H_2O) or $H_2CC_6H_4X$. Thus

although the action of O_2 on the carbon atom in the α-position relative to the C=O group constitutes the main pathway, it is not the only one: carbon atoms in other positions can also be acted upon by oxygen, as has been demonstrated for long-chain ketones.

Indeed Rif and coworkers showed in relation to the oxidation of 2-octanone[43] and 6-undecanone[44,45] that, apart from the compounds formed as a result of the dissociation of the chain in the α-position, several other substances are formed as a consequence of the dissociation of the chain in other positions.

2. The Effect of O_2 in the Presence of Ionising Radiation in a Neutral Medium

The photochemical oxidation of acetone and diethyl ketone under the influence of light at wavelengths in the range $267 < \lambda < 313$ nm at different temperatures has been the subject of numerous investigations which have been analysed by Bernard[21]. It has been shown that the primary reaction step consists in the formation of the radicals $R^2-\dot{C}=O$ (or $R^1-\dot{C}=O$ and $\dot{R}^2$), which are oxidised to the corresponding peroxy-radicals.

The final products are formed from the radicals $R^1O-\dot{O}$, $R^1-\dot{O}$, $R^2-C(=O)O\dot{O}$, and $R^2-(C=O)-O^{\cdot}$ and constitute a mixture of CO, CO_2, the acids R^1-COOH and R^2-COOH, as well as alcohols and aldehydes formed as a consequence of the disproportionation of the radicals $R^1O^{\cdot}$ and $R^2O^{\cdot}$.

3. The Effect of O_2 in an Alkaline Medium

Ketones can react with molecular oxygen also at a very low temperature in a highly alkaline medium in aprotic solvents with formation (as in a neutral medium) of an α-ketohydroperoxide as the primary product. The rate of reaction depends very markedly on the configuration of the carbon atom in the α-position relative to the C=O group. Thus it is very low for the primary carbon atom and very high for secondary and tertiary carbon atoms. However, in the former case the yield of hydroperoxides is low, since they rapidly decompose in an alkaline medium; in the case of a tertiary carbon atom it is possible to isolate hydroperoxides with a higher degree of purity and in a high yield.

The selection of temperature and reaction time is very important for the attainment of the maximum yield. (t-Hydroperoxides also decompose under the influence of alkali via the general mechanism $2ROOH \rightarrow 2ROH + O_2$ but at a much lower rate than secondary hydroperoxides[23].) It is noteworthy that in asymmetric ketones of the type $H_3C-(C=O).CH(CH_3)_2$ only the tertiary group is involved. We may note that the oxidation in a highly alkaline medium is possible not only for ketones but also for many other organic compounds with a tertiary α-carbon atom, for example, ethers, esters, nitriles, hydroxylamines, hydrazines, mercaptans, and phenols.

The influence of the solvent on the yield of hydroperoxide has been studied[46] in relation to isopropyl methyl ketone in the presence of the $(CH_3)_3COK/(CH_3)_3COH$ system at −8° for a reaction time between 4 and 10 min. It was shown that the yield of hydroperoxide decreases in the sequence dimethylformamide > dimethoxyethane > hexamethylphosphoramide > tetrahydrofuran > acetonitrile > toluene > acetic acid, the yields being in proportions of 87, 80, 72, 66, 56, 48, and 38% respectively.

Evidently in the first two solvents the reaction proceeds even in the presence of aqueous solutions of alkalies, while in others it is necessary to use stronger bases (such as alkoxides) and in aprotic solvents such as diglyme and hexamethylformamide the rate of reaction is much higher than in $(CH_3)_3COH$.

The first reaction stage is the ionisation of the initial compound (designated by RH) by the base $\ddot{B}$ with formation of the anion R^-, which then reacts with molecular oxygen:

$$RH + \ddot{B} \rightarrow R^- + BH \ ;$$

$$R^- + O_2 \rightarrow R^{\cdot} + {}^{-}O_2^{\cdot} \ ;$$

$$R^{\cdot} + O_2 \rightarrow RO-O^{\cdot} \xrightarrow{HR} RO-OH + R^{\cdot} \ .$$

Consequently this reaction involves the formation of the O_2^- radical-ion the properties and formation of which in the course of various chemical reactions have been described in a recent review[47].

The kinetic data and the mechanism of the oxidation in an alkaline medium, which is applicable to substances other than ketones, particularly to esters[48] and alkyl halides[49], have been discussed in detail in the literature.

III. OXIDATION OF SATURATED ALIPHATIC AND AROMATIC KETONES

The thermal oxidation of acetone has been the subject of numerous studies. Acetone contains only primary carbon atoms in the α-position relative to the C=O group; it is fairly resistant to the action of atmospheric oxygen and reacts with the latter (in the absence of any oxidation initiators) only above 250 °C, so that its thermal oxidation can be studied only in the vapour phase. Such oxidation has been the subject of two serious investigations[50,51] carried out using specially purified acetone in the temperature range 250–500 °C at acetone and oxygen pressures of 60 and 30 mmHg respectively. The reaction products were determined quantitatively and qualitatively at 284° and 498 °C. It was shown that at these temperatures considerable amounts of H_2O and CO are formed. On the other hand, the contents of CO_2 and HCHO are considerable at 284 °C and very low at 498 °C; furthermore, methane (in fairly large amounts) and ethyl methyl ketone (in much smaller amounts) are formed only at the latter temperature. At 284 °C there is an appreciable amount of methyl hydroperoxide (which was not detected at 498 °C) and also a very small amount of H_2O_2, H_2, CH_3OH, and OCH–CHO. These compounds are formed in accordance with the equations presented below, the first of which describes the reaction at 284 °C and the second at 498 °C:[50,51]

$$(CH_3)_2C=O+2.5O_2 \rightarrow 1.75H_2O+1.25CO+0.65CO_2+0.6CH_3\dot{O}OH + \\ + 0.5HCHO+0.1H_2 \ ;$$

$$(CH_3)_2C=O+O_2 \rightarrow 0.9H_2O+1.6CO+0.7CH_4 \\ + 0.3HCHO+0.07(C_2H_4+CO_2+H_2) \ .$$

The ratio of the contents of the same compounds (r) formed at 284° and 498 °C is 2 for H_2O, 0.8 for CO, and 9.3 for CO_2.

The results suggest the following reaction mechanism; in the first step, as in the liquid-phase autoxidation of ketones, at 498 °C hydrogen is abstracted from acetone with formation of a radical:

$$CH_3-\underset{\underset{O}{\|}}{C}-CH_3 + O_2 \rightarrow CH_3-\underset{\underset{O}{\|}}{C}-\dot{C}H_2 + {}^{\cdot}O-OH \ .$$

Its life is very short; it decomposes to keten and the radical $H_3C^{\cdot}$ before reacting with O_2:

$$CH_3-\underset{\underset{O}{\|}}{C}-CH_2^{\cdot} \rightarrow H_3C^{\cdot} + \underset{\underset{O}{\|}}{C}=CH_2 \ .$$

In the presence of O_2, keten decomposes almost exclusively to H_2O and CO with traces of CO_2 + C_2H_4, while $H_3CO-O^{\cdot}$ is formed from the radical $H_3C^{\cdot}$. The behaviour of this radical also depends on temperature: at an elevated temperature (498 °C) it decomposes mainly to H_2O and the $\dot{C}HO$ radical:

$$CH_3O-O^{\cdot} \rightarrow H_2O + H-\underset{\underset{O}{\|}}{C}^{\cdot} \ .$$

The latter can in its turn either recombine with formation of glyoxal or can react with O_2; in the latter case the products are CO and the radical $HOO^{\cdot}$:

$$H-\underset{\underset{O}{\|}}{C}^{\cdot} + O_2 \rightarrow CO + HO-O^{\cdot} \ .$$

The radical $HOO^{\cdot}$ can abstract hydrogen from acetone to form the radical $CH_3COCH_2^{\cdot}$ and H_2O_2.

At 284 °C the radical $H_3CCO^{\cdot}$ mainly abstracts hydrogen from acetone or HCHO to form CH_3CHO, partial decomposition of which yields HCHO and H_2O; the radical $CH_3COCH_2^{\cdot}$, whose lifetime at 284 °C is longer than at 498 °C, mainly reacts with CO_2 to form a radical which subsequently decomposes by the mechanism

$$CH_3-\underset{\underset{O}{\|}}{C}-CH_2O-O^{\cdot} \rightarrow CH_3^{\cdot} + CO_2 + HCHO \ .$$

The photochemical oxidation of acetone (particularly at λ = 313 nm) in the vapour phase in the range from room temperature to 250 °C and at different oxygen and acetone pressures has been described in extensive reviews[52-65] and the conclusions reached in them have been analysed in detail in Hoare's review[22]. The liquid-phase photochemical oxidation of acetone at 30 °C has also been studied[64].

In these investigations it has been shown that the principal compounds formed under different conditions are CO, CO_2, CH_3OH, AcOH, H_2O, and CH_3OOH with small amounts of HCOOH, CH_4, and C_2H_6.

It is noteworthy that compounds of the type RH are obtained only at low O_2 pressures (<1 mmHg) and, in order to suppress their formation, it is necessary to increase somewhat the oxygen pressure, raising simultaneously the temperature (for example, 0.0625 and 0.360 mmHg at 36° and 100 °C respectively).

Whereas the nature of the products formed is analogous to that of the compounds obtained in the thermal oxidation of acetone in the vapour phase at 280–320 °C, the relative compositions and kinetics of their formation are different and depend on the reaction time: in photochemical oxidation the amount of CH_3OH is much greater and OH is formed from the beginning of the reaction together with HCHO.

At a constant specified temperature the total amount of oxidation products increases with increase of the oxygen pressure (with the exception of CO, the amount of which decreases). It is of interest to note that more than 90% of the CO_2 is formed from the C=O group and CO is produced both from the CH_3 and C=O groups, the amount obtained from the latter group being smaller the higher the O_2 pressure; HCHO and CH_3OH are derived from CH_3 to an extent greater than 90%. Indeed, a study employing ^{14}C in the CH_3 group showed[61] that at 120 °C the amount of radioactive CO_2 is less than 10%. This result has been confirmed in studies[59,63] where the ^{18}O label was used over a wide temperature range, from 36° to 175 °C; the proportion of $^{16}O=C=^{18}O$ reached 92%. Furthermore, it has been shown[63] that proportion of $CH_3{}^{18}OH$ and $H_2C={}^{18}O$ is greater than 90%. In the first stage of the reaction acetone decomposes to methyl and acetyl radicals, this being followed by the partial decarbonylation of the latter, its extent increasing with increase of temperature and decreasing with increase of oxygen pressure:

$$H_3C-\underset{\underset{O}{\|}}{C}-CH_3 \rightarrow H_3C^{\cdot} + \cdot\underset{\underset{O}{\|}}{C}-CH_3 \ ;$$

$$\cdot\underset{\underset{O}{\|}}{C}-CH_3 \rightarrow CO + \cdot CH_3 \ .$$

In the absence of O_2, two $H_3C^{\cdot}$ radicals recombine and a disproportionation reaction takes place between the $H_3C^{\cdot}$ and $O=\dot{C}-CH_3$ radicals, which leads to the formation of C_2H_6, CH_4, and $O=C=CH_2$ respectively:

$$H_3C^{\cdot} + \cdot CH_3 \rightarrow H_3C-CH_3 \ ;$$

$$H_3C^{\cdot} + HCH_2-\underset{\underset{O}{\|}}{C}^{\cdot} \rightarrow CH_4 + H_2C=C=O \ .$$

In the presence of O_2 the radical $H_3C-\dot{C}=O$ gives rise to CO_2 and the radical $H_3CO^{\cdot}$, i.e.

$$H_3C-\underset{\underset{O}{\|}}{C}^{\cdot} \xrightarrow{O_2} H_3C-\underset{\underset{O}{\|}}{C}-O-O^{\cdot} \rightarrow \cdot\underset{\underset{O}{\|}}{C}-O-OCH_3 \rightarrow CO_2 + \cdot OCH_3 \ ,$$

while HCHO and the radical $^{\cdot}OH$ are formed from the radical $H_3C^{\cdot}$, i.e.

$$H-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}^{\cdot} \xrightarrow{O_2} H-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-O-O^{\cdot} \rightarrow \cdot\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-O-OH \rightarrow \underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}=O + \cdot OH$$

or H_2O and the radical $H-\dot{C}=O$ are produced:

$$\cdot\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-O-OH - H_2O + H-\underset{\underset{O}{\|}}{C}^{\cdot} \ .$$

The radicals $H_3C-C(=O)O^{\cdot}$ can be formed from the radicals $H_3C-\underset{\underset{O}{\|}}{C}-O-O^{\cdot}$:

$$H_3C-\underset{\underset{O}{\|}}{C}-O-O^{\cdot}$$

$$2H_3C-\underset{\underset{O}{\|}}{C}-O-O^{\cdot} \rightarrow 2H_3C-\underset{\underset{O}{\|}}{C}-O^{\cdot} + O_2 \ ,$$

while the radicals $H_3CO^{\cdot}$ can be formed from $H_3C-O-O^{\cdot}$:

$$2H_3CO-O^{\cdot} \rightarrow 2H_3CO^{\cdot} + O_2 \ .$$

The feasibility of the last reaction has been discussed in detail[66].

The products HCHO and H_3COH (the latter at least at the beginning of the reaction) are formed as a consequence of a disproportionation reaction between two methoxy-radicals:

$$H_3CO^{\cdot} + \cdot OCH_3 \rightarrow H_3COH + HCHO \ .$$

This reaction has also been discussed[66].

Carbon monoxide can be formed via the two reactions presented below from the formyl radical obtained from the radical $H\dot{C}OOH$, the second reaction occurring at low oxygen pressures:

$$H-\underset{\underset{O}{\|}}{C}^{\cdot} + O_2 \rightarrow HO-O^{\cdot} + CO \ ;$$

$$H-\underset{\underset{O}{\|}}{C}^{\cdot} + H-\underset{\underset{O}{\|}}{C}^{\cdot} \rightarrow H-\underset{\underset{O}{\|}}{C}-H + CO \ .$$

The role of the reactions involving the abstraction of hydrogen by the radicals $H_3CO^{\cdot}$, $H_3CO-O^{\cdot}$, $H_3C-C(=O)-O^{\cdot}$, and $H_3C-C(=O)-O-O^{\cdot}$ increases with increasing temperature at least up to 200 °C. It is noteworthy that the abstraction of hydrogen from formaldehyde proceeds much more readily than from acetone. Indeed, depending on reaction time, the amount of HCHO passes through a maximum and the ratio $H_3COH/HCHO$ increases continuously; furthermore, when HCHO is introduced, the H_3COH content and the reaction rate increase. A new source of $H-\dot{C}=O$ radicals arises and hence the formation of CO is initiated.

At 250 °C the reactions involving the dehydrogenation of acetone by the above radicals become dominant and the rate of formation of all the compounds rapidly increases. The $H_3C-C(=O)CH_2$ radicals formed are oxidised to the corresponding peroxy-radicals, which become a new source of HCHO and the radicals $H_3C^{\cdot}$ as well as all their derivatives as a consequence of decomposition via the mechanism

$$H_3C-\underset{\underset{O}{\|}}{C}-CH_2O-O^{\cdot} \rightarrow HCHO + CO_2 + H_3C^{\cdot} \ .$$

The liquid-phase photochemical oxidation (λ = 313 nm) of acetone at 30 °C has been studied[64] and it has been shown that virtually the same reaction products are obtained as in the vapour phase at 284 °C. However, the amount of O_2 dissolved in acetone is insufficient for the complete suppression of the formation of CH_4 and C_2H_6, which suggests a greater ability of the $H_3C^{\cdot}$ radicals to abstract hydrogen and to dimerise in the liquid phase.

The photochemical oxidation of diethyl ketone at 25°, 100°, and 200 °C, diethyl ketone pressures of 35 or 12.5 mmHg, and oxygen pressures from 0 to 1.25 mmHg [67] and at 30°, 70°, 100°, and 150 °C, a diethyl ketone pressure of 35 mmHg, and oxygen pressures ranging from 0.55 to 1.85 mmHg [69] has been described[67-69]. These studies have been analysed in a review[22].

The principal reaction products include CO, CO_2, CH_3CHO, and C_2H_5COOH with small amounts of C_2H_4 and C_2H_6. Furthermore, it has been possible to establish by an isotope method that almost the entire amount of CO is formed from the carbonyl group (in contrast to acetone where the amount of CO derived from C=O does not exceed 20%) and that CO_2 at 30 °C is derived almost exclusively from C=O but at 100 °C only to the extent of 30%, while the remainder of the CO_2 arises from a group with a secondary carbon atom.

The above facts can be explained by the much easier decarbonylation of the radicals $C_2H_5\dot{C}=O$ than the radicals $H_3C\dot{C}=O$ and the much greater mobility of the hydrogen atom linked to a secondary carbon atom compared with a primary carbon atom (in the case of acetone). Consequently, for diethyl ketone all the hydrogen abstraction reactions are more important than in the oxidation of acetone. Hence it follows that the radicals $C_2H_5-\dot{C}=O$, $\dot{C}_2H_5$, and $C_2H_5-C(=O)-\dot{C}H-CH_3$ are formed even at room temperature in the initial stage of the reaction. The formation of different compounds can be represented by a sequence of steps:

$$C_2H_5-\underset{\underset{O}{\|}}{C}-C_2H_5 \xrightarrow{h\nu} C_2H_5-\underset{\underset{O}{\|}}{C}^{\cdot} + C_2H_5^{\cdot} \ ;$$

$$C_2H_5-\underset{\underset{O}{\|}}{C}^{\cdot} \rightarrow C_2H_5^{\cdot} + CO \ ;$$

$$C_2H_5^{\cdot} + C_2H_5-\underset{\underset{O}{\|}}{C}-CH_2-CH_3 \rightarrow C_2H_6 + C_2H_5-\underset{\underset{O}{\|}}{C}-\dot{C}H-CH_3 \ ;$$

$$C_2H_5-\underset{\underset{O}{\|}}{C}-\dot{C}H-CH_3 \rightarrow C_2H_5-\underset{\underset{O}{\|}}{C} + H_2C=CH_2 \ ;$$

$$C_2H_5-\underset{\underset{O}{\|}}{C}^{\cdot} \xrightarrow{O_2} C_2H_5-\underset{\underset{O}{\|}}{C}-O-O^{\cdot} \rightarrow CO_2 + {}^{\cdot}OC_2H_5 \ ;$$

$$H_3C-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}-O-O^{\cdot} \rightarrow H_3C-\underset{\underset{H}{|}}{\overset{\overset{H}{|}}{C}}=O + {}^{\cdot}OH \ ;$$

$$C_2H_5-\underset{\underset{O}{\|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}^{\cdot} \xrightarrow{O_2} C_2H_5-\underset{\underset{O}{\|}}{\overset{\overset{H}{|}}{C}}-\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}-O-O^{\cdot} \rightarrow \underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}-O-O + C-C_2H_5 \ ;$$

$$\underset{\underset{CH_3}{|}}{\overset{\overset{H}{|}}{C}}-O-\underset{\underset{O}{\|}}{C}-C_2H_5 \rightarrow \overset{\overset{H}{|}}{C}=O + {}^{\cdot}O\underset{\underset{O}{\|}}{C}-C_2H_5 \ ;$$

$$C_2H_5-\underset{\underset{O}{\|}}{C}-O^{\cdot} + C_2H_5-\underset{\underset{O}{\|}}{C}-CH_2-CH_3 \rightarrow C_2H_5-\underset{\underset{O}{\|}}{C}-OH + C_2H_5-\underset{\underset{O}{\|}}{C}-\dot{C}H-CH_3 \ ;$$

$$H_3C-\underset{\underset{O}{\|}}{\overset{\overset{H}{|}}{C}} + R^{\cdot} \rightarrow H_3C-\underset{\underset{O}{\|}}{C}^{\cdot} + RH \quad (R = C_2H_5^{\cdot},\ C_2H_5-\underset{\underset{O}{\|}}{C}^{\cdot}) \ ;$$

$$H_3C-\underset{\underset{O}{\|}}{C}^{\cdot} \xrightarrow{O_2} H_3C-\underset{\underset{O}{\|}}{C}-O-O^{\cdot} \rightarrow CO_2 + {}^{\cdot}OCH_3 \ .$$

The reaction involving the abstraction of a hydrogen atom from H_3C-CHO is analogous to the abstraction of hydrogen from HCHO in the case of acetone. In the absence of oxygen, C_2H_6 and C_2H_4 are mainly formed[70].

The thermal oxidation of dipropyl ketone has been studied[35] and it has been shown that the maximum concentration of the hydroperoxide is 0.005 and 0.010 mole per mole of the initial substance at 110° and 120 °C respectively; these concentrations are reached after 24 and 5 h respectively. Under the same conditions, the concentrations of acids are 0.03 and 0.04 mol mol^{-1} and reach 0.05 and 0.08 mol mol^{-1} after 30 h at 100 °C and after 12 h at 120 °C.

The thermal oxidation of di-isopropyl ketone has been investigated[36] at 100° and 110 °C; the maximum content of the hydroperoxide reaches 0.05 and 0.04 mole per mole of the initial substance at 100° and 110 °C after 36 and 16 h respectively.

The oxidation of di-isopropyl ketone in a highly alkaline medium has been studied[46,49]. In the presence of $(CH_3)_3COK$ in a $(CH_3)_3COH$ + diglyme mixture the conversion of the ketone is complete after 45 h, the yield of the hydroperoxide amounting to 0.8 mol mol^{-1}.[49] The same alkoxide in solution in dimethyl formamide at −8 °C reacts completely after 4 min and the yield of the hydroperoxide is 0.87 mol mol^{-1}. Cubbon and Hewlett[46] studied the structure of the hydroperoxide

$$(CH_3)_2C(OOH)-CO-CH(CH_3)_2 \qquad \text{(IV)}$$

obtained by thermal oxidation at 100 °C as described by Scarp and Whitcome[36] or by base-catalysed oxidation at −8 °C as described by Gersmann and Bickel[48]. The absence of a cyclic structure of the type

$$(CH_3)_2C(OH)-C(O-O)-CH(CH_3)_2$$

was demonstrated by the retention of specific properties of the O–OH and C=O groups. Indeed, in the presence of phenylhydrazine it is possible to obtain the hydroperoxide

$$(CH_3)_2C(OOH)-C(=N-NHC_6H_5)-CH(CH_3)_2$$

and in the presence of $(C_6H_5)_3CCl$ the dialkyl peroxide

$$(CH_3)_2C(O-O-C(C_6H_5)_3)-COCH(CH_3)_2$$

can be synthesised.

The presence of a single hydroperoxy-group (with intramolecular and intermolecular hydrogen bonds) in the reaction product is fairly unexpected, because the simultaneous presence of two tertiary carbon atoms creates favourable conditions for attack at two positions simultaneously. The hydroperoxide decomposes via a radical mechanism (initiation of the polymerisation of vinyl monomers).

The oxidation of 2-octanone[42] at 130 °C and 15 atm in an alkaline medium in the presence of NaOH (from 0 to 4.25 *N*) has been studied[42] and it has been shown that, apart from the main attack on the 3-position (relative to the end of the chain), leading to the formation of C_2 and C_6 monobasic acids, there is attack on other positions albeit to a lesser extent. It is of interest to note that the direction of this attack varies with the alkalinity of the medium; with increase of alkalinity, the CH_2 group is involved to a lesser extent but the interaction with the CH_3 group in the α-position relative to C=O intensifies.

Thus in a neutral medium the overall yield of the C_2 and C_6 acids is 77% and the yield of α-oxoheptanoic acid is 2% of the overall yield of all the acids, while in an alkaline medium (NaOH, 6.25 *N*) the yields of the C_2 and C_6 acids are 63 and 18% respectively. On passing from a neutral to an alkaline medium, the yields of the C_3 and C_4 acids diminish somewhat, from 6.2 to 4.4% and from 8.4 to 6.5% respectively.

The thermal oxidation of γ-undecanone at 140 °C has been studied[43] under a pressure of 15 atm. As in the previous case, oxygen acts not only on the carbon atom in the 5-position relative to the end of the chain but also on all the carbon atoms although to a much smaller extent; this gives rise to the formation of both C_5 and C_6 acids, on the one hand, and of C_2, C_3, and C_4 acids, γ-oxovaleric acid, and β- and γ-oxocapric acids, on the other, as well as the formation of diketones (3,6- and 2,6-undecanediones) and methylethylbutyrolactone. The preferential attack on the 2-position (the α-position relative to the CH_3 group) is noteworthy. The amounts of the C_2, C_3, C_4, and C_5 acids formed relative to the C_6 acid are 0.17, 0.11, 0.10, and 0.66 respectively.

The amount of peroxides passes through a sharp maximum (8×10^{-2} mol mol^{-1}), which is attained after 20 min; after 2.5 h, the products contained 5×10^{-2} mol mol^{-1} of peroxides, 5×10^{-2} mol mol^{-1} of esters (after 3 h), and 1×10^{-2} mol mol^{-1} of lactones (after 3 h).

Esters can be formed partly as a result of the reaction with the initial ketone of the peroxide formed by the oxidation of the aldehydes formed. This is the classical Baeyer–Villiger reaction described by Hassall[71] and the present author[72].

The thermal oxidation of γ-undecanone has also been studied at 120° and 130 °C;[43] the maximum content of different compounds in the product is almost independent of temperature but is attained faster at higher temperatures. Thus the maximum amounts of products are formed after 180, 90, and 30 min for peroxides (8×10^{-2} mole), after 300, 180, and 90 min for acids (6×10^{-2} mole), and after 360, 180, and 150 min for esters (3×10^{-2} mole) at 120°, 130°, and 140 °C respectively.

It has been established[73] that benzyl mesityl ketone is converted at room temperatures into mesiteic acid and benzaldehyde on contact with even traces of atmospheric oxygen. The yield of the intermediate hydroperoxide $C_6H_5-\underset{\underset{O-H}{|}}{CH}-COMes$ is 0.07–0.08 mol mol^{-1} and is reached after a period ranging from 15 days to 6 months. The hydroperoxide isolated in a pure form is a crystalline substance which melts with decomposition at 134–135 °C. After reduction by treatment with KI or Na_2SO_3 in acetic acid, the corresponding ketoalcohol is obtained, while heating up to 100–110 °C at a pressure of 1 mmHg results mainly in the formation of mesiteic acid, benzophenone, and a small amount of dibenzoyl and water.

IV. SYNTHESIS AND STUDY OF THE DECOMPOSITION OF α-KETOHYDROPEROXIDES

1. Synthesis

Hydroperoxides of different types, presented in Tables 2 and 3, have been obtained[74] by oxidising aldehydes or ketones ketones in an alkaline medium at −20 °C in the presence of $(CH_3)_3COK$ in $(CH_3)_3COH$ (method I) or C_2H_5ONa in C_2H_5OH + DMF (method II) with subsequent recrystallisation of the reaction products from an appropriate solvent.

Table 2. Hydroperoxides of the type $XC_6H_4-\underset{\underset{O}{\|}}{C}-\underset{\underset{O-OH}{|}}{\overset{\overset{C_6H_5}{|}}{C}}-C_6H_5$.

X	Method	Solvent for recrystallisation	Purity, %	M.p., °C
H	I	petroleum ether	96	115—116
H_3CO-*p*	II	hexane + petroleum ether	85	118—119
H_3C-*p*	II	benzene + petroleum ether	77	112—114
Cl-*m*	II	benzene + petroleum ether	88	101—103
Cl-*m*	II	—	67	liquid

Table 3. Hydroperoxides of the type $C_6H_5-\underset{\underset{O}{\|}}{C}-\underset{\underset{O-OH}{|}}{\overset{\overset{C_6H_5}{|}}{C}}-CH_2C_6H_4X$-*p* obtained by method II.

X	Solvent of recrystallisation	Purity, %	M.p., °C
CH_3O	benzene + petroleum ether	29	105—108
H_3C	—	50	liquid
Cl	—	60	liquid

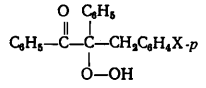
2. Various α-Ketohydroperoxide Decomposition Pathways

Various methods for the thermal[74] (at 250 °C in the vapour phase or at 130 °C in the liquid phase in chlorobenzene), photochemical[75], and alkali-catalysed[76] decomposition of α-ketohydroperoxides have been studied in very great detail. The papers indicated present the ratios of products in each individual instance and discuss the relevant mechanisms.

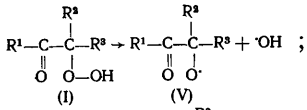
(a) The radical mechanism. The thermal decomposition of α-ketohydroperoxides in the vapour phase at 250 °C or in the liquid phase at 130° and 150 °C in C_6H_5Cl as well as their photochemical decomposition at room temperature give rise to the acid R^1COOH and the ketone R^2COR^3 as the main products

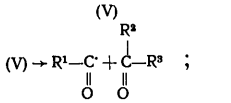
in yields of 0.75–0.80 and 0.75–1.00 mole per mole of the initial substance respectively. These products are formed as a result of the rupture of the bond between the carbon atom of the carbonyl group and the carbon atom linked to the hydroperoxy-group. Small amounts of R^1COCOR^2, the alcohol R^3OH, and the hydrocarbon R^3R^3 are also formed as a result of the dissociation of the C–C bond in the β-position relative to the C=O group. The ease of dissociation depends on the nature of R^3.

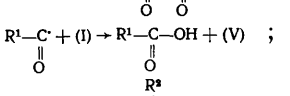
In the case of hydroperoxides

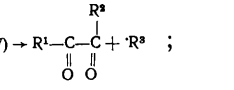


the yield of $C_6H_5-C(=O)-C(=O)-C_6H_5$ is 0.04, 0.054, and 0.08 mole per mole of the initial substance for X = Cl, H, and OCH_3 respectively. Consequently electron-accepting groups lower and electron-donating groups increase the rate of dissociation of the C–C bond in the β-position. The increased yield of the acid R^1COOH or the ketone R^2COR^3 as well as the fact that the rate of reaction in C_6H_5Cl is higher than in other solvents suggest that the thermal decomposition proceeds via a radical mechanism including a sequence of steps:


(1)


(2)


(3)

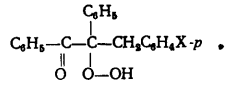

(4)

$$R^3 + (I) \rightarrow R^3OH + (V) \quad ; \qquad (5)$$

$$^{\cdot}R^3 + {}^{\cdot}R^3 \rightarrow R^3R^3 \quad . \qquad (6)$$

The first stage is the homolytic dissociation of the oxygen bridge in compound (I) with formation of radicals (V) and $^{\cdot}OH$; this is followed by reactions (2)–(6). The main reactions are (2) and (3) and the side reactions are (4), (5), and (6). The contribution of the ionic mechanism under the experimental conditions given above (dilution to a low concentration in a non-polar solvent) is apparently insignificant. Furthermore, since the yields are analogous to those quoted in the previous instance (for the formation of the acid R^1COOH and the ketone R^2COR^3 in the photochemical decomposition of the above hydroperoxides at room temperature), presumably this process also involves a radical chain mechanism[75].

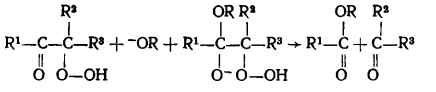
It is noteworthy that the oxidation-reduction reaction at 25 °C in aqueous 70% CH_3OH solution in the presence of $FeSO_4$ also proceeds via a radical mechanism analogous to that described by Sawaki and Ogata[74]. The hypothesis of the formation of the radicals R^1CO is also supported by the formation of the diketone R^1COCOR^1 in a yield of ~0.17–0.20 mol mol^{-1} for hydroperoxides of the type



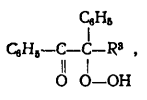
In contrast to cumenyl hydroperoxide, the α-ketohydroperoxide is not reduced to the corresponding alcohol. In the simultaneous presence of $FeSO_4$ and $FeCl_3$, R^1COOCH_3, $R^2R^3C=O$, and R^3Cl are formed in amounts of 0.4–0.6, 0.5–1.0 and 0.018–0.013 mole per mole of the initial substance respectively.

Kochi and Rust[77] discussed in detail the recombination of radicals in the presence of metal ions, while de la Mare and Kochi[78] published a similar discussion of the reduction and oxidation by metal salts.

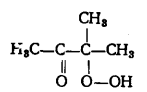
(b) Ionic decomposition catalysed by strong acids. This procedure has been studied in detail by Sawaki and Ogata[76]. It was shown that, in the presence of alkaline alkoxides ROM, where M = K or Na, in the corresponding alcohol or in an alcohol with added benzene at temperatures ranging from 0 °C to room temperature, the ester R^1COOR is formed almost exclusively with a small amount of the acid R^1COOH; however, the content of the latter increases with decrease of the ROM concentration and with increase of the amount of H_2O. Kinetic data suggest that the first reaction stage is the addition of the ^-OR anion to the carbonyl group followed by the heterolytic dissociation of the oxygen bridge and the C–C bond in the anion formed:



The rate of reaction evaluated from the amount of decomposed hydroperoxide varies very markedly with the structure of the hydroperoxide and also with the nature of the group linked to the C=O group compared with that linked to the COOH group. Thus for a hydroperoxide of the type



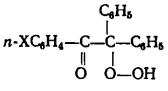
where R^3 = C_6H_5, CH_3, C_2H_5, or $C_6H_5CH_2$ (under the following identical conditions: temperature 0 °C, CH_3ONa concentration 0.10 M in a 1 : 1 mixture of CH_3OH and C_6H_6), the rates of decomposition (in relative units) are 308, 10.5, and 4.9 (the rate of decomposition of the hydroperoxide



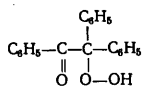
was adopted as unity). The replacement of the C_6H_5 group by C_2H_5 lowers the rate of decomposition by a factor of 30 and the replacement by $C_6H_5-CH_2$ lowers it by a factor of 60; the yield of the ketone R^2COR^3 decreases in the same sequence: from 0.98 for R^3 = C_6H_5 to 0.77 mole per mole of the initial substance for R^3 = $C_6H_5CH_2$.

It is noteworthy that the relative rate of decomposition of the hydroperoxide $(CH_3)_2CH-C(=O)-C(CH_3)_2$ (O–OH) is 0.078, diminishing by a factor greater than 13 on replacement of the CH_3 group by $(CH_3)_2CH$.

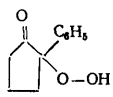
When the rate of decomposition for X = H is adopted as unity, the relative rates corresponding to X = CH_3O, CH_3, and Cl for hydroperoxides of the type



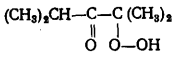
(the conditions were the same as above but CH_3ONa was replaced by C_2H_5ONa) are 0.11, 0.33, and 4.8, the rate diminishing by a factor of 14 following the replacement of the C_6H_5 group (linked to C=O) by CH_3 in



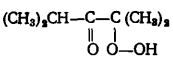
An especially high rate of decomposition of the hydroperoxide



has been noted. It is 7550 times greater than for the hydroperoxide

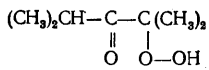


The above results depend mainly on the difference between the rates of addition of the anion ^-OR to the group C=O, caused by polar and particularly steric factors. Thus the rate of decomposition of the hydroperoxide

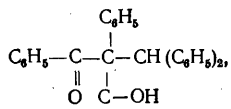


is extremely low due to steric hindrance. The rate of decomposition also varies with the RONa concentration: it increases by a factor of 4.5 for the $C_2H_5ONa/(CH_3COH + C_6H_6)$ system at 0 °C when the RONa concentration is raised by a factor of 20 (from 5×10^{-3} to 10^{-1} M) and increases by a factor of 25 with increase of temperature to 25 °C.

It is noteworthy that the ketone R^2COR^3 has been obtained in a yield of 0.8 mol mol^{-1} in a study[79] of the decomposition of the hydroperoxides

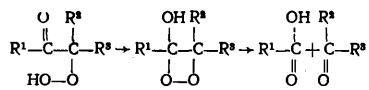


and



also in an alkaline medium but under other conditions (30 °C, $NaOH/CH_3OH + H_2O$ at a concentration of 0.1–0.5 M or CH_3ONa/CH_3OH at a concentration of 5×10^{-2}–5×10^{-1} M). Another compound formed was mainly the acid R^1COOH; the ester R^1COOCH_3 was obtained only in a yield of 0.13–0.16 mole per mole of the initial substance.

The results described suggest that the competitive addition of the groups RO^- and ^-OH to the carbonyl group leads to the formation of an ester and an acid. Furthermore, on the basis of kinetic data and luminescence phenomena, observed in the course of the decomposition of the hydroperoxides investigated, the authors[79] suggested that, as a consequence of the addition of the hydroperoxide hydrogen to the carbonyl group, a dioxetan is formed as an intermediate:



v. OXIDATION REACTIONS OF ALICYCLIC KETONES

1. Monocyclic Ketones

Three types of methods have been used to investigate monocyclic ketones, in particular cyclohexanone and its methyl derivatives:

(a) oxidation in a neutral medium at 100 °C of a purely thermal type or in the presence of catalysts based on variable-valence metal salts;

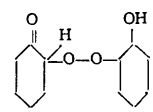
(b) oxidation in an acid medium at 60–70 °C;

(c) oxidation in a highly alkaline medium below room temperature.

In the first two cases the reaction products consist mainly of dicarboxylic acids (or their derivatives) formed as a result of ring rupture; in the third case the products are α-diketones (without ring dissociation), which are obtained by the dehydration of the intermediate hydroperoxides or from the products of their subsequent condensation.

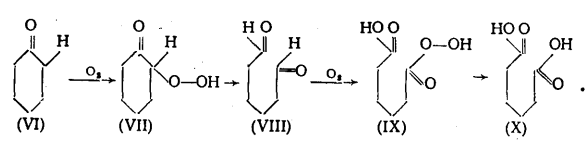
It has been shown[37] that the rate of oxidation of cyclohexanone in a neutral medium at 76 °C is low, becoming considerable at 100 °C. The kinetics of the formation of peroxides at 110°, 120°, and 130 °C have been determined by Denisov and Denisova[80]. Pritzkow[38] carried out the oxidation at 100 °C in the absence and presence of manganese laurate and determined the compounds obtained as well as the kinetics of the formation of peroxides and acids. It is noteworthy that in the presence of manganese laurate the maximum content of hydroperoxide is 9×10^{-3} mole per mole of the initial substance and is attained after only 2 h from the start of the reaction and the corresponding overall amount of the acids is 4.6×10^{-1} mole per mole of the initial substance, i.e. 7 times greater than in the absence of the catalyst.

By concentrating the crude oxidation product at a reduced pressure, it was possible[38] to obtain a product containing 10^{-1} mol mol^{-1} of peroxides. It decomposes 80 times faster in cyclohexanone than in cyclohexane, which suggests that cyclohexanone is involved in the formation of radical chains via the formation of the intermediate hydroperoxide



obtained as a consequence of the intermolecular addition of the hydroperoxide hydrogen to the carbonyl group[80]. The same phenomenon has been observed also in the general case where carbon compounds are treated with hydroperoxides[23].

The compounds obtained consist mainly of C_4, C_5, and C_6 dicarboxylic acids, with adipic acid predominating, and of smaller amounts of C_5 and C_6 monobasic acids; ω-hydroxycaproic acid and the corresponding lactone are also formed. Adipic acid is formed via a radical mechanism (probably a chain mechanism), which can be represented by the following simplified scheme:



(VI) (VII) (VIII) (IX) (X)

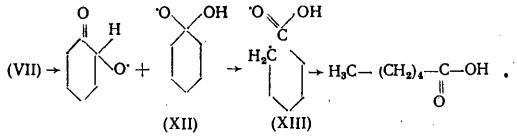
The C_5 dicarboxylic acid is formed as a result of the decarboxylation of the peracid (IX) with formation of radicals (XI) and $^{\cdot}OH$, the former being oxidised to the corresponding

semialdehyde via the classical mechanism

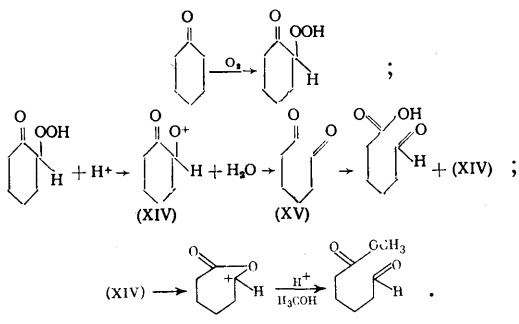
$$(IX) \rightarrow CO_2 + {}^{\cdot}OH + HO{-}CO(CH_2)_3{-}CH_2^{\cdot};$$

$$(XI) + O_2 \rightarrow HO{-}CO(CH_2)_3{-}CHO + {}^{\cdot}OH\ .$$

Monobasic acids may be formed from the hydroperoxide (VII) via the homolytic dissociation of the peroxy-bridge with subsequent dissociation of the carbon–carbon bond and the elimination of hydrogen:



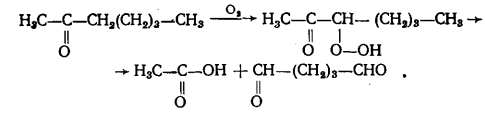
The oxidation process in an acid medium has been investigated[81] at 60 °C in CH_3OH in the presence of 4% H_2SO_4 relative to the ketone. As for the oxidation in a neutral medium, the main products (0.70 mole per mole of the initial substance) are formed via the ring dissociation; they consist of derivatives of adipic semialdehyde (0.45 mole), its oxidation product—adipic acid (0.15 mole), and ω-hydroxycaproic acid (0.10 mole). The acid group is bound in the form of the methyl ester and the aldehyde group is bound in the form of the dimethyl acetal. These compounds are formed in the presence of acids via an ionic mechanism:



Oxidation in an alkaline medium has been investigated[82] in the $(H_3C)_3COK{-}(CH_3)_3COH{-}$diglyme system. It was shown that at −20 °C the degree of dissociation of the ring is low and that the main product (0.6 mol mol^{-1}) is α-cyclohexanedione, adipic acid being formed in the smallest amount (0.1 mol mol^{-1}). Only tarry products are obtained at room temperature in the presence of CH_3ONa/CH_3OH,[83] but in hexamethylphosphoramide (HMP) solution in the presence of NaOH or CH_3ONa adipic acid is formed in a yield of 0.80 mol mol^{-1} at 24° or 80 °C.[84]

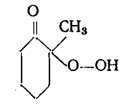
The oxidation of 2-methylcyclohexanone has been investigated in a neutral medium[85] at 100 °C in the presence of $(1–5) \times 10^{-4}$ mol mol^{-1} of copper stearate. The main products are α-ketohydroperoxide, ε-methylcaprolactone, and oxoheptanoic, caproic, and acetic acids with a small amount of methyladipic, glutaric, succinic, methylsuccinic, and $C_3–C_6$ monocarboxylic acids. Compared with the non-catalytic oxidation, the catalyst apparently drives the reaction towards the formation of acids and the amount of the latter depends little on its concentration.

The nature of the compounds obtained suggests that the main attack is directed to the carbon atom in the α-position (with the CH_3 group); this results in the formation of a tertiary hydroperoxide, which then decomposes via a radical mechanism to 6-oxoheptanoic acid. Using the reoxidation method, the latter can be used as a source of monobasic acids, namely acetic acid:



However, the formation of α-methyladipic acid indicates the attack of O_2 on the α-position relative to the secondary carbon atom.

The oxidation of 2-methylcyclohexanone has been investigated[46] in the presence of NaOH or CH_3ONa in dimethylformamide as the solvent. At −50 °C the hydroperoxide



can be isolated in the form of a liquid; at −10 °C the main reaction product is oxoheptanoic acid.

The oxidation of 3-methylcyclohexanone in the presence of cobalt stearate at concentrations from 5×10^{-4} to 5×10^{-2} mol mol^{-1} has been studied by Serov et al.[86] The main products consist of α-methyladipic, δ-oxocaproic, and acetic acids; the secondary compounds are dicarboxylic acids; β-methyladipic, α-methylglutaric, and methylsuccinic acids. The results confirm the hypothesis that oxygen attacks the two secondary carbon atoms in the α- and α′-positions relative to the C=O group and the tertiary carbon atom. The quantitative composition of the products and hence the intensity of the attack on these positions are influenced by the temperature, the reaction time, and concentration.

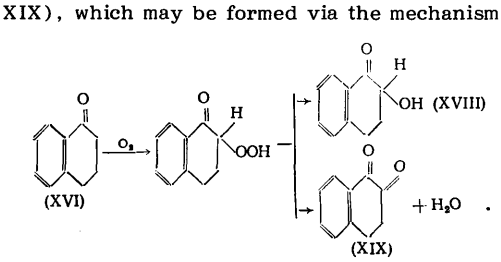
The thermal oxidation of methylcyclohexanone isomers has been investigated in detail[87] in the presence of cobalt(II) and manganese(II) stearates and cobalt(III) and manganese(II) acetylacetonates as catalysts.

Rao et al.[82] described the oxidation of $C_5–C_8$ cyclanones in the highly alkaline $(CH_3)_3COK{-}(CH_3)_3COH{-}$diglyme medium at −20 °C. It was observed that 1,2-cyclopentanedione and glutaric acids are formed from cyclopentanone in yields of 0.36 and 0.19 mole per mole of the initial substance respectively, while α-diones are obtained from the C_7 and C_8 cyclanones and then undergo aldolisation with formation of spiran derivatives[82].

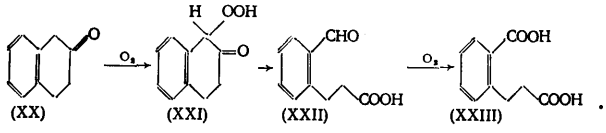
This difference in behaviour as a function of the type of ring can be due to the fact that the C_5 and C_6 diones almost always exist in the enolic form, which prevents the aldolisation reaction, while the C_7 and C_8 cyclanones exist in the keto-form and readily undergo this reaction[82].

2. Cyclanones with Condensed Rings

The thermal oxidation of α- and β-tetralinones in a neutral medium has been studied[37]. The products obtained from the α-isomer (XVI) consist of peroxides [most probably largely of the hydroperoxide (XVII)], naphthoquinol (XVIII), and the diene (XIX), which may be formed via the mechanism



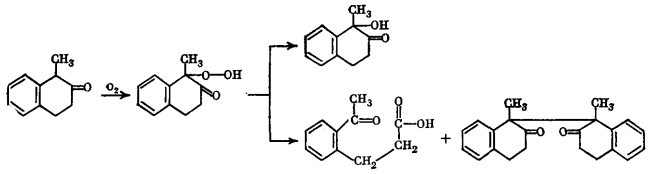
In the case of the β-isomer a single product was isolated—*o*-carboxyphenylpropionic acid (XXIII), which is apparently formed via an intermediate hydroperoxide (XXI):



(XX) (XXI) (XXII) (XXIII)

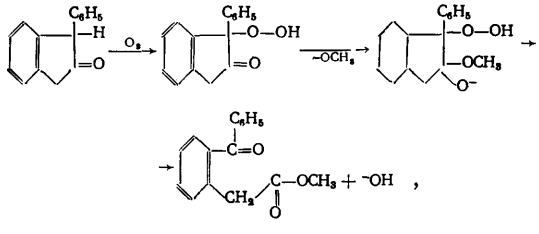
It is noteworthy that the rate of oxidation of the β-isomer is much higher than that of the α-isomer, because the carbon of the methylene group is located between the C=O and C_6H_5 groups.

The oxidation of α-methyl-β-tetralinone at room temperature has been studied by Naispuri et al.[88] The composition of the products formed via the mechanism



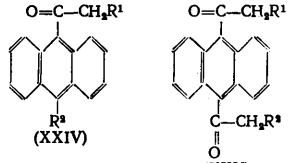
is as follows: 2-acetylphenylpropionic acid (main product, yield 0.3 mol mol^{-1}); 3,4-dihydro-1-hydroxynaphthalin-2(14)-one; 1,1-bis-3,4-dihydro-1-methylnaphthalin-2(14)-one. The latter is obtained as a result of the dimerisation of the initial keto-radical. It was not possible to isolate the hydroperoxide in a pure form.

The oxidation of 1-phenyl-2-indanone has been studied[89] in an alkaline medium (CH_3ONa/CH_3OH), and methyl *o*-benzoylphenylacetate, probably formed via the mechanism of Sawaki and Ogata[76], which in the given instance reduces to the mechanism



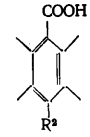
was obtained.

The oxidation (in an alkaline KOH/CH_3OH medium at room temperature) of α-monoketones and several anthracene α,α'-diketones having the general formula



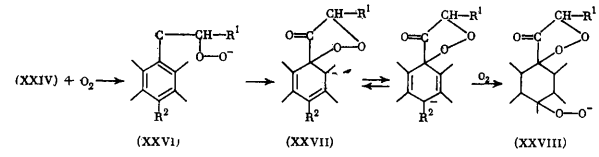
(XXIV) (XXV)

has been the subject of an interesting study by Rao et al.[90] In contrast to the classical mechanism, the products do not consist of the acid



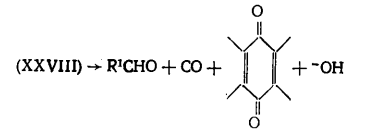
and the aldehyde R^1CHO; their nature depends on the substituent R^2. Thus anthraquinone is formed for R^2 = H and hydroxyanthrone is formed for $R^2 = C_6H_5$; in addition CO is produced in both instances.

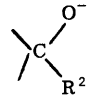
The formation of the above compounds can be accounted for by the following mechanism: the peroxide anion formed in the initial stage adds to the nearest carbon atom in the *meso*-position to form a five-membered ring, which causes the migration of the double bond and the appearance of a negative charge on another carbon atom in the *meso*-position, which is in its turn oxidised:

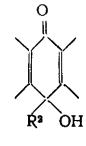


(XXVI) (XXVII) (XXVIII)

The course of the decomposition of compound (XXVIII) depends on the nature of R^2: the following reaction takes place when R^2 = H:

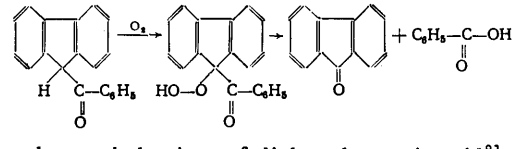


When $R^2 = C_6H_5$, the  groups are reduced to  (probably by the initial ketone) with formation of the OH group, which is followed by the formation of hydroxyanthrone:



The oxidation of fluorenyl phenyl ketone in an alkaline medium has been described[91]. In a neutral or weakly alkaline medium ($NaHCO_3$) at pH 8.4 oxygen is not absorbed and at pH 12 the absorption is very slow; it is significantly accelerated in a highly alkaline medium, for example in $KOH-C_2H_5OH-H_2O$, and the yield of fluorenone becomes 0.85 mol mol^{-1}.

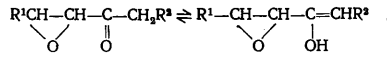
Fluorenone is formed by a general mechanism via the α-ketohydroperoxide:



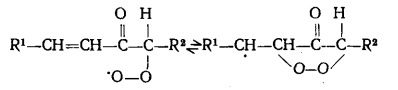
The analogous behaviour of diphenylpyruvic acid[91]—oxidation with formation of oxalic acid and benzophenone—is noteworthy. The intermediate hydroperoxide could never be isolated because of its instability.

VI. OXIDATION OF α,β-UNSATURATED KETONES

The oxidation of ketones of this type has been studied mainly in an alkaline medium (KOH/CH_3OH) above room temperature. In all cases the main reaction is the formation of an epoxyketone, which is in equilibrium with the corresponding unsaturated ketol:



This can be followed by hydrolytic oxidative dissociation steps with formation of various compounds. Hydrogen peroxide, formed by the hydrolysis of the allyl hydroperoxide produced initially, can serve as the epoxidising agent. It is noteworthy that attack by oxygen is more likely to be directed to the carbon atom located in the α-position relative to the double bond than to the carbon atom in the α-position relative to the C=O group. Indeed the peroxy-radical arising in the second case should have been stabilised, by virtue of its resonance structure, by addition to a double bond with formation of a five-membered ring:



Incidentally, it is known that α,β-unsaturated aldehydes are oxidised with much greater difficulty than the corresponding saturated aldehydes[8,10].

The oxidation of mesityl oxide[24], pent-3-en-2-one,[92] pulegone[93], piperitone[94,95], carvenone[96], carvone[97], 1-methylcyclohex-1,2-en-3-one, 1,5-dimethylcyclohex-1-en-3-one, verbenone, carvotanacetone, isophorone, and eucarvone[98] has been investigated.

VII. INTERACTION OF STEROID KETONES WITH OXYGEN

The oxidation of various steroid ketones in an alkaline medium has been considered by comparison with certain simple ketones[99] and examples of compounds formed depending on the nature of the initial ketone, have been given.

The studies of Bailey et al.[100] and of Gardner et al.[101] were concerned with the hydroxylation of pregnan-20-ones to the corresponding hydroxy-compounds. In principle, the process consists in the oxidation of the ketone in an alkaline medium (CH_3ONa/CH_3OH + DMF) with reduction of the α-ketohydroperoxide *in situ* to the corresponding ketoalcohol. The reducing agent can be H_2 [100] or $P(CH_3O)_3$.[101] The latter reduction method is more effective, because the yield of the ketoalcohol reaches 65%. This reaction has been discussed in detail by Gardner et al.[101]

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