LIQUID-PHASE OXIDATION
OF PARA-CYMENE

LIQUID-PHASE OXIDATION OF PARA-CYMENE: NATURE OF INTERMEDIATE HYDROPEROXIDES AND RELATIVE ACTIVITY OF THE ALKYL GROUPS

By

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SCOPE AND CONTENTS: Using photochemical and emulsion procedures, a study has been made of the liquid-phase oxidation of *p*-cymene with respect to the nature of the resulting hydroperoxides and their decomposition products, and the relative extent of oxidative attack at the methyl and isopropyl groups. Hydroperoxide decomposition was negligible in the photochemical oxidations at 60°C., and the product was shown to consist of 20% primary and 80% tertiary hydroperoxide by reduction of the total product and fractionation of the resulting alcohols. The following compounds were shown to be present in the emulsion oxidation product in addition to the above mentioned hydroperoxides: dimethyl-*p*-tolylcarbinol, *p*-methylacetophenone, *p*-isopropylphenylcarbinol, cumic acid, *p*-acetobenzoic acid, *p*-(α-hydroperoxyisopropyl) benzoic acid, and *p*-(α-hydroxyisopropyl) benzoic acid. By chromatographic separation of the acids and reduction of the other products, the relative extent of attack at the two positions was shown to be 1:4, identical with that of the photochemical oxidation. Pure tertiary hydroperoxide has been obtained for the first time.

ACKNOWLEDGEMENTS

The author wishes to express his sincere appreciation to Dr. A.N. Bourns for his helpful criticisms and advice in guiding this research.

The cooperation of Mr. F. Hunt and Mr. K. Wright, whose earlier investigations broke ground for this work, is gratefully acknowledged.

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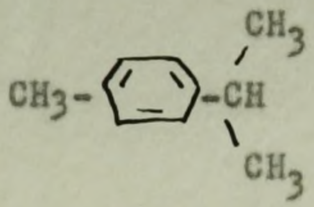
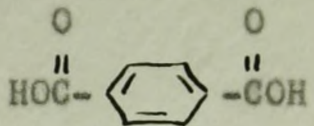
GENERAL INTRODUCTION

A study of the liquid-phase oxidation of *p*-cymene, I, with molecular oxygen has practical as well as fundamental significance. This compound, formed as a by-product of the sulfite pulping process, is a potential source of the industrially important terephthalic acid, II, which is used



I

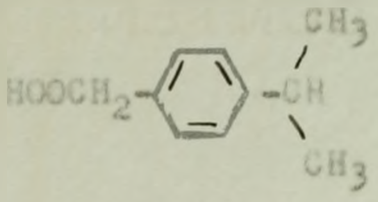


II

in the manufacture of a number of important plastics and synthetic fibres. This acid is at present prepared from *p*-xylene by either drastic oxidation with chemical oxidizing agents, such as permanganate, or by vapour-phase oxidation over vanadium pentoxide. Both the hydrocarbon and the methods for its oxidation are expensive and for this reason a cheaper method of producing the acid is highly desirable.

Preliminary studies, as yet unpublished, on the liquid-phase oxidation of *p*-cymene with air in the presence of cobalt napthenate as a catalyst have been carried out in this laboratory by Hunt. The results showed little promise, however, in so far as the formation of terephthalic acid was concerned. It was then decided that before continuing this more practical aspect of the problem, an effort should be made to gain a better understanding of the oxidation reaction itself. Accordingly the work reported in this thesis deals primarily with a study of the nature of the hydroperoxides formed as intermediates in cymene oxidation and the relative extent of oxidative attack on the methyl and isopropyl groups under different reaction conditions. In order to establish the latter it has been necessary to investigate the nature and composition of the products formed by decomposition of the hydroperoxides under the conditions used.

An examination of the structure of p-cymene reveals that the two most probable monohydroperoxides to result from the oxidation of this hydrocarbon are the primary compound, III, formed by the attack of oxygen on the methyl side chain, and the tertiary hydroperoxide, IV, resulting from oxygen attack at the tertiary carbon of the isopropyl group. In 1939, Helberger, Rebay, Fettback (1) carried out the oxidation of pure p-cymene with molecular oxygen at 60°C in the presence of sunlight and obtained a peroxidic product to which they assigned structure III on the basis of the isolation of cuminaldehyde, V, as its semicarbazone, from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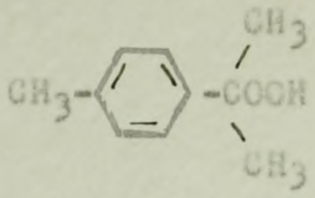
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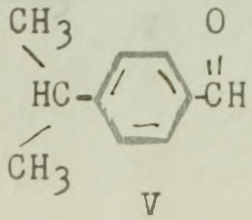
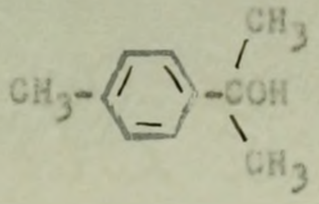

V

the products of the decomposition of the sodium salt in boiling water. More recently, a patent (84) has been issued in the name of Hercules Powder Co. dealing with the oxidation of aromatic hydrocarbons with air or oxygen in the presence of aqueous alkali. The peroxidic product obtained from a *p*-cymene oxidation, on reduction with sodium sulfide, furnished a product consisting of 90.5% dimethyl-*p*-tolylcarbinol, VI, and 9.5% *p*-methylacetophenone, VII. The absence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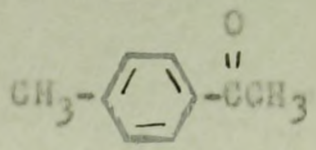
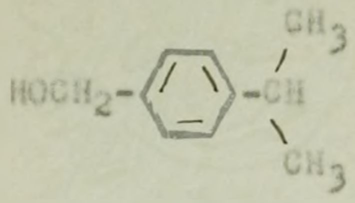

VII

of the reduction product of the primary hydroperoxide, III, namely *p*-isopropylphenylcarbinol, VIII, would suggest that

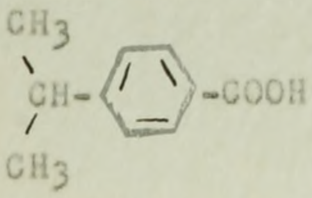

VIII

III was not a product of the oxidation under these conditions.

The seemingly contradictory results obtained using the two oxidation procedures is indeed surprising since current ideas concerning the mechanism of hydrocarbon autoxidation would strongly suggest a product of similar composition should be formed in each case. It was therefore proposed to re-investigate the oxidation of *p*-cymene by the two methods and, in each case, to carefully determine the composition of the total product. It was hoped that this study would not only indicate the nature of the hydroperoxides formed in the reaction but would also provide an accurate measure of the relative activity of the methyl and isopropyl groups toward oxidative attack.

The oxidation in the presence of aqueous alkali was carried out using a procedure recently developed by Armstrong, Hall, and Quinn (2) for the preparation of cumene hydroperoxide. It consists in passing gaseous oxygen into an emulsion of the hydrocarbon and aqueous sodium carbonate in the presence of sodium stearate as the emulsifying agent. This procedure will hereafter be referred to as an emulsion oxidation.

Employing methods described fully in the Experimental section, seven compounds were isolated from the products of the emulsion oxidation in addition to the expected primary and tertiary hydroperoxides, III and IV. These products were a ketone, p-methylacetophenone, VII, two alcohols, dimethyl-p-tolylcarbinol, VI, and p-isopropylphenylcarbinol, VIII, and four solid carboxylic acids, cumic acid, IX, p-acetobenzoic acid, X, p-(α-hydroperoxyisopropyl) benzoic acid, XI, and p-(α-hydroxyisopropyl) benzoic acid, XII.



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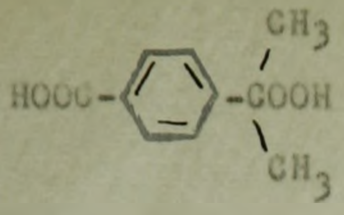
X



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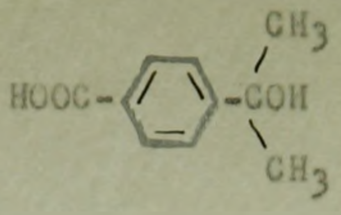


XII

In order to determine accurately the relative extent of oxidative attack at the two positions an aliquot of the emulsion oxidation product was reduced with lithium aluminium hydride, after removal of the carboxylic acids, and the reduction product carefully fractionated into its component alcohols. A procedure has also been developed for obtaining for the first time pure tertiary hydroperoxide, IV, free from its primary isomer, III, and the physical properties of the compound have been determined.

The procedure used in the photochemical reaction was similar to that described by Helberger _et al_ except that a mercury-vapour lamp was used as a source of illumination. Examination of the reaction product established the almost complete absence of products other than hydroperoxides. For this reason it was possible to determine both the composition of the hydroperoxide product and the ratio of attack at the primary and tertiary positions by reduction of the total oxidation mixture with lithium aluminium hydride and fractionation of the resulting alcohols.

HISTORICAL INTRODUCTION

Although organic hydroperoxides have been known since 1901, it has only been during the past decade that they have received close attention. Interest in this class of compounds followed the discovery that liquid-phase oxidation reactions proceed through a hydroperoxide intermediate. Since such oxidation reactions are of very great practical importance, this discovery resulted in an intensive investigation of methods for the production of hydroperoxides and of the nature of their decomposition reactions.

The present review will be restricted to a discussion of the methods which have been developed for the preparation of hydroperoxides with particular attention being given to studies on the mechanism of hydroperoxide formation in hydrocarbon oxidations. The question of the point of oxidative attack in those hydrocarbons providing alternate reaction sites will also be considered. Under each method of preparation tables will be presented listing the hydroperoxides which have been prepared by the method indicated. An effort has been made to include all hydroperoxides which have been reported in the literature up until the present time.

Hydroperoxide Formation by Hydrolysis of Alkyl Esters with Hydrogen Peroxide

This method was developed by Baeyer and Villiger (3) who applied it to the preparation of the first known organic hydroperoxides, methyl and ethyl hydroperoxide. The reaction of hydrogen peroxide on alkyl esters is given by the following general equation:

$$ROA + H_2O_2 \longrightarrow ROOH + AOH \qquad (i)$$

Further reaction of the resulting hydroperoxide with the alkyl ester leads to the formation of some peroxide:

$$ROA + ROOH \longrightarrow ROOR + HOA \qquad (ii)$$

Sulfate, perchlorate and phosphate esters (represented by ROA in above equations, where R is the organic radical and AOH the acid involved) have all been used for the preparation of hydroperoxides. It is also of interest to note that triphenyl methyl chloride has a sufficiently weak carbon-chlorine bond to yield the hydroperoxide by this method (4).

$$PH_3C\text{-}Cl + H_2O_2 \longrightarrow PH_3C\text{-}OOH + HCl \qquad (iii)$$

The method is fairly wide in scope since most organic alcohols can be readily converted to the corresponding ester. Yields are low, however, with the exception of the hydroperoxides prepared from the esters derived from tertiary alcohols. These have been prepared in up to 91per cent yields by Criegee and Dietrich (5). A serious fault of this method is the danger of violent decomposition reactions. Dietrich was critically injured in an explosion.

Hydroperoxides, isolated by this process, are shown in Table I.

TABLE I

HYDROPEROXIDES FORMED BY HYDROLYSIS OF ALKYL ESTERS WITH HYDROGEN PEROXIDE

Hydroperoxide	Ester	References
Methyl-	Dimethyl sulfate	3,6
Ethyl-	Diethyl sulfate	3,6
Propyl-	Propyl sulfate	7
Isopropyl-	Isopropyl sulfate	7
Tertiary butyl-	Tertiary butyl phosphate	8
	Tertiary butyl sulfate	5,9,10
Tertiary amyl-	Tertiary amyl sulfate	9
Triethylmethyl-	Triethylmethyl sulfate	11
Pentamethylethyl-	Pentamethylethyl sulfate	5,11
1,1,2,2-Tetramethylethyl	Tetramethylethyl sulfate	5
1-Methylcyclohexyl-	Methylcyclohexyl sulfate	11
1-Ethylcyclohexyl-	1-Ethylcyclohexyl sulfate	5
Decahydro-4-α-napthyl-	Decahydro-4-α-napthyl sulfate	5
Triphenylmethyl-	Triphenylmethyl chloride	4
Meso-diphenyldihydroanthracene	Meso-diphenyldihydroanthracene chloride	12
Phenyldibenzoxanthenyl-	Phenyldibenzoxanthene perchlorate	13
Meso-m-nitrophenyl-1,2,7,8-dibenzoxanthenyl-	Meso-m-nitrophenyl-1,2,7,8-dibenzoxanthenyl perchlorate	14

TABLE I (cont'd.)

Hydroperoxide	Ester	References
Meso-p-biphenyl-1,2,7,8-dibenzoxanthenyl-	Meso-p-biphenyl-1,2,7,8-dibenzoxanthene perchlorate	14
Meso-p-methoxyphenyl-1,2,7,8-dibenzoxanthenyl-	Meso-p-methoxyphenyl-1,2,7,8-dibenzoxanthene perchlorate	14
14-(Chlorophenyl) dibenzo-(aj)-xanthen-14-yl-	14-(Chlorophenyl)dibenzo-(aj)-xanthen-14-yl perchlorate	14

Preparation of Hydroperoxides by the Addition of Hydrogen Peroxide to Carbonyl Compounds

In 1931 Rieche (15,16) observed that in a cold mixture of aldehyde and hydrogen peroxide an equilibrium existed between the reactants, an hydroxyhydroperoxide, XIII, and a dihydroxyperoxide, XIV:

$$\begin{tikzcd}
H_2O_2 + RCHO \arrow[r, shift left] & RCH(OH)OOH \arrow[l, shift left] \arrow[d, shift left, "+ RCHO"] & XIII \\
 & RCH(OH)OOCH(OH)R \arrow[u, shift left] & \\
 & XIV &
\end{tikzcd}$$

(iv)

He further observed that compound XIV was the more stable of the two and in an aqueous medium tends to be formed to the greatest extent. In dry solvents, such as anhydrous ether, however, the equilibrium was such that there was a greater tendency for compound XIII to form, allowing an isolation of the hydroxyhydroperoxide in the pure form. Somewhat later Milas (17) extended the application of Rieche's method by employing cyclic ketones in the place of aldehydes.

The scope of the process is necessarily limited by the fact that only hydroxyhydroperoxides may be produced.

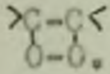
Hydroperoxides prepared by the Rieche-Milas method are listed in Table II.

TABLE II

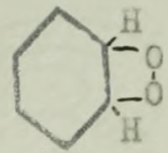
HYDROPEROXIDES FORMED BY ADDITION OF HYDROGEN PEROXIDE TO CARBONYL COMPOUNDS

Hydroperoxide	Carbonyl Compound	References
1-Hydroxymethyl-	Formaldehyde	18
1-Hydroxyethyl-	Acetaldehyde	19
1-Hydroxypropyl-	Propionaldehyde	19
1-Hydroxybutyl-	n-Butyraldehyde	19
1-Hydroxypentyl-	Valeraldehyde	19
1-Hydroxyhexyl-	n-Caproic aldehyde	19
1-Hydroxyheptyl-	Heptaldehyde	19
1-Hydroxyoctyl-	n-Caprylic aldehyde	19
1-Hydroxynonyl-	Nonanal	19,20
1-Hydroxydecyl-	Decanal	19,20
1-Hydroxyundecyl-	Undecanal	19,20
1-Hydroxydodecyl-	Dodecanal	19,20
1-Hydroxycyclopentyl-	Cyclopentanone	21
1-Hydroxycyclohexyl-	Cyclohexanone	17,21,22
1-Hydroxycycloheptyl-	Cycloheptanone	17,21
1-Hydroxycyclooctyl-	Cyclooctanone	17,21
1-Hydroxymethyl-cyclohexyl-	Methylcyclohexanone	21

Hydroperoxide Formation by the Oxidation of Hydrocarbons with Elemental Oxygen

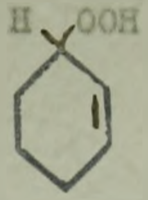
The oxidation of olefinic hydrocarbons by elemental oxygen has been the subject of intensive investigation for a number of years. Many early theories have been proposed to account for the oxidation reaction but the one which most nearly approached the theory generally accepted today was the "peroxidation theory" suggested in 1897 by Bach (23) and Engler and Wild (24,25,26), and later modified by Callendar (27), Egerton(28), and Ubbelohde (29). According to this theory the primary intermediate of olefin oxidation is a cyclic peroxide of the structure  $\underset{O-O}{>C-C<}$. Other schools of thought (30), however, held the view that the products of olefin oxidation reactions are formed directly without going through a peroxide intermediate.

In 1928 Stephens (31) discovered that cyclohexene, on treatment with oxygen in the sunlight, gave a liquid peroxide whose composition corresponded to the molecular formula $C_6H_{10}O_2$, and which could be isolated by distillation. He concluded that this peroxide had the structure XV .



XV

This peroxide was later isolated by Hock (32,33,34) who agreed with Stephens' formulation of its structure. Criegee, Pilz, and Flygare (35) in 1939, however, carefully studied the chemical behaviour of the peroxide compound formed from cyclohexene. They came to the conclusion that the Stephens' structure was incorrect, and that the compound actually was a hydroperoxide of structure XVI in which the double bond was still intact.



XVI

They based their conclusion upon the following evidence:

(a) The compound is reduced by sodium sulfite to cyclohexenol, XVII.

XVII

(b) One mole of bromine is absorbed per mole of compound.

(c) There is one atom of active hydrogen per molecule.

The isolation of other hydroperoxides of both unsaturated and saturated hydrocarbons (Table IV) led later investigators to the opinion, now generally held, that liquid phase hydrocarbon oxidation always proceeds through a hydroperoxide intermediate.

Mechanism of Hydroperoxide Formation

On the basis of the large amount of evidence which has accumulated during the past few years, it is now quite generally accepted that the oxidation of a hydrocarbon proceeds by a free radical chain mechanism (36,37,38,39). As in other chain reactions the general sequence of oxidative attack comprises initiation, propagation, and termination steps, and may be expressed by the following equations:

A. Initiation; $RH \xrightarrow{\text{activation}} R^\bullet + H^\bullet$ (v)

B. Propagation; $R^\bullet \quad O_2 \longrightarrow ROO^\bullet$ (vi)

$ROO^\bullet + RH \longrightarrow ROOH + R^\bullet$ (vii)

C. Termination; $R^\bullet + R^\bullet \longrightarrow RH + R(-H)$ (viii)

$ROO^\bullet + {}^\bullet OH \longrightarrow ROH + O_2$ (ix)

$R^\bullet + R^\bullet \longrightarrow R\text{-}R$ (x)

etc.

Initiation

$$RH \xrightarrow{\text{activation}} R^\bullet + H^\bullet \qquad (v)$$

To understand better the phases present in the initiation of hydrocarbon oxidation, it would be helpful to examine a representative hydrocarbon, the oxidation of which has been investigated intensively. Tetralin is such a compound (40,41,42,43).

In the absence of catalysts the autoxidation of tetralin at the 76°C passes through four distinct stages (43).

(a) An induction period lasting some hours with very little absorption of oxygen, but during which the peroxide content of the liquid gradually increases.

(b) An autocatalytic stage in which the reaction accelerates until the peroxide content is about 5 per cent.

(c) A steady state, with constant and fairly rapid

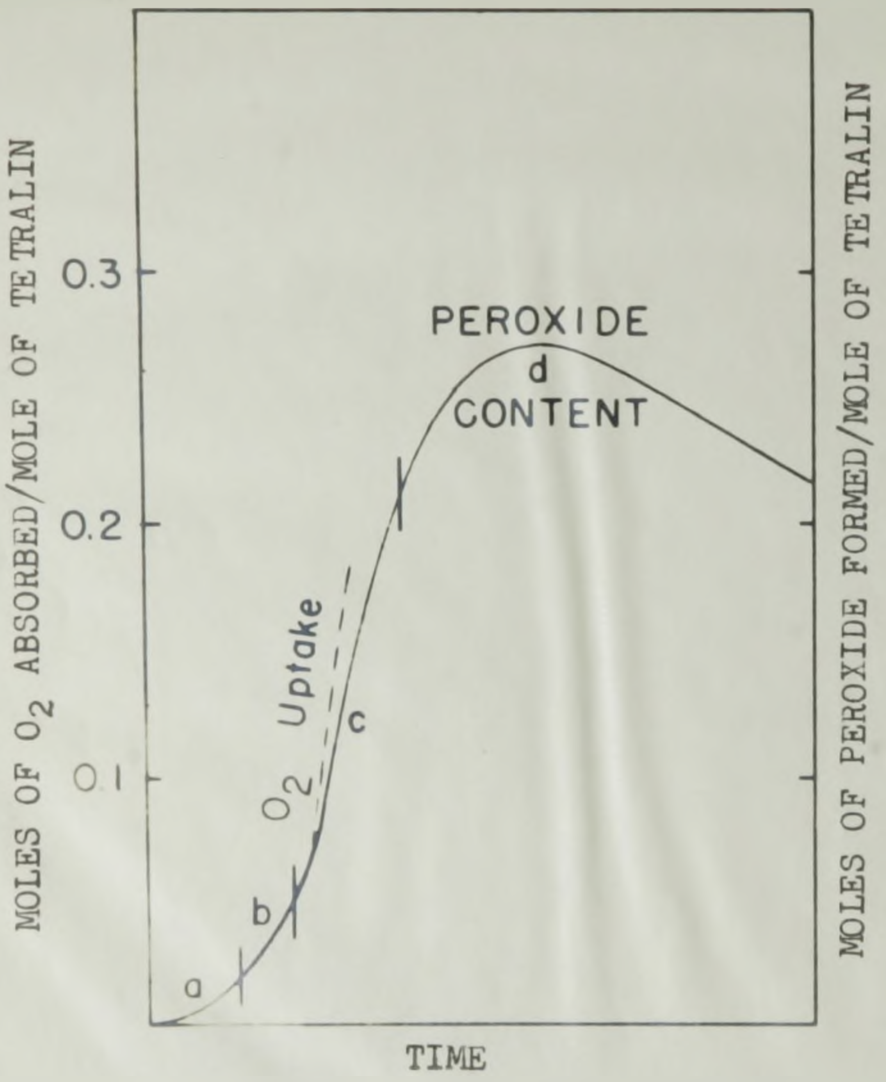

MOLES OF O_2 ABSORBED/MOLE OF TETRALIN
0.3
0.2
0.1
MOLES OF PEROXIDE FORMED/MOLE OF TETRALIN
PEROXIDE
d
CONTENT
O_2 Uptake
a
b
c
TIME

FIG 1

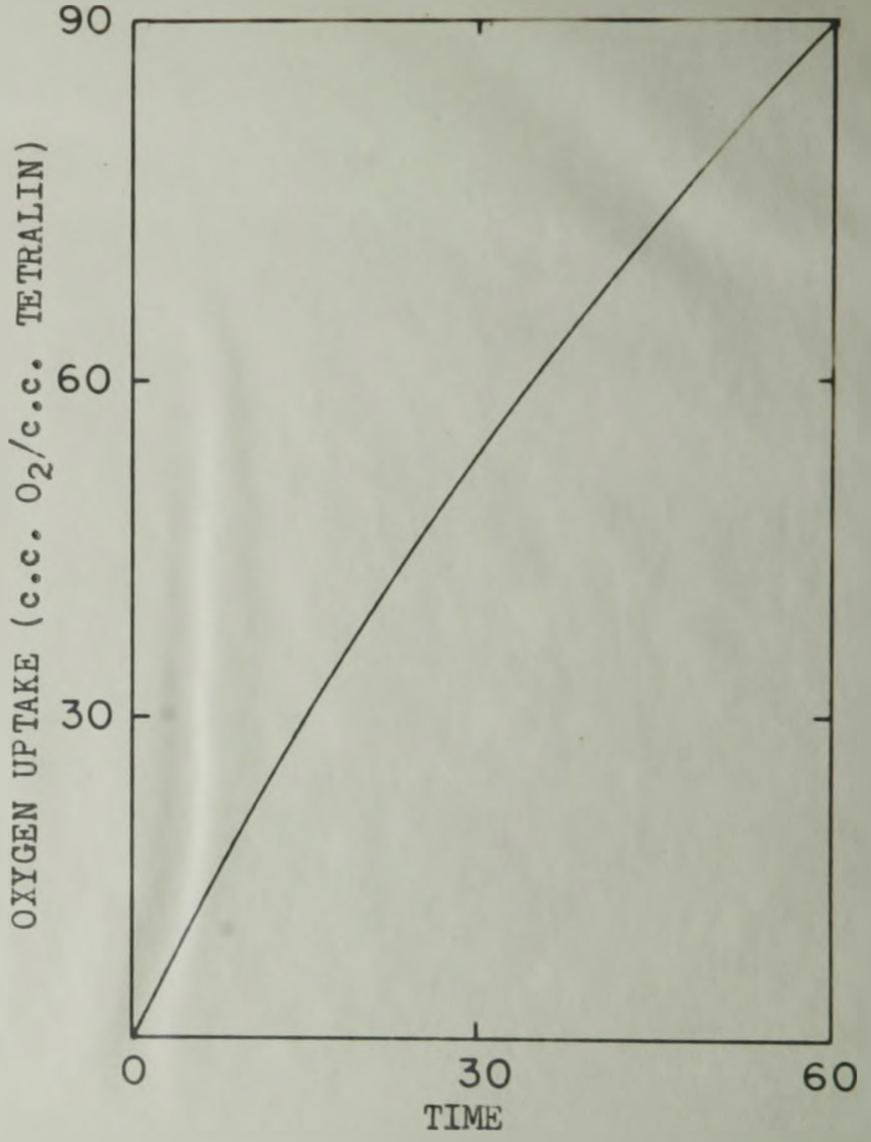

90
60
30
OXYGEN UPTAKE (c.c. O_2/c.c. TETRALIN)
0
30
60
TIME

FIG 2

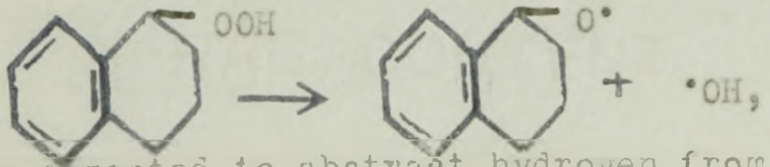
oxygen uptake, which persists until about 30 per cent of the tetralin has been oxidized.

(d) Finally a period in which there is a decline in the rate of autoxidation although a considerable percentage of unreacted hydrocarbon still remains.

Fig. I indicates the course of the reaction under these conditions. Throughout stages (a) and (b) the hydroperoxide is formed quantitatively, but its decomposition becomes apparent as a slight secondary reaction in stage (c). In stage (d) a point is reached at which the hydroperoxide is decomposing faster than it is being formed. Stage (a) and part of (b) are together often termed "the induction period".

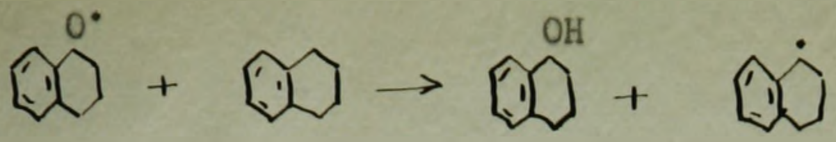
When the oxidation of tetralin is carried out in the presence of five per cent added tetralin hydroperoxide, the induction period is eliminated. A similar result is observed in an oxidation catalyzed by benzoyl peroxide, a compound known to initiate free radical reactions. These facts, therefore, strongly suggest that tetralin hydroperoxide, like benzoyl peroxide, is capable of initiating the reaction by generating free radicals. Additional evidence to support this explanation of the autocatalytic nature of the primary stage of autoxidation may be cited.

(a) If free radicals are produced by the reaction they

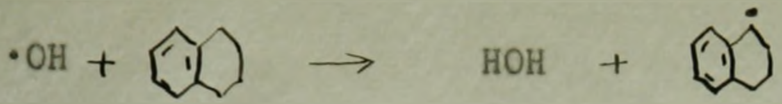


(xi)

would be expected to abstract hydrogen from available hydrocarbon molecules to form α-tetralol and water.



(xii)



(xiii)

These compounds are invariably found in the products of tetralin oxidation.

(b) Tetralin hydroperoxide has been shown to be a polymerization catalyst of the same order of efficacy as dibenzoyl peroxide.

Hydrocarbon-soluble salts of heavy-metals have been found to catalyze hydrocarbon oxidations. It is of interest, therefore, to compare Fig. 2, showing the variation of oxidation rate with time in a copper stearate catalyzed oxidation of tetralin (40),with the corresponding plot (Fig.1) for the uncatalyzed reaction. No induction period is evident with the former. The kinetics of the heavy-metal ion catalyzed oxidation of tetralin and that of the benzoyl peroxide sensitized reaction have been shown to be identical (40,42). This would suggest that a free radical mechanism holds for the metal catalyst reaction as well as for the benzoyl peroxide initiated oxidation. George and Robertson (41) concluded from kinetic considerations that metal ions initiate the reaction chains by activating the oxygen through the formation of an activated complex. In a review article by Frank (44a) the opinion was expressed that the metallic ions actually abstract hydrogen atoms from the hydrocarbon molecules to create free radicals. At the recent meetings of the Faraday Society in

Toronto, Bawn (44b) presented evidence that in cobalt catalyzed autoxidation reactions it is the trivalent state of the ion which is the active entity. This ion, he suggests, may initiate the oxidation by reaction with the reactant or with hydroperoxide formed by thermal reaction, and this reaction in all cases leading to the generation of a radical.

Propagation

$$R\cdot + O_2 \longrightarrow RO_2\cdot \qquad (vi)$$

$$RO_2\cdot + RH \longrightarrow RO_2H + R\cdot \qquad (vii)$$

The above equations represent the propagation steps of hydrocarbon oxidation. The fact that even the relatively stable triphenylmethyl radicals combine almost instantly with oxygen demonstrates the ease with which the reaction, expressed by equation (vi), proceeds. Cleavage of the R-H bond by $RO_2\cdot$, on the other hand, requires a much higher activation energy, and it is at this stage in the reaction sequence that the ease of oxidation of reactive hydrocarbons, such as tetralin, differs from that of less reactive compounds, represented by cyclohexane.

Termination

$$R^{\circ} + R\cdot \longrightarrow RH + R(-H) \qquad (viii)$$

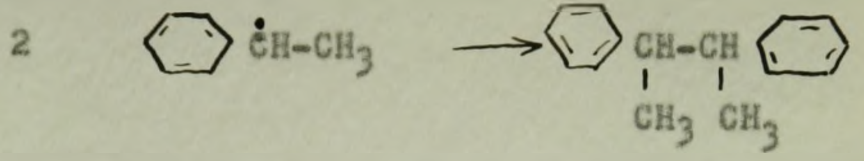
$$ROO\cdot + \cdot OH \longrightarrow ROH + O_2 \qquad (ix)$$

$$R\cdot + R\cdot \longrightarrow R\text{-}R \qquad (x)$$

etc.

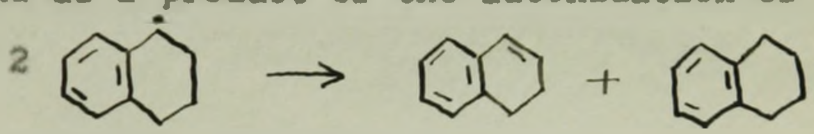
Chain termination, as a result of free radical destruction, may be brought about in a number of ways as indicated in the above equations. Robertson and Waters (43) have compiled a more complete list for tetralin:

(a) dimerization of R• :- although no dimer has been found with tetralin, it has been observed in the autoxidation of ethyl benzene (45,46)



(xiv)

(b) disproportionation of R• :- 1,2-dihydronapthalene is always found as a product of the autoxidation of tetralin



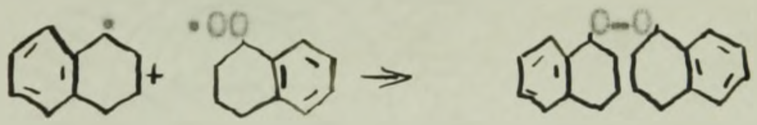
(xv)

(c) dimerization of ROO• :-

$$2ROO\cdot \longrightarrow ROOOOR \qquad (xvi)$$

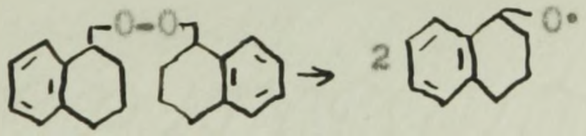
This is highly improbable.

(d) union of R• and ROO• :-



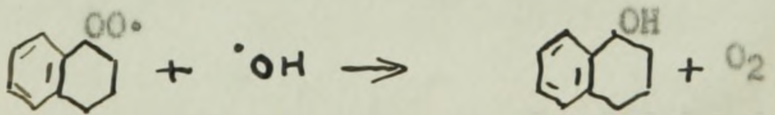
(xvii)

The reaction would not lead to a stable product but would decompose to initiate new radicals.



(xviii)

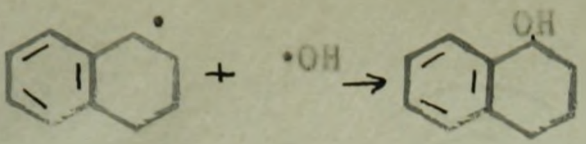
(e) formation of α-tetralol from RCHOO• :-



(xix)

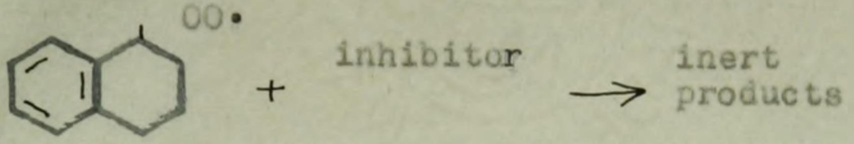
Direct scission of the hydroperoxide at the O-O bond yields the required •OH radicals (see pg. 15).

(f) direct formation of α-tetralol :-



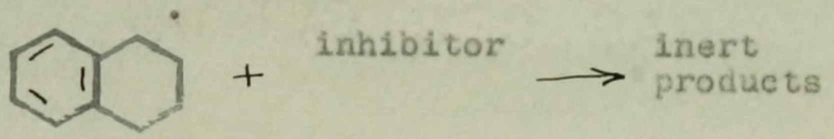
(xx)

(g) reaction of ROO• with an inhibitor :-



(xxi)

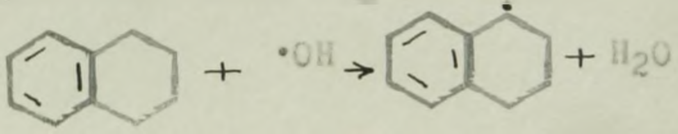
(h) reaction of R• with an inhibitor :-



(xxii)

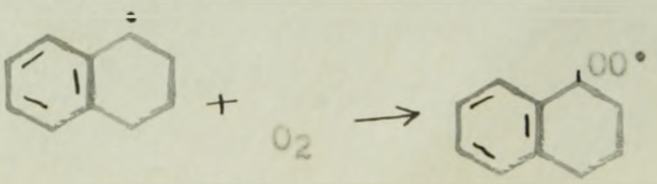
It has been found experimentally that the oxygen liberated when tetralin hydroperoxide is catalytically decomposed is approximately equal to the α-tetralol produced. Hence (e) is regarded as the main chain-stopping process when the hydroperoxide concentration has risen to a sufficiently high value. Mechanism (b) is probably the main reaction initially. Robertson and Waters conclude from these results and from considerations of the autocatalytic character of the uncatalyzed reaction that the main reaction sequence for tetralin can be represented in the following manner.

Chain Initiation;



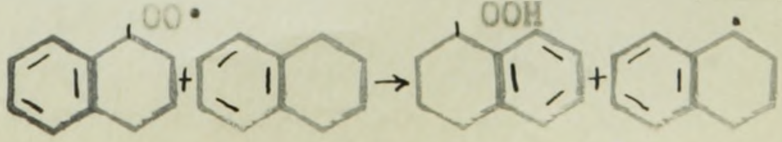
(xxiii)

Chain Propagation;

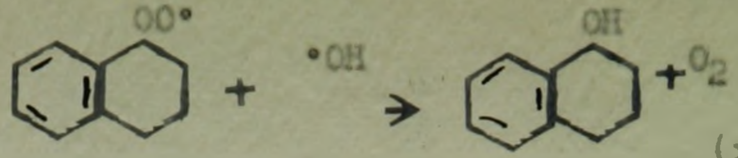


(xxiv)

(xxv)



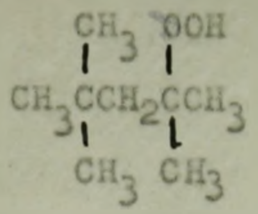
Chain Termination;



(xxvi)

Point of Oxidative Attack

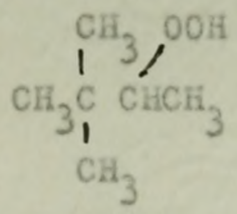
In early studies of the autoxidation of liquid hydrocarbons a great deal of confusion existed as to the actual positions favoured in the attack of oxygen. Grun (47), from experimental results, came to the conclusion that elemental oxygen preferred to enter a carbon chain at a point as far removed from a methyl group as possible. Burwell (48), using long straight-chain paraffins, also found that in practically no case was the end or methyl group attacked. Pope, Dykstra, and Edgar (49), from studies on the oxidation of octanes, arrived at the opposite conclusions, namely, that oxygen first attacks the methyl group at the end of the longest straight-chain. Stephens (45), on the other hand, found that oxidation of ethyl-and n-propylbenzenes led to the formation of acetophenone and propiophenone, respectively. Therefore the point of attack with benzene hydrocarbons is at a position α to the centre of unsaturation and not at the end of the carbon chain. Under the same conditions, tertiary butylbenzene was not oxidized, a fact which demonstrates the necessity of a hydrogen atom at the point of attack. Walsh (50,51), from his study of the oxidation of hydrocarbon fuels, found that a tertiary carbon atom is attacked in preference to a secondary carbon atom, and it, in turn, in preference to a primary atom. This generalization is illustrated by his work on the oxidation of 2,2,4-trimethylpentane and neo-hexane. 2,2,4-Trimethylpentane contains primary, secondary, and tertiary carbon atoms, but the product of oxidation is almost exclusively the tertiary hydroperoxide XVIII.



$$\begin{array}{c} CH_3\ \ OOH \\ |\qquad | \\ CH_3CCH_2CCH_3 \\ |\qquad | \\ CH_3\ \ CH_3 \end{array}$$

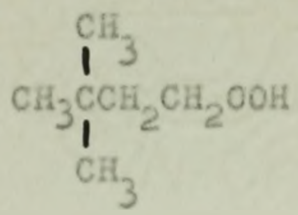
XVIII

neo-Hexane, a hydrocarbon with no tertiary carbon atom, on the other hand, gives rise to secondary XIX and primary hydroperoxides with the former predominating.



$$\begin{array}{c} CH_3\ \ OOH \\ |\quad / \\ CH_3C\ CHCH_3 \\ | \\ CH_3 \end{array}$$

XIX



$$\begin{array}{c} CH_3 \\ | \\ CH_3CCH_2CH_2OOH \\ | \\ CH_3 \end{array}$$

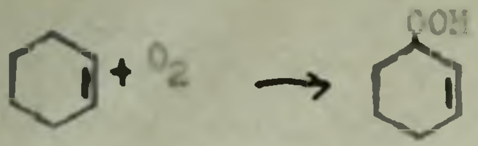
(or other primary hydroperoxides)

XX

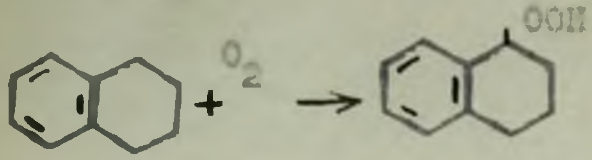
Walsh's generalizations appear to hold in the liquid phase at temperatures up to 150°C. At higher temperatures and also in the vapour phase, there is no doubt that different oxidative mechanisms occur. This is shown by the fact that in the gas phase at 200 - 265°C straight-chain paraffins undergo oxidation much more readily than branched chain compounds (52).

In the case of olefin oxidation, the work of Farmer (53, 54), Hock (55), and Criegee (35), has clearly demonstrated that the favoured position for attack is not at the double bond but at the activated carbon atom α to the double bond.

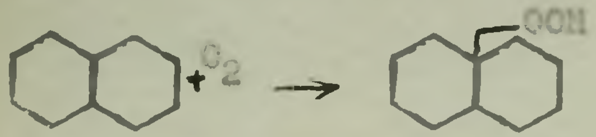
These generalizations concerning the preferred position of attack in hydrocarbon oxidation find support in the structure of the hydroperoxides formed in the following reactions:



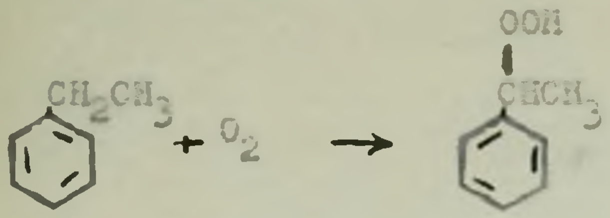
35,55 (xxvii)



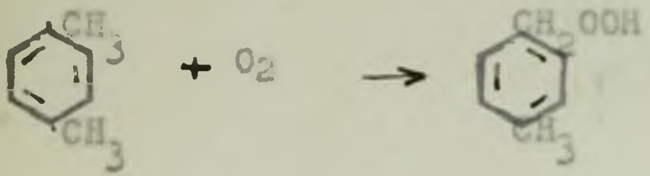
43,56 (xxviii)



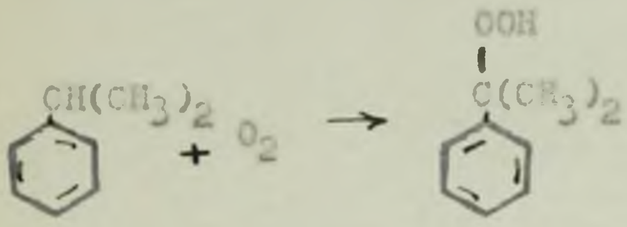
57 (xxix)



58 (xxx)



58 (xxxi)



59 (xxxii)

Further support is provided by the studies of George and Robertson (60) on the rates of the metal-ion catalyzed oxidation of a wide variety of hydrocarbons, the results of which are found in Table III.

TABLE III

RATES OF HYDROCARBON AUTOXIDATION

Hydrocarbon	Rate[1]
Aromatic	
Napthalene	0.0
Tetralin	125.0
Ethylbenzene	7.5
iso-Propylbenzene	6.0
Cymene	7.0
tert-Butylbenzene	0.02
Mesitylene	4.8
Napthenic	
Decalin	4.3
Ethylcyclohexane	1.5
iso-Propylcyclohexane	2.2
1-Methyl-4-isopropylcyclohexane	5.7
tert-Butylcyclohexane	0.35
1,2-Dimethylcyclohexane	0.5
1,4-Dimethylcyclohexane	5.0
1,3,5-Trimethylcyclohexane	11.2
Paraffinic	
Straight chain paraffins (C_{15}-C_{25} mixture)	0.25

---

[1] The rates are expressed in terms of the amount of oxygen absorbed by the hydrocarbons at 110°C using 0.5 copper stearate as a catalyst.

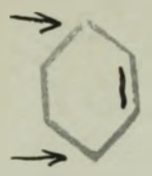
Theoretical interpretations of the empirical rules have been given by George and Robertson (60). Walsh suggests that since the oxidation of hydrocarbons undoubtedly follows a chain mechanism involving free radicals as carriers, the phrase "point of oxygen attack" means the point at which free radicals attack the hydrocarbon molecule. Free radicals are electrophilic in nature and therefore will preferentially attack the sites of greatest electron density. Since alkyl groups show a negative inductive effect, it follows that the order of increasing negative charge in the attacked carbon and therefore the order of reactivity of that carbon towards the attacking radical will be primary $<$ secondary $<$ tertiary. In addition, the reactivity will also depend upon the strength of the carbon-hydrogen bond which has been shown to follow the order primary $<$ secondary $<$ tertiary (61). According to Walsh, these two factors, relative electron density and relative carbon-hydrogen bond strength, account for the order of reactivity observed.

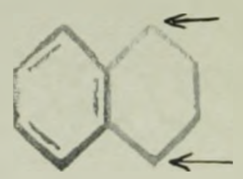
In the oxidation of unsaturated systems George and Robertson conclude that the point of attack is invariably at the weakest carbon-hydrogen bond. The strength of such a bond is given by the energy required to remove the hydrogen atom, and George and Robertson suggest that this separation may be thought of as proceeding in two steps:

(a) removal of the atom without alteration of the electronic structure of the radical

(b) delocalization of the free electron of the radical if resonance is possible.

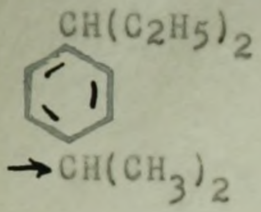
The first step will require energy roughly equal to the strength of the carbon-hydrogen bond in methane, whereas the second step will liberate energy amounting to the resonance energy of the radical. The larger the resonance energy of this radical the smaller the energy required to separate the hydrogen atom from the carbon being attacked. An illustration using toluene is given by these authors. In step (a) the hydrogen atom from the methyl group is removed and the valencies of the carbon atom remain tetrahedral. In step (b) the carbon valencies become planar and the π electrons of the ring then can conjugate with the unshared electron in the p orbital of the side chain carbon, thus stabilizing the radical through resonance energy. This interpretation accounts for the preferred position of attack in cyclohexene and tetralin, and

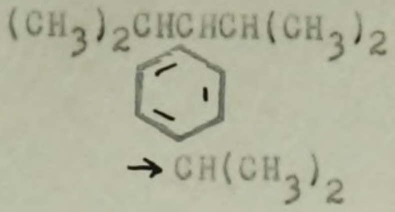


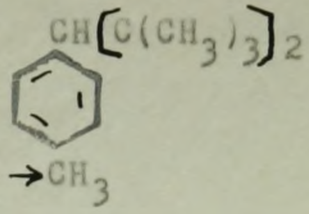


also explains why the carbon α to the aromatic nucleus is attacked in ethylbenzene and similar aromatic hydrocarbons.

The approach of George and Robertson may also be extended to account for the fact that a tertiary carbon is attacked in preference to a secondary carbon and it, in turn, in preference to a primary. If a methyl group is joined to the carbon atom from which hydrogen has been removed in the formation of the radical, then this radical will be stabalized by hyperconjugation with the three carbon-hydrogen bonds of the methyl group. If two methyl groups are so joined, then six carbon-hydrogen bonds will hyperconjugate with the electron of the trivalent carbon providing even greater stabilization. An ethyl group will be less effective than methyl and an isopropyl group still less effective since there are but two and one carbon-hydrogen bonds, respectively, which can enter into hyperconjugation. One may make certain predictions which would be interesting to verify:







In the latter example the tertiary radical will not be stabalized by hyperconjugation, and it might be expected that it would have no greater tendency to form (ignoring the weaker inductive effect) than the primary radical from the p-methyl group. In fact, the steric factor might actually favour primary radical formation.

A somewhat more fundamental approach to the problem of relative activity in free radical reactions is to consider the energy of the transition state relative to that of the initial state, i.e., the energy of activation. It is not possible, of course, to evaluate the energy of the transition state quantitatively. Nevertheless, quantitative predictions can be made by considering the transition state to have a structure intermediate between reactant and product. It follows that any substituent which will stabalize the product (radical) relative to the reactant (hydrocarbon) will also tend to stabalize the transition state, and therefore will lower the energy of activation. This approach is, in the final analysis, equivalent to that of George and Robertson's. It differs only in focusing attention on the transition state rather than solely on the product. Theoretical chemists now generally agree that this approach to the problem of reactivity in organic reactions is, in general, to be preferred to the electrostatic approach of Walsh discussed earlier.

Oxidation Techniques

A number of techniques have been developed for the preparation of hydroperoxides by oxidation of hydrocarbons. These may be grouped under three main headings;

(a) Photochemical Oxidation
(b) Metal Catalysed Oxidation
(c) Emulsion Oxidation

Photochemical Oxidation

Stephens, in 1928, (31) oxidized cyclohexene to the hydroperoxide by passing elemental oxygen through the hydrocarbon with concurrent exposure to sunlight. Criegee (35) later altered Stephens' procedure by employing a mercury discharge lamp as a source of high energy ultra-violet light. Since then, particularly in the hands of Hock, the Stephens-Criegee photochemical oxidation has become the favoured method for hydroperoxide formation (See Table IV).

Metal Catalysed Oxidation

The discovery that the presence of heavy-metal catalysts accelerated the rate of hydrocarbon oxidation (62) focused attention on these compounds. As a result a large number of heavy-metal catalysts have been found useful in hydroperoxide formation. Heavy-metal catalysts not only increase the rate of hydroperoxide formation but also catalyse hydroperoxide decomposition. In general, heavy-metal soaps, such as copper stearate and cobalt napthenate, which dissolve in the hydrocarbon to be oxidized,have been found to be most efficient (63). Other forms of heavy-metal catalysts, however, such as copper chloride and lead tetraethyl have also been found to be effective.

Emulsion Oxidation

An interesting variation of the oxidation techniques previously employed was reported in 1950 by Armstrong, Hall, and Quinn (2). It involves passing gaseous oxygen into an emulsion of the hydrocarbon and water. (This emulsion is created by agitation of the hydrocarbon with a basic solution of sodium stearate). It is claimed by these authors that this procedure more intimately mixes oxygen with the hydrocarbon, resulting in higher yields of hydroperoxide.

A large number of hydroperoxides have been prepared by the direct oxidation of hydrocarbons employing the three techniques outlined above. These compounds are listed in Table IV.

TABLE IV

HYDROPEROXIDES FORMED BY HYDROCARBON OXIDATION WITH ELEMENTAL OXYGEN

Hydroperoxide	Hydrocarbon	Catalyst	References
tert-Butyl-	iso-Butane	HBr	64,65,66
α-Ethoxyethyl-	Diethyl ether	None	67
2-Pentenyl-	2-Pentene	Light	68
3-Methyl-2-butenyl-	3-Methyl-2-butene	Light	69
2-Methyl-2-butenyl-	2-Methyl-2-butene	Light	69
1-Hexenyl-	1-Hexene	Metal	70
Cyclohexenyl-	Cyclohexene	Light	32,35,55
iso-Propoxyethyl-	iso-Propyl ether	Light	71
Methylcyclopentyl-	Methylcyclopentane	Emulsion	72
n-Heptyl-	n-Heptane	None	73
1-Methylcyclohexenyl-	1-Methylcyclohexene	Light	35,53,74
Methylcyclohexyl-	Methylcyclohexane	Light	72,75
Dimethylcyclopentyl-	Dimethylcyclopentane	None	76
1,2-Dimethylcyclohexenyl-	1,2-Dimethylcyclohexene	None	53,74
p-Xylyl-	p-Xylene	Light Metal	58,(mono) 77,(di)
m-Xylyl-	m-Xylene	Metal	77
1-Phenylethyl-	1-Phenylethane	Light	58

TABLE IV (cont'd.)

Hydroperoxide	Hydrocarbon	Catalyst	References
Indan-	Indan (Hydrindene)	Light	78
Hexahydroindan-	Hexahydroindan	None	79
Cuminyl-	Cumene	Light Emulsion	59 2,80,81, 82,83
Cyminyl-	Cymene	Light Emulsion	1,(prim.) 83,84, (tert.)
Tetralin-	Tetralin	None Metal	56,85 86,87,88,89
Decalin-	Decalin	Light	57,90
2,7-Dimethyloctyl-	2-7-Dimethyloctane	Light	91
α-Methyl-αethyl-benzyl-	Secondary butylbenzene	Light Emulsion	92 83,93
Dihydronapthyl-	Dihydronapthalene	None	94
1-Methyltetralin-	1-Methyltetralin	Light	95
Dicyclopentadienyl-	Dicyclopentadiene	None	94
Di-iso-propylphenyl-	Di-iso-propylbenzene	Emulsion	96,97
Diphenylmethyl-	Diphenylmethane	Light	59
Fluorenyl-	Fluorene	None	98
2-iso-propylnapthyl-	2-iso-propylnapthalene	Emulsion	99

TABLE IV (cont'd)

Hydroperoxide	Hydrocarbon	Catalyst	References
tetra-Hydrocarbazolyl-	tetra-Hydrocarbazole	None	100
octa-Hydroanthracenyl-	octa-Hydroanthracene	Light	101
Menthenyl-	Carvomenthene	Light	102
meso-Phenylanthranol-	meso-Phenylanthranol	None	103
Methyloleate	Methyloleate	Light	104,105
Dihydromyrcene- (a mixture of mono- and poly- hydroperoxides)	Dihydromyrcene	Light	106
Dihydrofarnesene- (a mixture of mono- and poly- hydroperoxides)	Dihydrofarnesene	Light	106
Squalene- (a mixture of mono- and poly- hydroperoxides)	Squalene	Light	106

Hydroperoxide Formation by Ether Hydrolysis with Hydrogen Peroxide

In searching the literature for a preparative procedure for hydroperoxide formation, one example was found of a method which does not logically fit into any of the preceding categories and therefore will be presented separately.

Kadowaki (107) treated a slightly acid solution of methoxymethyl urea, $H_2NCONHCH_2OMe$, with a 3% solution of hydrogen peroxide and evapourated the mixture to dryness. The hydroperoxide $HOOCH_2NHCONH_2$ resulted by what appears to be an ether cleavage with hydrogen peroxide:

$$H_2NCONHCH_2OMe + HOOH \rightarrow H_2NCONHCH_2OOH + CH_3OH \quad (xxxiii)$$

No other literature references for this method were found and the above hydroperoxide is apparently the only one isolated in this manner.

EXPERIMENTAL

General

As outlined in the General Introduction the object of the investigation reported in this thesis has been to determine the relative extent of attack at the methyl and isopropyl groups, the composition of the hydroperoxide, and the nature and amount of other products resulting from the oxidation of p-cymene by both the emulsion and photochemical procedures. The oxidation, employing the emulsion technique, was studied at two different temperatures, 85°C and 60°C, while the photochemical oxidation was carried out at the one temperature of 60°C. The reaction temperature of 85°C was chosen since Armstrong, Hall, and Quinn (2) have shown this to be a suitable temperature for the oxidation of cumene, a homologue of p-cymene, using the emulsion technique. The reaction temperature of 60°C for the photochemical oxidation was selected in order to simulate the conditions employed by Helberger, Rebay, and Fettback in their oxidation of p-cymene under the action of sunlight (1). The emulsion oxidation at 60°C was carried out for the purpose of drawing a direct comparison between the two methods, and also for the purpose of studying the one oxidation method at two different temperatures in order to determine the effect, if any, of temperature on the relative extent of oxidative attack at the two available positions.

Preliminary emulsion oxidation experiments indicated that the products formed contained, in addition to hydroperoxides, a ketonic product, alcohols, and solid carboxylic acids. Attempts were first made to separate the reaction products quantitatively into three fractions, (a) carboxylic acids, (b) hydroperoxides, (c) neutral compounds (alcohols and ketone), and then to analyze each fraction separately. It was found, however, that the separation of hydroperoxides by the usual method of precipitation as their sodium salts (1) was not quantitative, since appreciable quantities were retained in both organic and aqueous layers of the filtrate, and decomposition, particularly of the primary hydroperoxide, occurred to a certain extent.

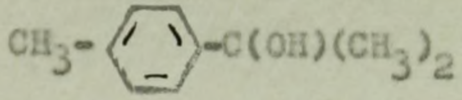
After considerable experimentation on the products of the emulsion oxidation, a method of analysis was developed by means of which it was possible, with fair accuracy, to determine the relative extent of oxidative attack on the two alkyl positions of p-cymene. A description of this method follows.

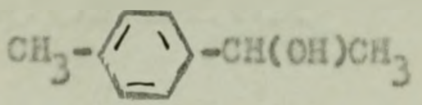
On completion of the oxidation reaction the aqueous layer, containing the sodium salts of the carboxylic acids, was separated and acidified, and the precipitated acids were then analyzed by partition chromatography. The organic layer was analyzed iodometrically for hydroperoxide content, and was then divided into two portions. One portion was reduced with lithium aluminium hydride to give a product consisting of three alcohols:

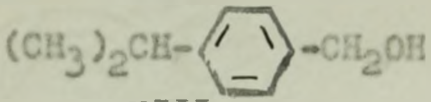
(a) a tertiary alcohol, dimethyl-p-tolylcarbinol, VI, the greater amounts of which being formed by the reduction of the tertiary hydroperoxide although some was formed during the oxidation reaction by the decomposition of the hydroperoxide,

(b) a small amount of secondary alcohol, methyl-*p*-tolylcarbinol, XXI, resulting from the reduction of *p*-methylacetophenone,

(c) a primary alcohol, *p*-isopropylphenylcarbinol VIII, formed both by the decomposition of primary hydroperoxide during oxidation and by reduction of primary hydroperoxide.


VI


XXI


VIII

The mixture of the three alcohols was fractionally distilled to give a main fraction consisting of the secondary and tertiary alcohol, VII, and VI , and a higher boiling, easily-separated fraction, consisting of primary alcohol,[1] VIII.

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[1] Fractionation of a synthetic mixture indicated that the primary and tertiary alcohols did not form an azeotropic pair.

From the results of this fractionation and the chromatographic analysis of acids it was possible to calculate the relative degree of oxidative attack on the two available positions.

Although for reasons indicated above it was not possible to separate the total hydroperoxide product, it seemed desireable, in view of the work of Helberger et al (1), to determine the nature of the hydroperoxide isolated by the sodium salt precipitation method. To accomplish this, the second portion of reaction product (from which the acids had been previously removed) was treated with a concentrated solution of sodium hydroxide to precipitate the hydroperoxide as the slightly soluble sodium salt. The hydroperoxide was then liberated from the sodium salt by means of carbon dioxide, reduced with lithium aluminium hydride, and the resulting alcohol product carefully fractionated.

Additional information concerning the nature of the products of emulsion oxidation was obtained by examining the organic layer present in the filtrate after removal of the sodium salt of the hydroperoxide. This organic layer contains the neutral products, i.e., p-methylacetophenone VII, tertiary alcohol VI , and primary alcoholVIII, formed during the oxidation reaction. Fractionation of test mixtures of p-methylacetophenone and tertiary alcohol showed that these two compounds could not be readily separated by fractional distillation. Therefore a different procedure for analysis was necessitated. The ketone content of the organic layer was first determined by a volumetric hydroxylamine hydrochloride method. The layer was then fractionated to separate any primary alcohol from the tertiary alcohol-ketone fraction. The tertiary alcohol content could then be determined by subtracting the weight of ketone from the tertiary alcohol-ketone fraction.

Preliminary work on the photochemical oxidation showed that acids were present only in very small quantities, (less than 0.6% of the total oxidation product), and mainly in the form of cumic acid. For this reason no effort was made to separate the acid product by alkaline extraction and the total reaction mixture at the end of the oxidation period was directly reduced with lithium aluminium hydride. The alcohols formed were then fractionally distilled. Since the total weight of this reduction product was almost identical to the theoretical weight of alcohols which would result by reduction of the known amount of hydroperoxide in the oxidation reaction mixture and since yields in such reductions are practically quantitative, it could be concluded that the photochemical oxidation product was almost completely in the form of the hydroperoxide and very little neutral material (ketone or alcohols) was present. The composition of the oxidation mixture as well as the extent of oxidative attack at the two available positions were thus given directly by the results of the fractional distillation of the reduction product into the dimethyl-p-tolylcarbinol VI and p-isopropylphenylcarbinol VIII.

In a second photochemical oxidation, the hydroperoxides were isolated as their sodium salts. These sodium salts were used in certain tests in an effort to confirm the experimental results of Helberger _et al_ (1) on which they based their conclusion that the oxidation product was the primary hydroperoxide.

Purification of p-Cymene

_p_-Cymene (Eastman Kodak White Label) used in this investigation was allowed to stand over "Drierite" for a week and was then fractionated over sodium using a 35 plate, glass-helices column. Of a total charge of 1,000 ml., approximately 200 ml. was collected as a prerun and 100 ml. was left behind as residue in the distillation pot. The purified material had the physical constants, b.p.$_{(12\ \mathrm{mm.})}$ 62.5 °C, n_D^{20} 1.4908. A recent literature value for the refractive index of pure _p_-cymene is n_D^{20} 1.4909 (108).

Hydroperoxide Analysis

An iodometric procedure, suggested to us by Hercules Powder Co., Wilmington, Delaware, was used for the analysis of hydroperoxide in all samples (109). The method is based upon the oxidation, by the hydroperoxide, of iodide to free iodine.

$$RO_2H + 2I^- + 2H^+ \longrightarrow I_2 + ROH + H_2O. \qquad (xxxiv)$$

The liberated iodine is then determined by titration with standard thiosulfate solution.

In determining the amount of hydroperoxide present during and at the completion of the oxidation reaction, two-gram samples of the reaction mixture were withdrawn and analyzed for hydroperoxide content. Smaller samples (0.2-0.3 g.) were used for the analysis of the solid hydroperoxide salt and concentrated solutions of the hydroperoxide. Each sample was weighed into a 250 ml. standard-taper Erlenmeyer flask. Ninety-nine per cent isopropanol (100 ml.) was added together with 10 ml. of glacial acetic acid and 1 ml. of saturated potassium iodide solution. The flask was connected to a reflux condenser and the solution heated gently on a low flame for three to four minutes. The condenser was washed down with 10 ml. of isopropanol and the sides of the flask rinsed with 25 ml. of distilled water. The liberated iodine was titrated with 0.05 N sodium thiosulfate solution to the disappearance of the yellow color[1]. Blank determinations carried out concurrently were of the order 0.1 ml.

An indication of the precision and accuracy of the method is shown from the values obtained in the analysis of a sample of cumic acid hydroperoxide which had been recrystalized to a constant melting point and therefore was presumably quite pure. The values obtained from two determinations were 99.8 % and 100.2 %.

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[1] Soluble starch fails as an indicator under these conditions but isopropanol intensifies the color of free iodine to provide a sharp end-point.

Ketone Analysis

The method for ketone analysis employed in this work was the hydroxylamine hydrochloride procedure described by Siggia (110). A modification of this method reported by Smith and Mitchell (111) was first employed, but a satisfactory end-point could not be obtained and the method was abandoned in favour of Siggia's procedure.

Emulsion Oxidation

Apparatus

The apparatus used for the emulsion oxidations is shown in Fig. III. Oxygen from cylinder A was passed through a purification train consisting of, an activated charcoal tower, C, a sodium hydroxide tower, D, back-splash trap, E, sulphuric acid trap, F, and a Pyrex glass wool tower, G. The rate of gas flow was controlled by the micro-valve, B, and measured by means of a mercury flowmeter, H. The oxygen then passed through a"fritted"glass dispersion tube, I, into the reaction vessel, J. The reaction vessel was a standard-taper three-necked 5 l. flask fitted with a mercury-seal stirrer, K, a reflux condenser, L, and a thermometer, M. The exhaust gases were led from the top of the condenser into a dry ice-acetone trap, N, and thence through a wet-test gasmeter, O, to the atmosphere.

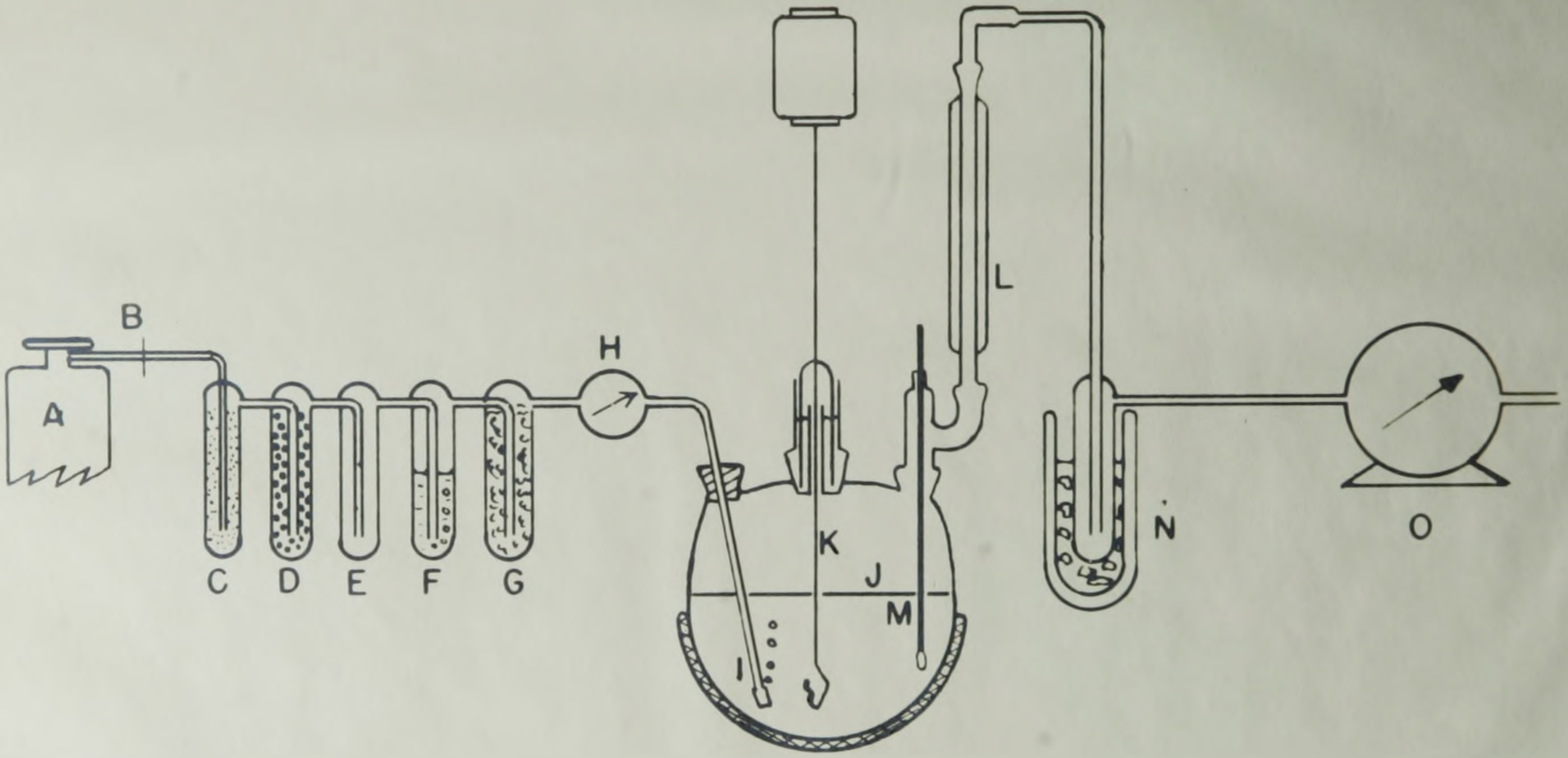

FIG. 3

F

Emulsion Oxidation Procedure

85°C Oxidation

Composition of the reaction mixture is given in Table V. This ratio of the reactants has been shown by Armstrong et al (2) to provide optimum conditions for emulsion in the oxidation of cumene.

TABLE V

COMPOSITION OF THE EMULSION OXIDATION REACTION MIXTURE

Reagent	Weight (g.)
Water	2,000.0
p-Cymene	340.0
Stearic acid	3.0
Sodium carbonate	27.0
Cymene hydroperoxide	0.4
Total weight	2370.4

The temperature of the reactants was raised to 85°C before the oxygen flow was initiated. This flow was then started and adjusted to a rate of 7.0 l. per hour, by means of the microvalve, B. The oxidation reaction was followed by hydroperoxide analysis of samples periodically removed from the reaction flask by means of a pipette substituted for the thermometer, M. In preliminary work with emulsion autoxidations it was found that an induction period of considerable length existed. This period was obviated by the addition of a small amount of cymene hydroperoxide as indicated in Table V. The reaction was stopped when the hydroperoxide concentration reached 40 %[1] by weight. This required a period of 35.5 hours. At this point, the emulsion broke, making sampling very difficult. On cooling, the reaction mixture separated into two layers. The lower aqueous layer was separated and washed with petroleum ether (b.p. 30-60°C.) to remove dissolved hydrocarbons, care being taken to leave the flocculent sodium stearate behind with the aqueous layer. The ether washings were then added to the separated upper hydrocarbon layer. The oxidized p-cymene layer was dried by removing the greater portion of petroleum ether under reduced pressure and at room temperature. In this manner the water present was removed in the form of an azeotropic pair with the petroleum ether. The residue, consisting of the liquid oxidation products and unchanged p-cymene, was weighed, analyzed for hydroperoxide content, and then divided into two aliquots which were set aside for further treatment.

The aqueous layer of the reaction product was acidified with dilute hydrochloric acid and the precipitated carboxylic acids removed by extraction with diethyl ether. The ether was then removed under reduced pressure and room temperature leaving a solid residue of carboxylic acids.

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[1] The extent of oxidation is given as a per cent hydroperoxide content with respect to the original weight of p-cymene, i.e., the water present in the reaction mixture is not included. In this way a direct comparison may be obtained between the extent of oxidation in the emulsion and photochemical reactions.

60°C Oxidation

The procedure for the emulsion oxidation at 60°C was similar to that used in the 85°C oxidation with the exception that a longer oxidation period was required. After 197.2 hours, in the course of which a hydroperoxide concentration of 19.1 % was attained, the oxidation was stopped. Because of the smaller conversion the oxidized cymene layer was divided into two equal aliquots in order to provide sufficient material in each portion for subsequent treatment.

Chromatographic Separation of Acids

The solid acids from both the 85°C and 60°C emulsion oxidations were separated by a column partition chromatographic procedure developed in this laboratory by Hunt (112).

The column was constructed of a Pyrex glass tube, 3.5 cm. in diameter and 49 cm. long, at the bottom of which was sealed a tube 6 mm. in diameter and 2.5 cm. long. A small Pyrex wool plug was placed securely in the neck of the constriction at the base of the column. A disc of white blotter paper of the same diameter as the inside of the column was tamped down snugly on top of the wool plug.

The column packing was prepared by grinding 150 g. of Mallinkrodt analytical grade, 100 mesh, silicic acid ($SiO_2 \cdot XH_2O$) in a mortar together with 200 ml. of methanol, 7.5 ml. of bromocresol green indicator solution (200 mg. in 25 ml. of methanol), and 60 drops of 1 N ammonium hydroxide. This grinding process was continued until a homogeneous and virtually dry powder was produced. The powder was then slurried with 300 ml. of benzene and poured into the previously prepared tube. A dense and uniformly packed column was obtained by applying air pressure at the top and tapping the walls of the tube. When the silicic acid had "settled down", the pressure was released and a disc of blotter paper was placed loosely on top of the packing. Benzene, which previously had been redistilled and equilibrated with a solution of 90 % methanol and 10 % water (hereafter called "equilibrated" benzene) was then forced through the column under air pressure until all excess indicator was removed as indicated by a colorless eluent. To neutralize the slight, unavoidable excess of ammonium hydroxide on the column, a small amount of cumic acid (0.5 g.) was dissolved in 20 ml. of "equilibrated" benzene and placed carefully on the top of the packing. The column was then connected to the pressure source and pressure applied. At the precise moment when the last of the solution had passed into the gel the pressure was released. The column was then washed down with a further 20 ml. of "equilibrated" benzene following the same procedure. "Equilibrated" benzene was then passed continuously into the column until the yellow band, produced by the presence of cumic acid, had been completely eluted. The column, thus prepared, was considered satisfactory if the acid bands formed in an actual separation were clearly visible and well separated.

A two gram sample of the acid product from an emulsion oxidation was dissolved in 25 ml. of "equilibrated" benzene and the solution passed into the column in the same manner described for the cumic acid used in the column neutralization. After the mixed acids had been washed into the column a continuous elution with "equilibrated" benzene was carried out at a pressure sufficient to maintain a flow rate of three drops every two seconds. Under these conditions four, distinct, yellow bands were formed. These bands were washed from the column into separate containers and the solvent removed at reduced pressures and room temperature leaving four acid residues which were carefully washed with small portions of diethyl ether into weighed beakers. The ether was permitted to evaporate and the weights of the acid residues determined.

Melting point determinations were made on each of the separated acids both before and after a single recrystallization. Confirmation of the identity of these acids was obtained from mixed melting point determinations on the acids mixed with samples of acids prepared and fully characterized in this laboratory by Hunt (112). The hydroperoxide acid was further characterized by a hydroperoxide analysis (See p.39).

The first band to be eluted was found to be a mixture of stearic and cumic acids. These two acids could not be separated by this chromatographic procedure although a single recrystallization from a water-ethanol solvent yielded pure cumic acid. Since care had been taken, however, to retain all precipitated sodium stearate in the aqueous layer of the reaction product, it was possible to make a reasonably accurate correction for the stearic acid present in this band. The other acid products were cleanly separated by the chromatographic technique.

The composition of the acid product (corrected for stearic acid content) and the melting points of the separated acids obtained from the 85°C emulsion oxidation are given in Table VI and from the 60°C oxidation in Table VII. In the analysis of the acids, acid recoveries from the chromatographic column were 98 % and 96 % for the 85°C and 60°C runs, respectively.

Lithium Aluminium Hydride Reduction[1] of Aliquot I of the Liquid Oxidation Products

Aliquot I of each run (one-half of the oxidized hydrocarbon layer from the 60 C run and three-quarters from the 85 C run) was diluted with 500 ml. of dry ether and the resulting solution added dropwise with stirring to a 25 %

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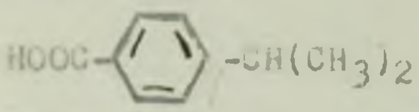
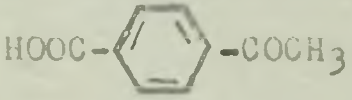
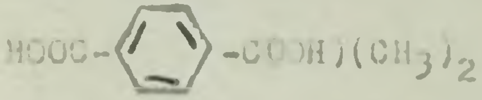
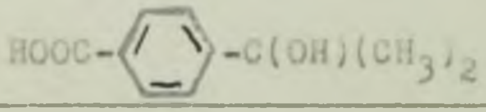
[1] Lithium aluminium hydride was chosen as the reducing agent because of the relatively mild conditions involved, with little decomposition of hydroperoxide, and because of the high yields obtainable. A test reduction of 20 g. of p-methylacetophenone yielded 97 % of the expected alcohol. Similarly in a test reduction of 7.6 g. of cymene hydroperoxide an alcohol yield of 91 % was obtained. The lower yield in the latter case is explained on the basis of the small quantity of hydroperoxide reduced.

TABLE VI

AROMATIC ACIDS OF THE 85°C EMULSION OXIDATION

Band Number	Acids	Weight of Separated Acid (g.)	Total Weight of Each Acid (g.)	Composition of Acid Product (% by wt)	M.P.[1] (°C) (a) Crude Product (b) Recrystallized (c) Lit. Value
I	Cumic acid 	1.0888[2]	23.8	62.5	(a) 112-116 (b) 117.6-118.1 (c) 118.2 (112)
II	p-Acetobenzoic acid 	0.1100	2.4	6.3	(a) 195-198 (b) 203.6-204.9 (c) 205.2 (112)
III	p-(α-hydroperoxy-isopropyl) benzoic acid 	0.3241	7.1	18.6	(a) 143-146 (b) 147.5-148.4 (c) 148.2 (112)
IV	p-(α-hydroxyisopropyl) benzoic acid 	0.1782	3.9	10.2	(a) 147-151 (b) 156.4-157.1 (c) 157.3 (112)

1. Melting and boiling point temperatures in Tables of Results are corrected.

2. The weight given here is the weight of the first band less the weight of stearic acid.

TABLE VII

AROMATIC ACIDS OF THE 60°C EMULSION OXIDATION

Band Number	Acids	Weight of Separated Acid (g.)	Total Weight of Each Acid (g.)	Composition of Acid Product (% by wt)	M.P. (°C) (a) Crude Product (b) Recrystallized (c) Lit. Value
I	Cumic acid	1.0475[1]	7.1	76.9	(a) 81-96 (b) 115.6-118.0 (c) 118.2 (112)
II	p-Acetobenzoic acid	0.0173	0.1	1.3	(a) 200-201.9 (b) 204.0-205.5 (c) 205.2 (112)
III	p-(α-hydroperoxy-isopropyl) benzoic acid	0.1530	1.1	11.4	(a) 145-147.3 (b) 147.5-148.2 (c) 148.2 (112)
IV	p-(α-hydroxyisopropyl) benzoic acid	0.0320	0.3	2.4	(a) 148.7-151.4 (b) 150.2-157 (c) 157.3 (112)

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[1] Weight of first band less the weight ofstearic acid.

excess[1] of a 2 M solution of lithium aluminium hydride in ether. The rate of addition was such as to maintain the ether solution of the reactants at a steady rate of reflux. Care was taken to insure a moisture free atmosphere in the reaction flask. When the addition was complete, water was added cautiously, until reaction stopped, in order to destroy excess lithium aluminium hydride, and this was followed by just sufficient 10 % aqueous sulfuric acid to barely dissolve the basic aluminium salts. The ether layer was separated and the aqueous layer washed with petroleum ether. The ether layer and petroleum ether washings were combined and were then washed thoroughly with 10 % sodium bicarbonate solution. The solvents were removed under reduced pressure and the residual cymene and reduction products fractionated in a 35 plate "Podbielniak Type" (113) column using benzohydrol[2] as a chaser.

The results of the fractional distillation of the products from reduction of Aliquot I of the 85 °C oxidation are given in Table VIII and of Aliquot I of the 60 °C oxidation in Table IX. Since a preliminary investigation on a test

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[1] From a preliminary oxidation run the weights of alcohols, hydroperoxides, and ketone were determined and from these it was possible to calculate the quantity of lithium aluminium hydride necessary to reduce these components leaving a 25 % excess of reducing agent.

[2] It was found that benzohydrol did not form a azeotrope with any of the reaction products.

mixture of dimethyl-*p*-tolylcarbinol and methyl-*p*-tolylcarbinol had shown that separation was impossible with the fractionation columns in our laboratory, these alcohols were collected as one fraction in the fractional distillation of the reduction product. This limitation, however, was not too important as the quantity of secondary alcohol present could be indirectly obtained by a ketone analysis on Aliquot II (See p. 50).

Experimental verification of the assumption that the primary and tertiary alcohols, *p*-isopropylphenylcarbinol and dimethyl-*p*-tolylcarbinol respectively, could be quantitatively separated by fractional distillation was, on the other hand, very important. This verification was obtained by fractionating a test mixture of these alcohols (both obtained for the purpose of this test, from sources other than the oxidation of *p*-cymene). Weighed quantities of the two alcohols were fractionally distilled and their weights determined again after separation. The two sets of weights obtained corresponded closely, thereby indicating that the primary and tertiary alcohols could be separated by fractionation and that the two did not form an azeotropic pair.

Treatment of Aloquot II

Aliquot II of the separated oxidation product of each run was added slowly with stirring to twice its volume of 25% sodium hydroxide solution thoroughly cooled by an ice bath. The reaction mixture, containing the product from the 65°C

TABLE VIII

REDUCED PRODUCTS OF ALIQUOT I FROM THE 85°C OXIDATION

Product	B.P. (°C) (12mm)	Weight (g)	Composition of Alcohol Product (% by wt)	Refractive Index (n_D^{20}) (a) Found (b) Lit. Value
p-Cymene	62.0-62.5	118.9		(a) 1.4906-1.4909 (b) 1.4909 (108)
Dimethyl-*p*-tolylcarbinol	105.0-106.0	104.5	90.9	(a) 1.5178-1.5182[1] (b) 1.5156- (114)
Methyl-*p*-tolylcarbinol				(b) 1.5220 (115)
p-Isopropylphenylcarbinol	125.5-126.5	10.5	9.1	(a) 1.5202-1.5205 (b) 1.5205 (116)

1. The high refractive index is due to the presence of methyl-*p*-tolylcarbinol (n_D^{20} 1.5220) and traces of α, *p*-dimethylstyrene (n_D^{20} 1.5283) formed by dehydration of the tertiary alcohol dimethyl-*p*-tolylcarbinol.

TABLE IX

REDUCED PRODUCTS OF ALIQUOT I FROM THE 60°C OXIDATION

Product	B.P.$_{(12mm)}$ (°C)	Weight (g.)	Composition of Alcohol Product (% by wt)	Refractive Index (n_D^{20}) (a) Found (b) Lit. Value
p-Cymene	62.0-62.5	137.1		(a) 1.4906-1.4909 (b) 1.4909 (108)
Dimethyl-*p*-tolylcarbinol	105.0-106.0	26.3	88.3	(a) 1.5178-1.5181 (b) 1.5156 (114)
Methyl-*p*-tolylcarbinol				(b) 1.5220 (115)
p-Isopropylphenylcarbinol	125.5-126.5	3.5	11.7	(a) 1.5202-1.5205 (b) 1.5205 (116)

oxidation, was then seeded with a small amount of the sodium salt of p-cymene hydroperoxide in an effort to reduce the precipitation time and thus decrease the extent of hydroperoxide decomposition during the sodium hydroxide treatment. Immediately after seeding a flocculent white precipitate separated. The seeding technique was not used in treating Aliquot II of the 60°C oxidation with sodium hydroxide and as a result a much longer precipitation time (two hours) was required. The precipitated sodium salt was filtered as rapidly as possible using a coarse "fritted" glass funnel surrounded by an ice bath. The crystals were carefully washed several times with petroleum ether and were then allowed to dry in a vacuum desiccator.

When the sodium salt dried to a crumbling white powder, it was weighed and analyzed for its hydroperoxide content. The product from the 85°C oxidation was found to be 64 % pure sodium hydroperoxide salt and that from the 60°C oxidation 61 % pure. The impurities were considered to be largely water and sodium hydroxide. The recovery of the hydroperoxide in the form of the sodium salt was 84 % from the 85°C oxidation and 79 % from the 60°C experiment. The loss was due to both decomposition of the hydroperoxide and incomplete precipitation, the former being greater in the 60°C than in the 85°C run due to the longer precipitation time. The aqueous layer from the filtration of the sodium salt was found by analysis to contain approximately 3 % of the total hydroperoxide and the organic layer of the filtrate approximately 9 % of the total. More complete precipitation could not be achieved by further treatment with 25 % sodium hydroxide.

The hydroperoxide was liberated by suspending the sodium salt in distilled water and passing carbon dioxide into the suspension until a pH of approximately eight had been reached. At this hydrogen ion concentration the sodium salt was completely converted to the free hydroperoxide. This hydroperoxide was extracted with petroleum ether (b.p. 30-60°C) and the ether then removed under reduced pressure, any water present being carried over in the form of an azeotrope. The colorless oil which remained analyzed as 98-99 % pure cymene hydroperoxide. This residue was diluted with dry ethyl ether and reduced with lithium aluminium hydride by the procedure previously described. The reduction product was then carefully fractionated in the 35 plate "Podbielniak" column using benzohydrol as a chaser.

It was found that the product of the reduction of the hydroperoxide from both the 85°C and 60°C oxidations distilled over a very narrow range, 105-106°C, the boiling point corresponding to that of the tertiary alcohol, VI, dimethyl-*p*-tolylcarbinol. The yield of the reduction product from the 85°C run was 93.0 % based on the sodium hydroperoxide salt and 77.8 % based on the hydroperoxide content of the original oxidation mixture. For the 60°C run the corresponding yields were 90.7 % and 70.6 %, respectively. The refractive index of the product was somewhat high for the tertiary alcohol, n_D^{20} 1.5173-1.5175 compared to the literature value of 1.5156 (114). This was attributed to a small amount of decomposition of the tertiary alcohol to α,p-dimethylstyrene (n_D^{20} 1.5283) since it was found that when the column was maintained under conditions of total reflux a short time water droplets appeared on the condenser of the column head, the temperatures of the vapour dropped, and the refractive index of the distillate increased. Furthermore, fractionation of a synthetic sample of the tertiary alcohol failed to give a product of refractive index in any closer agreement with the literature value. There was no indication of primary alcohol, p-isopropylphenylcarbinol, in the product of the reduction of the hydroperoxide. From this it must be concluded that the hydroperoxide, isolated as the sodium salt from the products of the emulsion oxidation of p-cymene, is essentially the pure tertiary compound[1].

The organic layer of the filtrate from the sodium salt filtration was separated and the petroleum ether solvent and traces of water removed under vacuum. The residue was heated at atmospheric pressure to decompose any hydroperoxide present which would otherwise interfere with the subsequent ketone analysis. A small sample of the product was removed and analyzed for its ketone content by the

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[1] See footnote pg. 57.

method already described[1]. The remainder was fractionally

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[1] That p-methylacetophenone was the only carbonyl compound present was strongly indicated by the following results. A negative fuchsin-aldehyde test was given by the oxidation product. A 2,4-dinitrophenylhydrazone derivative readily formed, however. After one recrystallization from ethyl acetate its melting point was 259.8-260.6°C (corr.). The melting point of the 2,4-dinitrophenylhydrazone of p-methylacetophenone reported in the literature is 260°C(117). A mixed melting point with an authentic sample of 2,4-dinitrophenylhydrazone of p-methylacetophenone gave no temperature depression.

[2] In a preliminary oxidation at 85°C, the sodium salt isolated in the manner described above, was converted to the free hydroperoxide by means of carbon dioxide, and then reprecipitated. This sodium salt after being dried in a vacuum desiccator, was 97.4 % pure. The purified salt was then treated with carbon dioxide and the liberated hydroperoxide extracted with petroleum ether. Removal of the petroleum ether under vacuum left a colorless oily liquid which analyzed for 98.9 % cymene hydroperoxide. This material was the vacuum distilled to give a product b.p. (1mm) 88-91°C; n_D^{20} 1.5207; d_4^{25} 1.0403; hydroperoxide content 99.1 %. On the basis of the results from the reduction studies presented above, the product was considered to be essentially pure tertiary cymene hydroperoxide.

distilled in the 35 plate column using benzohydrol as a chaser. Both the ketone, *p*-methyltolylketone, and tertiary alcohol,αdimethyl-*p*-tolylcarbinol, came over as one fraction due to the proximity of their boiling points (108°C and 105°C at 12 mm respectively). The amount of tertiary alcohol present, however, could be calculated by subtracting from the weight of this fraction the weight of ketone previously determined by ketone analysis.

This fractionation of the neutral fraction of the reaction product from both oxidations gave no evidence of the presence of the primary alcohol. *p*-isopropylphenylcarbinol, the boiling point climbing rapidly from that of the ketone-tertiary alcohol fraction to that of the chaser. The amount of material being fractionated, however was very small, less than ten grams in each run, and since the primary alcohol was a minor reaction product it could easily have been missed. That primary alcohol was actually a component of the neutral fraction of the 60°C oxidation was demonstrated in the following way. The product obtained from the fractionation of the neutral fraction of the 60°C run was reduced with lithium aluminium hydride and the resulting alcohols carefully fractionated. The main fraction was a mixture of the tertiary alcohol and methyl-*p*-tolylcarbinol, the latter being formed by reduction of the ketone. A very small fraction was collected between the boiling point of the main fraction and that of the chaser. The presence of primary alcohol in this fraction was confirmed by the preparation of a urethan derivative, which, after one recrystallization, gave the correct melting point for the urethan of p-isopropylphenylcarbinol; m.p. found 61.3-62.1°C, literature value 62°C (118).

The results of the ketone analysis and of the fractionation of the neutral products are presented in the following section.

Composition of the Total Product from the Emulsion Oxidation

The composition of the reaction products from the emulsion oxidation at 85°C is given in Table X and from the oxidation at 60°C in Table XI. The weights of the acids given in these tables are those presented earlier in Tables VI and VII. The weight of primary cymene hydroperoxide plus p-isopropylphenylcarbinol is obtained from the results of the reduction of Aliquot I, Tables VIII and IX. Subtraction of the amount of ketone, as determined by analysis, from the amount of tertiary and secondary alcohol obtained by reduction of Aliquot I, gives the amount of tertiary hydroperoxide and dimethyl-p-tolylcarbinol, taken together. The amount of the tertiary alcohol alone is obtained from the results of the fractionation of the neutral fraction from Aliquot II. Knowing the amount of tertiary alcohol, the amount of tertiary hydroperoxide is readily calculated.

Although the sum of the weights of tertiary alcohol

TABLE X

COMPOSITION OF THE PRODUCTS OF THE 85°C EMULSION OXIDATION

Product	Weight (g.)	Composition of the Oxidation Product	
		(a) % by wt	(b) mole %
Unreacted p-cymene	158.9		
Primary hydroperoxide + p-isopropylphenylcarbinol[1]	15.5	(a) 7.7	(b) 7.5
Tertiary hydroperoxide	101.9	(a) 50.4	(b) 49.4
Dimethyl-p-tolylcarbinol	41.6	(a) 20.6	(b) 22.3
p-Methylacetophenone	5.6	(a) 2.8	(b) 3.4
Cumic acid	23.8	(a) 11.8	(b) 11.7
Keto-acid	2.4	(a) 1.2	(b) 1.1
Hydroperoxy-acid	7.1	(a) 3.5	(b) 2.9
Hydroxy-acid	3.9	(a) 1.9	(b) 1.7

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[1] Weight expressed as hydroperoxide.

TABLE XI

COMPOSITION OF THE PRODUCTS OF THE 60°C EMULSION OXIDATION

Product	Weight (g.)	Composition of the Oxidation Product (a) % by wt (b) mole %
Unreacted *p*-cymene	274.2	
Primary hydroperoxide + *p*-isopropylphenylcarbinol[1]	7.4	(a) 10.0 (b) 9.7
Tertiary hydroperoxide	45.4	(a) 61.4 (b) 60.0
Dimethyl-*p*-tolylcarbinol	8.4	(a) 11.4 (b) 12.3
p-Methylacetophenone	4.2	(a) 5.7 (b) 6.9
Cumic acid	7.1	(a) 9.6 (b) 9.5
Keto-acid	0.1	(a) 0.1 (b) 0.1
Hydroperoxy-acid	1.1	(a) 1.5 (b) 1.2
Hydroxy-acid	0.3	(a) 0.4 (b) 0.4

1. Weight expressed as hydroperoxide.

and tertiary hydroperoxide is quite accurate, since it is based on the results of total reduction and ketone analysis, the relative amount of each is subject to considerable error. This is due to the fact that at least some of the tertiary alcohol isolated from the neutral fraction of Aliquot II undoubtedly was formed by decomposition of the tertiary hydroperoxide during the precipitation of the sodium salt. Therefore the reaction mixture at the end of the oxidation probably contained more tertiary hydroperoxide and less tertiary alcohol than the data presented in Tables X and XI would indicate.

Because of the ready decomposition of primary hydroperoxide in the sodium hydroxide treatment of Aliquot I, there is no way of even estimating the relative amounts of primary alcohol and primary hydroperoxide in the reaction products. The total of the two components given in the tables is, however, quite accurate.

Photochemical Oxidation

Apparatus

The apparatus employed in the photochemical oxidation of p-cymene was identical to that used in the emulsion oxidation excepting for the following minor modifications. The reaction vessel was of two litre size and was surrounded by an insulated box lined with aluminium foil. This insulated chamber was fitted with a light bulb which was connected to a "Variac" to produce a source of variable heat. A quartz D.C. mercury vapour tube 18 inches long was aligned across one end of the box 6 inches from the reaction vessel. This lamp acted as a source of high energy light. This serves as a more steady and controllable source of light than sunlight used by Helberger _et al_.

Oxidation Procedure

Two similar oxidations were carried out at 60°C using the photochemical technique. _p_-Cymene (850 g.) was placed in the reaction flask, the temperature raised to 60°C, and the oxygen flow started and adjusted to the rate of 7.0 l. per hour. Periodic checks of the hydroperoxide content were made[1]. The reactions were stopped after hydroperoxide concentrations of 5.5 % and 5.0 % had been built up. These

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[1] Despite the use of high energy light an induction period of considerable length was noticed in a preliminary oxidation. This was attributed in part to the use of a Pyrex glass reaction vessel which filtered out light of higher frequency. In the subsequent photochemical oxidations, no such induction period was observed. This was traced to the presence, on the sintered glass oxygen bubbler, of cymene hydroperoxide from the previous run which acted as a reaction initiator.

concentrations were attained after reaction periods of 117.7 hours and 119.0 hours, respectively.

Treatment of the Product of Oxidation No. I

Since a preliminary oxidation had demonstrated the absence of appreciable amounts of carboxylic acids, the product of the first oxidation was treated directly with lithium aluminium hydride[1], employing the procedure described earlier. Following reduction the alcohols formed were fractionally distilled, using a benzohydrol chaser. The results of this fractionation are given in Table XII. The total yield of alcohols corresponded closely to what would be expected from the reduction of the total hydroperoxide present i.e. a theoretical yield of 42.4 g. based on the hydroperoxide content of the oxidation product and an actual alcohol yield of 42.9 g. It was therefore concluded that very little neutral materials, i.e., alcohols and ketone were formed during the oxidation reaction. The composition of the product of the photochemical oxidation, calculated on the assumption that the total tertiary alcohol isolated was formed by the reduction of tertiary hydroperoxide and the total primary alcohol by reduction of the

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1. It was at first feared that a large excess of p-cymene might interfere with the reduction by precipitating the lithium aluminium hydride from ether solution. This did not prove to be the case, however.

primary hydroperoxide, was 79.5 % tertiary cymene hydroperoxide and 20.5 % primary cymene hydroperoxide.

TABLE XII

COMPOSITION OF REDUCED PHOTOCHEMICAL OXIDATION NO. I

Product	Weight (g.)	Composition of Reduced Product (mole %)
Unreacted p-cymene	801.6	
Dimethyl-p-tolylcarbinol	34.1	79.5
p-Isopropylphenylcarbinol	8.8	20.5

Treatment of Reaction II

The greater portion of unreacted p-cymene (790 g.) from the second reaction product was removed at 1 m.m. pressure and in the temperature range 28-35°C. The residual hydroperoxides were treated with a cooled sodium hydroxide solution and the sodium salts of the hydroperoxides precipitated as previously described. The product was filtered, washed thoroughly with petroleum ether, and dried in a vacuum desiccator. A small sample of the salt was refluxed with water for a period of fifteen minutes. The resulting oil was found to give a positive Schiff test for aldehyde and when treated with semicarbazide hydrochloride gave a derivative melting at 211.1-212.0°C. The literature value for the semicarbazone of p-isopropylbenzaldehyde is 212°C (1). This latter test was the one performed by Helberger, Rebay, and Fettback on which they based their conclusion that the product of the photochemical oxidation is exclusively the primary hydroperoxide. An explanation for this result is presented in the discussion.

Relative Extent of Oxidative Attack on Tertiary and Primary Carbon Atoms in the Oxidation of p-Cymene

The relative extent of oxidative attack on the tertiary and primary carbon atoms of p-cymene in both the emulsion and photochemical oxidations is shown in Table XIII. In the calculation of the relative extent of attack on the two available positions of p-cymene, the question of the proper allocation of the di-substituted acids arose. Since both

TABLE XIII

PER CENT ATTACK ON THE PRIMARY AND TERTIARY POSITIONS OF p-CYMENE

Position of Attack	Per Cent Attack in Emulsion Oxidation		Per Cent Attack in Photochemical Oxidation
	85°C	60°C	60°C
Primary carbon	22.0	20.0	20.5
Tertiary carbon	78.0	80.0	79.5

positions of the p-cymene molecule had been attacked the di-substituted compounds did not belong completely in either the tertiary or the primary groups. The solution to this problem was found to lie in a consideration of the rate constants operative and in the employment of the assumption that these rate constants in both primary and tertiary attack remain the same regardless of the nature of other substituents[1]. Thus from Fig.IVwe see that the ratio k_1/k_2 will be the same as the ratio of A/B or $k_2A = k_1B$ where A is

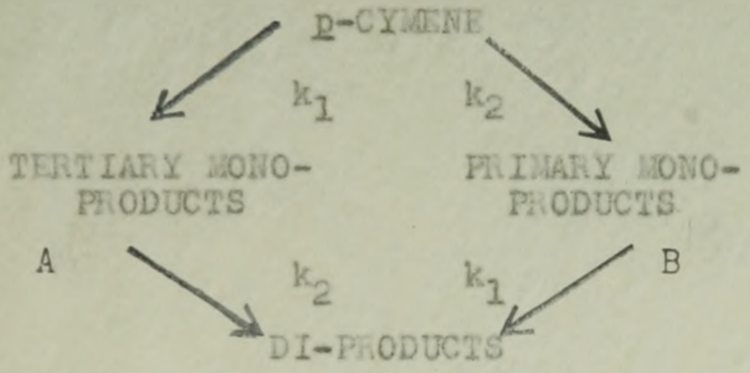

Fig. IV

the concentration of tertiary mono-products and B is the concentration of the primary mono-products. The quantity k_2A represents the rate of formation of the di-products from the tertiary mono-substituted compounds and similarly k_1B represents the rate of formation from the primary mono-substituted compounds. Since these two quantities are equivalent then the di-products must have been derived in equal

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[1] This assumption is not unreasonable in view of the fact that the influence of the substituents will be of second order importance since they are not attached directly to the benzene ring.

amounts from both available sources. Therefore the extent of attack on the primary position of p-cymene was determined by summing the mole per cent of primary hydroperoxide, the mole per cent of cumic acid, and one-half the mole per cent of substituted acids[1]. Similarly the extent of attack on the tertiary carbon was determined by adding the mole per cent of tertiary hydroperoxide, the mole per cent of tertiary alcohol, the mole per cent of p-methylacetophenone and one-half the mole per cent of the di-substituted products[1].

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1. These values are found in Tables X, XI, and XII.

DISCUSSION

The results reported in Table XIII indicate that, within the limit of experimental error, the relative extent of oxidative attack at the methyl and isopropyl groups of *p*-cymene is the same. This is not surprising. The nature of the major proportion of the product will be determined by the identity of the propagation steps and these are the same for oxidation under the two reaction conditions, namely;

$$R^\bullet + O_2 \rightarrow RO_2^\bullet \qquad (\text{vi})$$

$$RO_2^\bullet + RH \rightarrow RO_2H + R^\bullet \qquad (\text{vii})$$

where $R^\bullet$ is either the primary or tertiary cyminyl radical and RO_2H is the corresponding hydroperoxide. Some product will be attributable to the initiation and termination steps, but since the reaction chains are probably fairly long under the conditions used in this study (119) this will constitute a very minor proportion of the total. Furthermore it would seem reasonable that the relative reactivity of a radical towards a primary and tertiary carbon atom would be approximately the same regardless of its nature. Thus, in the emulsion oxidation, some reaction chains may possibly be initiated by $RO^\bullet$ and $HO^\bullet$ radicals formed by hydroperoxide decomposition. (See pg. 15). However the relative reactivity of these radicals with respect to the alternative reaction sites should correspond closely to that of the $RO_2^\bullet$ radical acting in the propagation step.

This conclusion finds support from a comparison of the results of the present study with those reported by Kooyman (120), who has recently developed a somewhat unique method for the determination of hydrocarbon activities in free radical reactions. This method is based upon a comparison of the inhibiting action of different hydrocarbons on the propagation step of the peroxide catalyzed addition of carbon tetrachloride to olefins.

$$CCl_3^{\bullet} + RCH_2CH{=}CH_2 \longrightarrow RCH_2CHCH_2CCl_3 \qquad (xxxv)$$

$$RCH_2CHCH_2CCl_3 + CCl_4 \longrightarrow RCH_2CHClCCl_3 + CCl_3^{\bullet} \qquad (xxxvi)$$

Hydrocarbons possessing one or more hydrogen atoms on a carbon α to a center of unsaturation are capable of inhibiting the reaction by removing the $CCl_3^{\bullet}$ radical by the following reaction:

$$CCl_3^{\bullet} + RCH_2CH{=}CH_2 \longrightarrow CHCl_3 + RCHCH{=}CH_2 \qquad (xxxvii)$$

Kooyman has derived a relationship between α-methylenic activity and the retarding effect shown above which he expressed in the equation,

$$\frac{\Delta P}{(R)} = Kr \int \frac{dA}{(O)}$$

where ΔP = amount of peroxide consumed by retarder

R = concentration of retarder

dA = amount of olefin to which CCl_4 is attached

and O = concentration of olefin

With all concentrations constant Kr becomes a relative measure of α-methylenic reactivity.

In Table XIV Kr values obtained by Kooyman are given for a number of aromatic compounds.

TABLE XIV

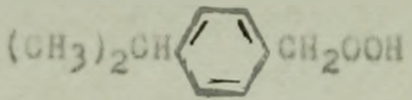
HYDROCARBON Kr VALUES

Compound	Kr x 10^2
Toluene	0.42
Cumene	1.75
p-Xylene	0.95
m-Xylene	0.84
o-Xylene	1.02

It is seen that the α-methylenic activity (Kr value) of the isopropyl group of cumene to that of the methyl group of toluene is 4.2:1. This corresponds very closely to the 4.0:1 ratio obtained in the present study for the relative extent of oxidative attack on the two positions of p-cymene. In other words the relative reactivity of the $RO_2^{\bullet}$ and $CCl_3^{\bullet}$ radicals towards primary and tertiary carbon atoms on a benzene ring is approximately the same.

It will be noted from Table XIV that the Kr value for m-xylene is exactly twice the Kr value for toluene. This is to be expected since m-xylene has twice the number of carbon-hydrogen bonds. In o- and p-xylene, however, the Kr values are slightly more than double. This indicates the presence of an intereaction effect between groups in the ortho and para positions. The ratio of activities of the two alkyl groups of p-cymene, as determined in the present study, is therefore not a true measure of the relative activity of methyl and isopropyl groups attached to the benzene nucleus because of a mutual interaction between groups in the para position. As a proposal for further work, it is suggested that the true ratio be determined by oxidation of *m*-cymene in the manner applied to *p*-cymene in the present study. On the basis of Kooyman's results one would predict that the ratio of activity for the two groups would be slightly smaller for the meta isomer.

Helberger *et al* (1) in their study of the photochemical oxidation of *p*-cymene proposed that the sole hydroperoxide formed was the primary compound III .



III

As pointed out in the General Introduction of this thesis their conclusion was based upon the isolation of cuminaldehyde by means of its semicarbazone from the products of the decomposition of the sodium salt of the hydroperoxide in boiling water. A similar treatment of the hydroperoxide salt isolated from the photochemical oxidation in the present investigation gave an identical result. On the other hand, the reduction of the oxidation product with lithium aluminium hydride has established quite conclusively that the product was a mixture of two hydroperoxides, the primary and the tertiary with the latter being present as the major component.

It is not difficult to account for these seemingly conflicting results. It has been well established that primary hydroperoxides decompose very readily in the presence of alkali to furnish aldehydes. Thus Hock and Long (58) obtained p-methylbenzaldehyde in good yield by warming p-xylyl hydroperoxide with one equivalent of aqueous alkali for a few minutes. Tertiary hydroperoxides, on the other hand,,are considerably more stable towards an alkali, particularly when one or more equivalents are present, thus converting the hydroperoxide completely to its sodium salt. Kharasch (121) has recently shown that at 90°C in the presence of excess alkali only 70% of cumyl hydroperoxide is decomposed in six hours. Furthermore the main reaction product is cumyl alcohol. As a result, subsequent treatment of the reaction product with semicarbazide hydrochloride allows the isolation of the semicarbazone of p-methylbenzaldehyde only. The mechanism of the decomposition of hydroperoxides in the presence of alkali will be discussed later in another connection.

It will be noted from an inspection of Tables X and XI that in the emulsion oxidations of p-cymene considerable quantities of hydroperoxide decomposition products, alcohols, ketone, and carboxylic acids, were formed during the oxidation reaction. This however was not the case in the photochemical oxidations. Thus, the product formed by the lithium aluminium hydride reduction of the total photochemical oxidation product corresponded to within 1% of the amount expected on the basis of the known hydroperoxide content of the oxidation mixture. Furthermore, only a very small amount of cumic acid (less than 0.5% of the total oxidation product) was isolated, and this may well have been formed by decomposition of the primary hydroperoxide during the extraction with sodium bicarbonate. The question naturally arises as to whether the presence of the hydroperoxide decomposition products in the emulsion oxidation is a consequence of the aqueous alkaline medium or the relatively high extent of conversion. (It will be recalled that the hydroperoxide content of the 60° C emulsion oxidation product was 19% and that of photochemical oxidation product only 5%). Certainly the almost complete absence of alcohols, ketone or acids in the photochemical reaction product would suggest that their formation in the emulsion process was promoted by the presence of the alkaline medium.

This conclusion finds support in the results of the recently reported investigation by Kharasch (121), on the decomposition of cumyl hydroperoxide under the influence of alkali. He observed that this tertiary hydroperoxide decomposed in the presence of aqueous alkali at an elevated temperature (above 50° C) into oxygen and cumyl alcohol together with small amounts of acetophenone, benzoic and other unidentified acids. This reaction is very much faster with 20 mole per cent than with a full equivalent of alkali. Furthermore it is markedly accelerated by the presence of certain "additives" such as succinonitrile which bring about a rapid and almost quantitative evolution of oxygen at room temperature. In the presence of easily oxidized compounds, i.e. primary and secondary alcohols, the "additives" cause the hydroperoxide to decompose without the evolution of oxygen and the alcohol is oxidized, often in high yield, to the corresponding aldehyde or ketone. Since above 50°C a rapid decomposition occurs even in the absence of "additives" Kharsch has suggested that the essential role of the "additive" is to accelerate a reaction which at room temperature is slow.

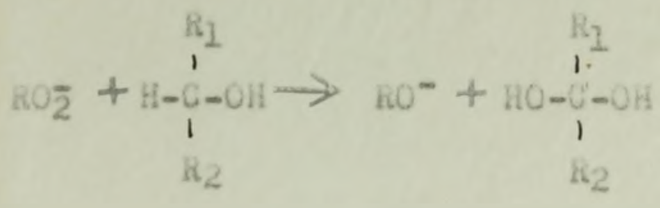
Kharsch has interpreted these results in terms of the following mechanism. The hydroperoxide in the presence of the alkaline medium, is considered first to be converted to the RO_2^- anion which is the active oxidizing species.

$$ROOH + OH^- \rightarrow RO_2^- + H_2O \qquad (xxxviii)$$

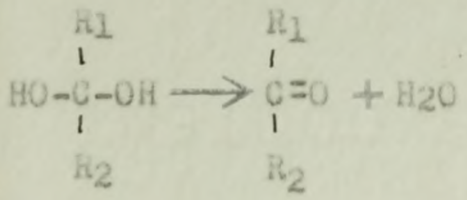
In the absence of other reducing components, oxygen is then transferred from the RO_2^- anion to the undissociated peroxide resulting in the formation of alcohol and oxygen.

$$RO_2^- + ROOH \rightarrow RO^- + ROH + O_2 \qquad (xxxix)$$

In the presence of an added alcohol, or some other reducing component, the RO_2 anion may transfer its oxygen to this component as follows:



$$RO_2^- + H\text{-}\overset{R_1}{\underset{R_2}{C}}\text{-}OH \rightarrow RO^- + HO\text{-}\overset{R_1}{\underset{R_2}{C}}\text{-}OH \qquad (xxxx)$$



$$HO\text{-}\overset{R_1}{\underset{R_2}{C}}\text{-}OH \rightarrow \overset{R_1}{\underset{R_2}{C}}{=}O + H_2O \qquad (xxxxi)$$

The extent to which this reaction occurs will depend upon the reducing power of the alcohol as compared to the hydroperoxide, and upon the relative concentrations of these reactants. Primary and secondary alcohols will be oxidized very readily and in their presence oxygen evolution can be completely supressed. A tertiary alcohol obviously will be more resistant and will yield oxidation products, ketones and acids, only at an elevated temperature and then in small amounts.

The results obtained in the present study are in complete accord with this interpretation. Thus, hydroperoxide decomposition, occurring during the emulsion oxidation because of the alkaline medium provided by the aqueous carbonate, produces a concentration of RO_2^- ions derived from both primary and tertiary hydroperoxides. These may act by oxygen transfer upon undissociated tertiary hydroperoxide to furnish the tertiary alcohol, dimethyl-*p*-tolylcarbinol, or upon undissociated primary hydroperoxide to give isopropylphenylcarbinol. This primary alcohol, however, may also serve as a reducing component and will be converted, in part, to the corresponding aldehyde, *p*-methylbenzaldehyde. This, in turn, will be further oxidized, probably by the oxygen gas being furnished to the system, to give cumic acid. To a minor extent the tertiary alcohol may serve as a reducing component and as a result a small amount will be converted into *p*-methylacetophenone.

The possibility is not precluded of some homolytic decomposition of hydroperoxide to $RO\cdot$ and $HO\cdot$ radicals, particularly in the case of the primary hydroperoxide which is thermally the less stable. The $RO\cdot$ radical could then react with excess hydrocarbon to form alcohol,

$$RO^{\bullet} + RH \rightarrow ROH + R^{\bullet} \qquad (vii)$$

and new radical R• so produced initiate a new hydroperoxide producing chain reaction. Other reactions of the RO• radical leading to ketone or acid formation might also occur (122). In view of the lack of products in the photochemical reaction and the results of Kharsch's investigation outlined above, however, it is suggested that the ionic alkali-induced decomposition is the more important in the emulsion oxidation.

On the basis of the present results, it is impossible to say whether, in the emulsion oxidation, all of the primary hydroperoxide had been decomposed to alcohol or acid at the completion of the reaction. Certainly the product obtained after precipitation of the sodium salt and liberation of the hydroperoxide with carbon dioxide was the essentially pure tertiary compound. Since it would seem unlikely that extensive decomposition of the primary hydroperoxide would occur at the ice-bath temperatures used in the precipitation process, this would suggest that the major portion of the primary hydroperoxide had decomposed during the oxidation reaction itself. Some of the resulting primary alcohol would then be converted to cumic acid (by the mechanism outlined above).

It remains now to discuss the significance of the variation with temperature of the relative extent of oxidative attack at the two reaction sites of cymene, and to outline a proposal for further study relating to this point.

It has now been well established that the relative ease of free-radical abstraction of hydrogen from hydrocarbon systems is in the order tertiary > secondary > primary. Walsh (50,51) observed that the oxidation of a saturated hydrocarbon containing the three carbon types yielded a product which was almost exclusively the result of attack at the tertiary site. He accounted for this on the basis of differences in the energy of activation required for that step of the reaction in which the hydrogen is removed from carbon. Thus, the activation energy for reaction at a tertiary carbon will be least since the resulting free radical will derive maximum stabilization through hyperconjugation. This conclusion is supported by the recent work of Trotman-Dickenson, Birchard, and Steacie (123) on the reaction of methyl radicals with paraffins. They have reported energies of activation varying from 10.4 K cal. for ethane, 8.3 K cal. for butane, to 7.6 K cal. for 2-methylpentane.

The same order of relativity has been observed by Bolland (119) from a kinetic study of the oxidation of a number of ethylenic compounds. He was able to evaluate the rate constant for the reaction,

$$RO_2^{\bullet} + RH \longrightarrow RO_2H + R\cdot \qquad \text{(vii)}$$

and found that a substitution of an alkyl group on the carbon to the ethylenic linkage increased its reactivity by a factor of 3.3^n, where n was the total number of substituents introduced. Furthermore, by making use of the plot of the logarithm of the rate constants against activation energies for a number of hydrocarbons he estimated that the difference in activation energy for the abstraction of hydrogen from a primary and secondary carbon to be approximately 1.6 K cal.

Trotman-Dickenson and Steacie (124), on the other hand, obtained very different results when they extended their study of the reaction of methyl radicals with hydrocarbons to compounds of the ethylenic series. Thus, although substitution of alkyl groups on the α-methylenic carbon greatly increased the reaction rate, the activation energies for all olefins studied, except ethylene, were in the range 7.8±0.3 K cal. In other words, it would appear that in the ethylenic series the difference in reactivity of primary, secondary, and tertiary carbon atoms is due mainly to changes in the steric factor.

Trotman-Dickenson and Steacie have criticized the method used by Bolland for the determination of activation energies and consider that their values are unreliable. It would seem to the writer, however, very unusual that the differences in reactivity at primary, secondary, and tertiary carbon atoms is due mainly to energy of activation differences with saturated hydrocarbons and to changes in the steric factor with olefins.

Returning now to the results of the present investigation, it can be seen from Table XIII that there was a slight but quite definite variation in the relative activity of the isopropyl and methyl groups of cymene with temperature.

DISCUSSION

The results reported in Table XIII indicate that, within the limit of experimental error, the relative extent of oxidative attack at the methyl and isopropyl groups of p-cymene is the same in the emulsion and photochemical reactions. This is not surprising. The nature of the major proportion of the product will be determined by the identity of the propagation steps and these are the same for oxidation under the two reaction conditions, namely,

$$R\cdot + O_2 \rightarrow RO_2^{\cdot} \qquad \text{(vi)}$$

$$RO_2^{\cdot} + RH \rightarrow RO_2H + R\cdot \qquad \text{(vii)}$$

where R· is either the primary or tertiary cyminyl radical and RO_2H is the corresponding hydroperoxide. Some product will be attributable to the initiation and termination steps, but since the reaction chains are probably fairly long under the conditions used in this study (119) this will constitute a very minor proportion of the total. Furthermore it would seem reasonable that the relative reactivity of a radical towards a primary and tertiary carbon atom would be approximately the same regardless of its nature. Thus, in the emulsion oxidation, some reaction chains may possibly be initiated by RO· and HO· radicals formed by hydroperoxide decomposition. (See pg. 15). However the relative reactivity of these radicals with respect to the alternative reaction sites should correspond closely to that of the$_2^{\cdot}$ radical acting in the propagation step.

The emulsion oxidation was studied at two different temperatures, 60°C and 80°C, and the relative reaction rates, as measured by the ratio of the products formed by attack at the tertiary and primary positions, was 4:1 and 3.5:1, respectively. This variation is too great to be attributed to experimental error, particularly in view of the excellent agreement between the results of the emulsion and photochemical reactions at the same temperature. Furthermore, the effect of temperature is in the direction expected if one considers that the difference in reactivity is due in all or part to a difference in activation energy. The slower reaction will have the higher energy of activation and the greater temperature coefficient. Therefore, as the temperature is increased the ratio of the reaction rates will approach unity.

It is suggested, as a proposal for further work, that a careful study be made of the variation of the relative extent of oxidative attack at the two positions of cymene as a function of temperature. From this data a fairly accurate value of ΔE, the difference in activation energy for abstraction of hydrogen from a primary and tertiary carbon atom in an aromatic system, and of $\frac{P_p}{P_t}$, the ratio of the probability factors for the two reactions, may be calculated. This has a distinct advantage over the usual method in which absolute values of the rate constants for the reactions being compared are determined and ΔE then is calculated as a difference between two large numbers. It is further suggested that this study be extended to p-ethyltoluene, m-cymene m-ethyltoluene. By comparing the results obtained for the para and meta isomers the effect, if any, of the mutual intereaction of para groups on activation energy can be calculated.

REFERENCES

1. Helberger, J.H., Rebay, A., and Fettback,H., Ber. 72 B, 1643, 1939; Chem. Abstr., 33, 9297, 1939
2. Armstrong, G.P., Hall, R.H., and Quinn, D.C., J. Chem. Soc., 666, 1950
3. Baeyer and Villiger, Ber., 34, 738, 1901; Biel.,I, 323
4. Wieland, H., and Maier, J., Ber., 64 B, 1205, 1931; Chem. Abstr. 25, 3984, 1931
5. Criegee, R., and Dietrich, H., Ann. 560, 135; Chem. Abstr. 43, 6189, 1949
6. Rieche, A., and Hitz, F., Ber., 62 B, 245, 1929; Chem. Abstr. 24, 1079, 1930
7. Medvedev, S., and Alekseeva, E., Ber., 65 B, 133, 1932; Chem. Abstr. 26, 2412, 1932
8. Milas, N.A., and Harris, S., J. Am. Chem. Soc., 60, 2434, 1938
9. Milas, N.A., and Surgenor,D., J. Am. Chem. Soc. 68, 205, 1946
10. Rust, F., and Vaughan, W., U.S. Patent 2,573,947, Nov. 6, 1951; Chem. Abstr. 46, 5073, 1952
11. Milas, N.A., and Perry, L., J. Am. Chem. Soc., 68, 1938; 1946
12. Pinazzi, C., Compt. rend., 226, 929, 1948; Chem. Abstr. 42, 5445, 1948
13. Quint, F.W., and Dilthey, W., Ber., 64 B, 2082, 1931; Chem. Abstr. 26, 141;1932

REFERENCES (cont'd)

14. Dilthey, W., and Dahm, F., J. prakt. Chem. 141, 61, 1934; Chem. Abstr. 29, 163, 1935

15. Rieche, A., "Alkyl Peroxyde and Ozonide", Dresden, Steinkopf; Chem. Abstr. 25, 1258, 1931

16. Rieche, A., Ber., 64 B, 2328, 1931; Chem. Abstr. 26, 81, 1932

17. Milas, N.A., J. Am. Chem. Soc., 61, 2430, 1939

18. Rieche, A., and Meister, R., Ber., 68 B, 1465, 1935; Chem. Abstr. 29, 6877, 1935

19. Rieche, A., Ber., 64 B, 2328, 1931; Chem. Abstr. 26, 81, 1932

20. Spath, E., Pailer, M., and Schmid, M., Ber., 74 B, 1557, 1941; Chem. Abstr. 37, 77, 1943

21. Milas, A., U.S. Patent 2,298,405, Oct. 13, 1942; Chem. Abstr. 37, 1448, 1943

22. Cooper, W., J. Am. Chem. Soc., 1340, 1951

23. Bach, A., Compt. rend. (Paris), 124, 951, 1897

24. Engler, C., and Wild, E., Ber. 30, 1669, 1897

25. Engler, C., and Wild, E., Ber. 31, 3046, 1898

26. Engler, C., and Wild, E., Ber. 33, 1090, 1900

27. Callender, H.L., Engineering 123, 147, 1927

28. Egerton, A.C., Nature, 121, 10, 1928

29. Ubbelohde, A.R., Proc. Roy. Soc. (London) A., 152, 354, 1935

REFERENCES (cont'd)

30. Szent Gyorgyi, A.v., Biochem. Z. 146, 246, 1924

31. Stephens, H.N., J. Am. Chem. Soc. 50, 568, 1928

32. Hock, H., and Shrader, O., Naturwiss 24, 159, 1936; Chem. Abstr. 30, 4472, 1936

33. Hock, H., and Shrader, O., Angew. Chem. 49, 595, 1936

34. Hock, H., Oel.u. Kohle. 13, 697, 1937; Chem. Abstr. 31, 4472, 1937

35. Criegee, R., Pilz, H., and Flygare, H., Ber. 72 B, 1799, 1939; Chem. Abstr. 33, 9292, 1939

36. Faraday Society, Trans. Faraday Soc. 42, 99, 1946

37. Faraday Society, Discussions Faraday Soc. 2, 1947

38. Waters, W.A., Chem. Soc., London, 42, 130, 1945

39. Waters. W.A., "The Chemistry of Free Radicals", Second Edition, Oxford Univ. Press. London 226, 1948

40. George, P., Rideal. E.K., and Robertson, A., Proc. Roy. Soc. A. 185, 288, 1946

41. George, P., and Robertson, A., Proc. Roy. Soc. A. 185, 309, 1946

42. George, P., Proc. Roy. Soc. A. 185, 337, 1946

43. Robertson, A., and Waters, W.A., Trans. Faraday Soc. 42, 201, 1946

44a. Frank, C., Chem. Rev. 46, 155, 1950

44b. Bawn, C.E.H., Faraday Soc. Discussion, Toronto, Sept. 1952

45. Stephens, H.N., J. Am. Chem. Soc., 48, 2920, 1926

REFERENCES (cont'd)

46. Stephens, H.N., and Roduta, F.L., J. Am. Chem. Soc., 57 2380, 1935

47. Grun, S., Ber. 53, 887, 1920

48. Burwell, A.W., Ind. Eng. Chem. 26, 204, 1934

49. Pope, J.C., Dykstra, F.J., and Edgar, G., J. Am. Chem. Soc. 51, 1875; 2203; 2213; 1929

50. Walsh, J., Trans. Faraday Soc. 42, 269, 1946

51, Walsh, J., Trans. Faraday Soc. 43, 297, 1947

52. Cullis, C.F., and Hinshelwood, C.N., Discussions Faraday Soc. 2, 1947

53. Farmer, H., and Sundralingham, A., J. Chem. Soc. 121, 1942

54. Farmer, H., Trans. Faraday Soc. 38, 340, 348, 1942

55. Hock, H., and Ganniche, K. Ber. 71, 1430, 1938; Chem. Abstr. 32, 7899, 1938

56. Hock, H., and Susemihl, W., Ber. 66, 61, 1933

57. Criegee, R., Ber. 77, 22, 1944; Chem. Abstr. 40, 6433, 1946

58. Hock, H., and Lang, S., Ber. 76, 169, 1943; Chem. Abstr. 37, 5362, 1943

59. Hock, H., and Lang, S., Ber. 77, 257, 1944; Chem. Abstr. 39, 3526, 1945

60. George, P., and Robertson, A., J. Inst. Pet. 32, 400, 1946

61. Polanyi, M., and Baughan, E.C., Trans. Faraday Soc. 37, 377, 1941

62. Maureu, H., and Dufraisse, C., Chem. Rev. 3, 113, 1926

REFERENCES (cont'd)

63. Lawrence, A.S.C., Trans. Faraday Soc. 34, 660, 1938

64. Vaughan, W., and Rust, F., U.S. Patent 2,403,777 July 9, 1946; Chem. Abstr. 40, 5757, 1946

65. Rust, F., and Vaughan, W., Ind. Eng. Chem. 41, 2595, 1949

66. Ross, W., and Fountain, E.B., Brit. Patent 636,754 May 3, 1950; Chem. Abstr. 44, 8360, 1950

67. Rieche, A., and Meister, R., Angew. Chem. 49, 101, 1936; Chem. Abstr. 30, 2549, 1936

68. Gray, V., and Steiner, H., U.S. Patent 2,558,844 July 3, 1951; Chem. Abstr. 46, 1023, 1952

69. Gray, V., and Steiner, H., Brit. Patent 614,455 Dec. 15, 1948; Chem. Abstr. 43, 5032, 1949

70. Hock, H., and Newwirth, F., Ber. 72 B, 1562, 1939; Chem. Abstr. 33, 8167, 1939

71. Ivanov, K., Savinova, V., and Mikhailova, E.G., J. Gen. Chem. (U.S.S.R.) 16, 1003, 1946; Chem. Abstr. 41, 2692, 1947

72. Hawkins, E., J. Chem. Soc. 2798, 1950

73. Ivanov, K., Doklady. Akad. Nauk. U.S.S.R. 72, 9036, 1950; Chem. Abstr. 44, 8316, 1950

74. Farmer, H., and Sutton, D., J. Chem. Soc. 10, 1946

75. Ivanov, K., and Savinova, V., Doklady. Askd. Nauk. U.S.S.R. 59, 493, 1948; Chem. Abstr. 42, 1948

76. Farkas, A., and Stribley, A., U.S. Patent, 2,430,864 Nov. 18, 1947; Chem. Abstr. 42, 1966, 1948

REFERENCES (cont'd)

77. Hochwalt, C., U.S. Patent 2,552,278 May 8, 1951; Chem. Abstr. 46, 139, 1952

78. Hock, H., and Lang, S., Ber. 75 B, 1051, 1942; Chem. Abstr. 37, 4387, 1943

79. Criegee, R., and Zogel, H., Chem Ber. 84, 215, 1951; Chem. Abstr. 45, 7558, 1951

80. Hall, R., and Quinn, D., Brit. Patent 610,293 Oct. 13, 1948; Chem. Abstr. 43, 3459, 1949

81. Hall, R., and Quinn, D., Nature 164 834, 1949

82. Hall, R., and Quinn, D., Brit. Patent 629,637, Sept. 23, 1939; Chem. Abstr. 44, 4489, 1950

83. Hall, R., and Quinn, D., U.S. Patent 2,547,938 April 10, 1951; Chem. Abstr. 45, 8042, 1951

84. Lorand, E.J., U.S. Patent 2,484,841 Oct. 18,1949; Chem. Abstr. 44, 5908, 1950

85. Hussle, [illegible]., Perkins, G.W., and Jolnnies, G., Am. J. Pharm. 107, 29, 1935

86. Hartmann, M., and Seiberth, M., Helv. Chem. Acta. 15, 1390, 1932

87. Hartmann, M., and Seiberth, M., U.S. Patent 1,924,786 Aug. 29, 1933; Chem. Abstr. 27, 5341, 1933

88. Soc. pour l'ind chim à Bâle, Brit. Patent 39[illegible],351 Aug. 3, 1933; Chem. Abstr. 28, 494, 1934

89. Johnson, R., U.S. Patent 2,5[illegible]8,039, 1952; Chem. Abstr. 46, 5089, 1952

REFERENCES (cont'd)

90. Ivanoy, K., and Savinova, V., Compt. rend. acad. sci. U.S.S.R. 48, 31, 1945; Doklady. Akad. Nauk. U.S.S.R. 48, 32, 1945; Chem. Abstr. 40, 4706, 1946

91. Ivanov, K., Savinova, V., and Zhakhovskoya, P., Doklady. Akad. Nauk. U.S.S.R. 59, 703, 1949; Chem. Abstr. 42, 6739, 1948

92. Ivanov, K., Savinova, V., and Zhakhovskoya, P., Doklady. Akad. Nauk. U.S.S.R. 59, 905, 1948; Chem. Abstr. 42, 6768, 1948

93. Hawkins, E., J. Chem. Soc. 2070, 1949

94. Hock, H., and Depke, [illegible]., Chem Ber. 84, 356, 1951; Chem. Abstr. 46, 1455, 1952

95. Hock, H., and Bergahad, K., Chem. Ber. 84 1, 1951; Chem. Abstr. 45, 5139, 1951

96. Hawkins, E., and Quinn, D., Brit. Patent 646,102 Nov. 15, 1950; Chem. Abstr. 45, 5723, 1950

97. Hawkins, E., Quinn, D., and Salt, F., Brit. Patent 641,250 Aug. 9, 1950; Chem. Abstr. 45, 8042, 1951

98. Hock, H., Lang, S., and Knavel, G., Chem. Ber. 83, 227, 1950;.Chem. Abstr. 44, 9946, 1950

99. Webster, [illegible]., and Quninn, D., Brit. Patent 654,035; Chem. Abstr. 46, 2580, 1952

100. Beer, R., McGrath, L., and Robertson, [illegible]., J. Chem. Soc. 2118, 1950

REFERENCES (cont'd)

101. Hock, H., and Lang, S., Ber. 76 B, 1130, 1943; Chem. Abstr. 38, 4935, 1944

102. Hock, H., and Lang, S., Ber. 75 B, 300, 1942; Chem. Abstr. 37, 3748, 1943

103. Dufraisse, C., and Etienne, A., Bull. Soc. Chem. (France) 1948, 804; Compt. rend. 226, 1773, 1948; Chem. Abstr. 43, 620, 1949

104. Farmer, H., and Sutton, D., J. Chem. Soc. 119, 1943

105. Ross, J., Gebhart, A., and Gerecht, F., J. Am. Chem. Soc. 71, 282, 1949

106. Farmer, H., and Sutton, D., J. Chem. Soc. 139, 1942

107. Kadowaki, H., Repts. Imp. Ind. Research Inst., Osaka, Japan, 14, No. 11, 1, 1934; Bull. Chem. Soc., Japan 11, 248, 1936; Chem. Abstr. 30, 5945 and 7543, 1936

108. Birch, S.F., Dean, R.A., Fidler, F.A., and Lowry, R.A., J. Am. Chem. Soc. 71, 362, 1949

109. Hercules Powder Co., Wilmington Delaware, Private Communication

110. Siggia, S., "Quantitative Organic Analysis Via Functional Groups", J. Wiley and Sons, New York, pg. 16

111. Smith, D., and Mitchell, J., Anal. Chem. 22 #6, 750, 1950

112. Hunt, F., McMaster University, Private Communication

113. Elliott, C., M.Sc. Thesis, McMaster University

114. Lorand, E.J. to Hercules Powder Co., Wilmington Delaware,

REFERENCES (cont'd)

U.S. Patent 2,484,841 Oct. 18, 1947; Chem. Abstr. 44, 5908, 1950

115. Auwers and Kolligs, Ber. 55, 42; Biel. VI 2(508)

116. Bert, Bull. Soc. Chim. Fran. (4) 37, 1580; Biel. VI, 2(543)

117. Shriner, R.L., and Fuson, R.C., "The Identification of Organic Compounds", J. Wiley and Sons, New York pg. 263

118. Cooke, R.G., Gillespie, E.F., and Killen MacBeth, A., J. Chem. Soc. 1825, 1938

119. Bolland, J.L., Quart. Rev. 3, 1, 1949

120. Kooyman, E.C., Discussions Faraday Soc., 10, 163, 1951

121. Kharasch, M.S., Fono, A., and Nudenberg, W., J. Org. Chem. 17, 212, 1952

122. Kharasch, M.S., Fono, A., and Nudenberg, W., J. Org. Chem. 16, 113, 1951

123. Trotman-Dickenson, A.F., and Steacie, E.W.R., J. Chem Phys. 19, 163, 1950

124. Trotman-Dickenson, A.F., and Steacie, E.W.R., J. Chem Phys. 19, 169, 1950