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Stable Phenoxy-radicals

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The present review is devoted to an examination and analysis of published data on reactions leading to the formation of phenoxy-radicals, and the structures and properties of these radicals.
In the description of the methods of preparing phenoxy-radicals, we examine the interaction of sterically hindered phenols with organic peroxides and inorganic oxidising agents, the mechanism of the thermal decomposition of cyclohexadienones, the autoxidation of sterically hindered phenols, and also the action of γ-radiation and ultraviolet radiation on phenols.
In the section devoted to the properties of phenoxy-radicals, we discuss the influence of steric hindrance of the reactive centre, and also the degree of delocalisation of the unpaired electron, on the stability of the phenoxy-radicals.
The available published data on the chemical transformations of substituted phenoxy-radicals are reviewed. Their recombination, disproportionation, isomerisation, and reaction with oxygen and halogens are examined. The influence of the steric and polar properties of substituents on the kinetics and mechanism of the transfer of hydrogen from organic compounds to stable phenoxy-radicals is analysed. The bibliography contains 180 references.

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I. INTRODUCTION

Sterically hindered phenols are now widely used as inhibitors of the thermal-oxidative degradation of polymeric materials, and the oxidation of motor fuels, oils, and edible fats[1-3]. Moreover, as shown by Emanuel' and coworkers[4-6], sterically hindered phenols can be used as physiologically active substances in various areas of biological studies.

The protective action of inhibitors of the phenol type is associated with the removal, from the substrate being oxidised, of the $RO_2^{\cdot}$ and $R^{\cdot}$ radicals responsible for the chain reaction: $RO_2^{\cdot} + PhOH \rightarrow ROOH + PhO^{\cdot}$. As a result of this reaction, the active $RO_2^{\cdot}$ or $R^{\cdot}$ radicals are replaced by the $PhO^{\cdot}$ radicals, which have a low activity and are incapable of maintaining the autoxidation chain reaction.

The retarding action of the inhibitor added to the substance being oxidised depends on[1,3]: (1) the activity of the $PhO^{\cdot}$ radical (the lower the activity of the $PhO^{\cdot}$ radical, the stronger the retarding effect), and (2) the rates of the reactions of the radicals $RO_2^{\cdot}$ and $R^{\cdot}$ with the inhibitor.

The development of a modern theory of the action of inhibitors, which might make it possible to control the selection and application of these inhibitors, is closely related to the development of the chemistry of free radicals and the establishment of the regular features of the dependence of their formation and behaviour on structure. In recent years, significant results have been obtained in this field, but these have not been reviewed to a sufficient extent in the chemical literature.

The present review examines reactions leading to the formation of stable phenoxy-radicals from sterically hindered phenols, and also the structure and behaviour of these radicals.

II. REACTIONS LEADING TO THE FORMATION OF PHENOXY-RADICALS

The chief method for the preparation of phenoxy-radicals is by the interaction of phenols with various organic and inorganic oxidising agents, leading to the removal of a hydrogen atom from the hydroxyl group. Phenoxy-radicals can also be obtained by the action of γ-radiation and ultraviolet radiation on phenols, and also as a result of homolytic bond rupture in various organic molecules. In the present chapter we shall examine reactions leading to the formation of stable phenoxy-radicals from sterically hindered phenols, that is, phenols containing various bulky substituents in the *ortho*-position relative to the hydroxyl group.

1. Reaction of Sterically Hindered Phenols with Peroxo-compounds

The thermal decomposition of organic peroxides in inert solvents is a spontaneous unimolecular reaction which takes place with the formation of free radicals[7,8]:

$$ROOR \rightarrow RO^{\cdot} + RO^{\cdot}$$

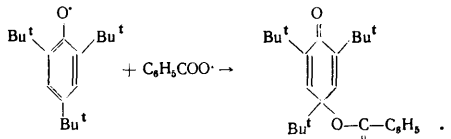
The $RO^{\cdot}$ radicals formed in this reaction can attack phenol molecules, giving the corresponding phenoxy-radicals:

$$PhOH + RO^{\cdot} \rightarrow PhO^{\cdot} + ROH .$$

Phenols react in analogous fashion with the free radicals formed by the decomposition of hydroperoxides, catalysed by cobalt naphthenate[9,10].

The reaction of 2,4,6-tri-t-butylphenol with benzoyl peroxide produces in the solution the blue colour characteristic

of the 2,4,6-tri-t-butylphenoxy-radical (I)[11]. Spectrophotometric study of this process[12] showed that the reaction obeys a second-order kinetic equation and includes as an intermediate stage the formation of the corresponding phenoxy-radical, which subsequently disappears, apparently according to the reaction:



(I) (II)

The direct detection of phenoxy-radicals in the reaction of sterically hindered phenols with peroxo-compounds is now possible using electron paramagnetic resonance (EPR). It was found that the reaction of 2,6-di-t-butyl-4-methylphenol[13,14], 2,6-di-(1,1-dimethylpropyl)-4-methylphenol, 2,6-di-(1,1-dimethylhexyl)-4-methylphenol[13], and 2,4,6-tri-t-butylphenol[14] with benzoyl peroxide, *p*-t-butylcumenyl hydroperoxide, or cyclohexyl peroxocarbonate, leads to the production of EPR spectra which show good agreement with the structures of the corresponding phenoxy-radicals. An interesting feature is that in the work cited no change in the structure of the EPR spectra was observed during the reaction. This indicates that the radicals formed by the decomposition of the peroxides react rapidly with the phenoxy-radicals, and this prevents their further transformation. The nature of the alkyl substituents in the *ortho*- and *para*-positions relative to the phenoxy hydroxyl group influences not only the structure of the final products of the reaction of the phenols with the peroxides, but also its velocity. The study of the dependence of the rate of the reaction of peroxo-radicals with phenols on the structure of the substituents in the phenol molecule is of considerable practical as well as purely theoretical interest, since the retarding action of inhibitors is to a large extent determined by the rate of the reaction of the peroxo-radicals with the inhibitor molecules (the efficiency of the inhibitor); when various inhibitors are introduced into a reaction in equal concentrations, the most effective inhibitor is that which reacts most rapidly.

Ingold[15], in a study of the oxidation of mineral oil in the presence of a number of 2,6-di-t-butyl-4-substituted phenols, found that electron-donating substituents in the *para*-position of the phenol, if their volume is small, increase the relative activity of the inhibitor. A linear relationship is observed between $\lg(k/k_0)$ (where k and k_0 are the rate constants of the inhibitor being studied and a standard inhibitor for the given reaction) and the Hammett constants σ of the substituents. A similar good correlation between the inhibiting activity of 2,6-di-t-butyl-4-alkylphenols and the Hammett constants σ was observed for the oxidation of methyl oleate[16]. With bulky substituents in the *para*-position, the relative inhibiting activities show a good correlation with the Taft constants of the substituents[15], which make allowance for steric factors. Study of the reaction of t-butoxy-radicals with 2,6-di-t-butyl-4-methylphenol† and 2,6-di-t-butylphenol, both deuteriated in the OH group, and also the reaction of styrylperoxo-radicals with 4-alkylphenols, revealed kinetic isotopic effects ($k_H/k_D = 6.14$[17] and $k_H/k_D = 10.5$[18] respectively), indicating that the stage limiting the rate of the process is the transfer of hydrogen from the phenol molecules to the attacking radical. To investigate the influence of substituents on the ease of formation of the polar transition state in the reaction of styrylperoxo-radicals with *meta*-, *para*-,[18] and *ortho*-substituted phenols[19], and also in the reaction of the t-butoxy-radical with 2,4,6-trialkylphenols[20], a correlation was established between the logarithms of the rate constants and the Brown constants σ^+ for electrophilic substituents. A linear relationship was observed with values of the constants for the reaction ρ equal to 1.30 for 2,6-dimethylphenol and 1.11 for 2,6-di-t-butylphenol. The small value of ρ for these phenols indicates only slight separation of the charges in the transition state of this reaction.

Like the RO· and ROO· radicals, hydroxyl radicals react with phenols with the formation of peroxo-compounds of the type PhO–OPh and PhO–OH.[21,22] The system $H_2O_2 + FeSO_4$ (Fenton's reagent) is usually employed as source of ·OH radicals. The formation of phenoxy-radicals in the reaction of 2,6-di-t-butyl-4-methylphenol with hydroxyl radicals was observed by Ershov and Zlobina[23] using the EPR method. The source of hydroxyl radicals used in this instance was peroxonitrous acid, which undergoes homolytic splitting in solution with the formation of ·OH and $\cdot ONO \rightleftharpoons \cdot NO_2$ radicals[24,25]. Analogous results were obtained by Ershov and coworkers[26] using alkyl nitrites as oxidising agents; these compounds readily undergo homolytic splitting with the formation of RO· and NO· radicals. The decomposition of alkyl nitrites in the presence of alkylphenols leads to the production of the corresponding phenoxy-radicals, detected both from the appearance of the characteristic colour and from the EPR spectra.

2. Reaction of Sterically Hindered Phenols with Inorganic Oxidising Agents

The reactions of sterically hindered phenols with peroxo-compounds, described above, generally produce, in addition to the primary phenoxy-radical, various products of the addition of the peroxide residue to this radical. In order to study the stability and behaviour of phenoxy-radicals it is necessary to carry out the oxidation of the phenols in such a way that the substrate containing the PhO· radicals does not contain other active radicals capable of recombining with the PhO· radicals. These requirements are satisfied by such oxidising agents as lead dioxide[12,14,27-33,35-37], silver oxide, potassium hexacyanoferrate(III)[38-42], and cerium(IV) sulphate[43,44]. The oxidation of phenols by these oxidising agents can be represented in general form as follows:

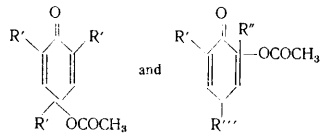
$$PhOH + M^{n+} \rightarrow PhO^{\cdot} + M^{(n-1)+} + H^+.$$

Using these oxidising agents, it has been established that the phenoxy radicals formed by the oxidation of phenols have different stabilities, and this determines their ability to undergo further transformations. Thus the oxidation of 2,4,6-tri-t-butylphenol[28,45-48] and various other phenols leads to the formation of phenoxy-radicals which are able to "live" in the absence of oxygen for a very prolonged period. On the other hand, the oxidation of 2,6-di-t-butyl-4-methylphenol produces a less stable phenoxy-radical, transformation of which gives various final products. Phenols which do not contain bulky substituents in the *ortho*-position are oxidised with the formation of even less stable radicals, whose lifetimes decrease to hundredths of a second. In order to study these radicals by the EPR method, it is necessary to establish a steady-state concentration of the radicals sufficient for their detection. Parti-

† In the Russian text here and subsequently this compound is incorrectly referred to as Ionol [which is 2-(3-hydroxybutenyl)-1,3,3-trimethylcyclohexene]. This has been corrected in the translation (Ed. of Translation).

cularly fruitful results have been obtained using a flow system in which the solutions of the phenol and the oxidising agent are mixed directly in the resonator of the EPR spectrometer. Stone and Waters[43,44] used this method to study the EPR spectra and structure of the radicals formed in the oxidation of a number of unhindered or weakly hindered phenols. In some instances, when the oxidation of the phenols takes place too rapidly, a milder oxidising agent—mercuric oxide HgO—is used[37]. The formation of phenoxy-radicals in the oxidation of 2,6-di-t-butyl-4-methylphenol by HgO is observed only when the solution is heated to 60°C,[50] whereas oxidation by means of PbO_2 or $K_3Fe(CN)_6$ leads to the immediate production of phenoxy-radicals even at room temperature[50-53].

The oxidation of phenols by lead tetra-acetate [$Pb(CH_3COO)_4$] and acetyl peroxide leads to the formation of the corresponding *p*- and *o*-quinol acetates[54-58]:



where R′ = CH_3, R″ = CH_3 or H, and R‴ = CH_3.

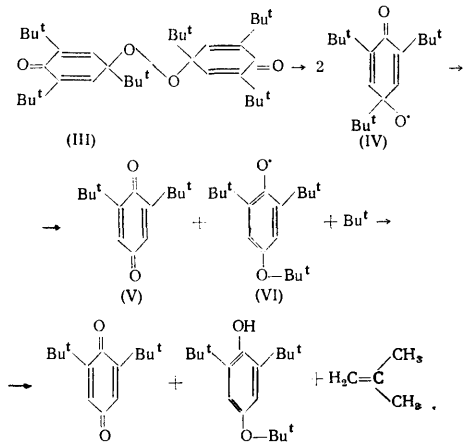
The radical mechanism of the reaction of phenols with $Pb(CH_3COO)_4$ was proved by Emanuel' and coworkers[59] by the production, in the EPR spectra, of signals due to primary phenoxy radicals from 2,4,6-tri-t-butylphenol, 2,6-di-t-butylphenol, and 2,6-di-t-butyl-4-ethylphenol. These workers also noted the formation of radicals from unhindered phenols such as *p*-cresol, *p*-ethylphenol, and phenol, confirming that this reaction also takes place by a radical mechanism with unhindered phenols. The formation of radicals from unhindered phenols in this instance is rather surprising, since when other oxidising agents were used, these radicals could not be recorded, because of their extremely low stability. It may be suggested that the short-lived radicals produced in the oxidation of phenols by lead tetra-acetate may form a complex with the oxidising agent or with its decomposition products, leading to their stabilisation.

The oxidation of sterically hindered phenols by salts of carboxylic acids, for example $Cu(OCOR)_2$, probably also takes place by a radical mechanism, since the chief reaction products, as in the reactions of such one-electron oxidising agents as PbO_2 and $K_3Fe(CN)_6$, are dimers, which are paired in the *ortho*- and *para*-positions, depending on the structure of the original phenol[60].

Phenoxy-radicals were observed directly by the EPR method by Razuvaev and coworkers[61,62] in a study of the oxidation of phenols in the presence of a complex Cu^{2+} + amine catalyst.

3. Decomposition of Cyclohexadienones

As already noted, the homolytic mechanism of the decomposition of organic peroxides of the type ROOR is now generally accepted[36]. The production of radicals in their decomposition has been confirmed by various methods, in particular from the initiation of autoxidation and polymerisation in the presence of the decomposing peroxide, from the decrease in the rate of decomposition of the peroxide in the presence of inhibitors of free-radical reactions, etc. Until recently, however, it was not possible to observe free radicals directly in the thermal decomposition of organic peroxides, since these radicals are insufficiently stable for detection by the EPR method. Brodskii and Pokhodenko[63] tried to prove the homolytic mechanism of the decomposition of peroxides using the EPR method. They started from the assumption that if the RO residues in the molecule of the peroxide ROOR were stable phenoxy-radicals, the decomposition by a homolytic mechanism would give radicals sufficiently stable to be recorded by the EPR method. For this purpose, bis-(1,3,5-tri-t-butyl-4-oxocyclohexa-2,5-dienyl) peroxide (III) was synthesised[27,28,46,64]. It was previously found[28,65] that the products of the decomposition of this peroxide are 2,6-di-t-butyl-4-t-butoxyphenol, 2,6-di-t-butylbenzoquinone, and 2-methylpropene. To explain the formation of these products, Muller[65] suggested that the decomposition of the peroxide takes place by an ionic mechanism with transfer of the t-butyl residue from the carbon atom to the oxygen atom. When this peroxide was heated to 200°C, however, an intense EPR signal was observed[63], consisting of three components 1 : 2 : 1 with a splitting between them equal to 1.3 Oe. The infrared spectra of the decomposition products of the peroxide[63], unlike the spectrum of the original peroxide, showed a band at 3650 cm^{-1}, corresponding to the OH group of sterically hindered phenols. On this basis, the following mechanism was proposed for the decomposition of the peroxide (III); this mechanism explains the production of the final products:

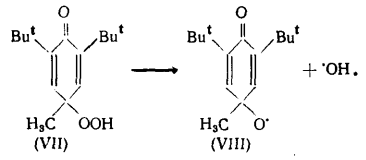


The observed EPR spectrum of the decomposition products of the peroxide is due to the phenoxy-radical (VI), in which the unpaired electron interacts with two equivalent *m*-hydrogen atoms. The constant for the splitting between the components of this signal has a value which is close to that previously obtained[53] for this radical, formed by the oxidation of the corresponding phenol. The suggestion[66,67] that the triplet EPR signal observed in the decomposition of the peroxide is due to the radical (IV), in which the presence of the oxygen atom in the *para*-position leads to a decrease in the splitting constant, which is usually equal to 1.7 Oe for the 2,4,6-tri-t-butylphenoxy-radical, to 1.3 Oe, appears erroneous if allowance is made for the low probability of the observation of this radical in the EPR spectra, resulting from its low stability, which is due to the impossibility of delocalisation of the unpaired electron in the benzene ring and the absence of bulky groups screening the reactive centre.

The radical mechanism for the decomposition of the peroxide (III) was later proved by the EPR method by carrying out the reaction in xylene solution at 80°C.[68]

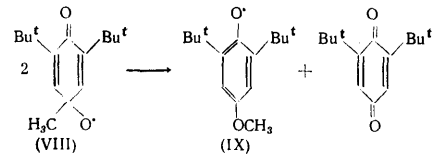
The thermal decomposition of 2,6-di-t-butyl-4-hydroperoxy-4-methylcyclohexa-2,5-dienone (VII) is also accompanied by the formation of phenoxy-radicals[69]. On the

basis of generally accepted ideas, this process should be represented as follows:



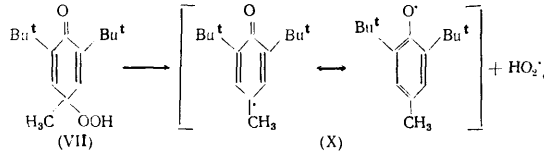
(VII) (VIII) (I)

Subsequent disproportionation of the radicals (VIII) should produce the phenoxy-radical (IX), as described above:



(VIII) (IX) (2)

The EPR signal observed in this work (1 : 3 : 3 : 1 quadruplet, 1 : 2 : 1 triplet, a_1 = 11 Oe, and a_2 = 1.7 Oe), however, cannot be attributed either to radical (VIII) or to radical (IX), formed according to schemes (1) and (2). The parameters of this spectrum (the number of lines, the ratio of the intensities, and the splitting constants) correspond completely to the 2,6-di-t-butyl-4-methylphenoxy-radical (X)[51,52,66]. On this basis it was suggested[69] that the first stage in the decomposition of the hydroperoxide is the removal of the hydroperoxo-radical with the formation of a phenoxy-radical:



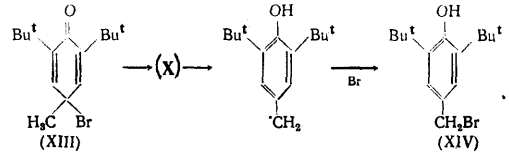
(VII) (X)

This unusual course of the thermal decomposition of organic peroxo-compounds without rupture of O–O bonds was also observed by the action of heat on 2,6-di-t-butyl-4-t-butylperoxy-4-methylcyclohexa-2,5-dienone (XI), leading to the formation of 2,6-di-t-butyl-4-methylphenoxy-radicals[70], and on bis-(3,5-di-t-butyl-4-oxo-1-phenyl-cyclohexa-2,5-dienyl) peroxide (XII), accompanied by the formation of 2,6-di-t-butyl-4-phenylphenoxy-radicals[71].

The radicals formed by the thermal decomposition of organic peroxides are effective initiators of polymerisation processes[7,8]. The thermal decomposition of the peroxide (III)[50], which, as indicated above, takes place with rupture of the O–O peroxide bond, gives radicals which initiate the polymerisation of methyl methacrylate. On the other hand, the decomposition of the hydroperoxide (VII) in the presence of methyl methacrylate and vinyl acetate does not lead to polymerisation of the latter[69], in agreement with the earlier observation[71] that the polymerisation of acrylonitrile is not initiated by the decomposition products of the peroxide (XII), whose decomposition also takes place without rupture of the peroxide bond.

It can be seen from the foregoing that the peroxo-compounds formed from sterically hindered phenols may decompose in two ways when heated: with splitting of the peroxide bond [peroxide (III)] or with splitting of the C–O bond of the C–O–O–R group [peroxides (VII), (XI), and (XII)]. In this instance, when splitting takes place at the O–O bond, active radicals of type (IV), which initiate the polymerisation of monomers, are produced. On the other hand, the phenoxy and peroxo-radicals produced in the decomposition of peroxides with rupture of the C–O bond of the C–O–O–R group do not initiate the polymerisation of monomers, because of their comparatively high stability.

One example of the decomposition of cyclohexadienone structures with the formation of phenoxy-radicals is the quinonone-benzyl rearrangement of 2,6-di-t-butyl(-4-methylphenol quinobromide (XIII)[72], which reacts when heated to give the corresponding hydroxybenzyl bromide (XIV). The available published data could be used to ascribe to this process either an ionic mechanism[73] or a radical mechanism[74]. According to recent results[72], thermal treatment of (XIII) in the resonator of an EPR spectrometer leads to the production of an EPR signal corresponding to the 2,6-di-t-butyl-4-methylphenoxy-radical (X)[51,52]. On this basis, the following reaction scheme was suggested[72]:



(XIII) (XIV)

The phenoxy-radical (X) is also formed when (XIII) is treated with benzoyl peroxide, metallic mercury, or ultraviolet light. The formation of the corresponding phenoxy-radical has also been recorded by similar treatment of the quino-bromide of 2,4,6-tri-t-butylphenol[72].

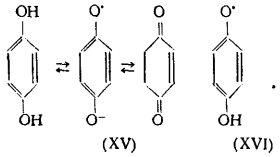
4. The Autoxidation of Sterically Hindered Phenols

The autoxidation of organic compounds is accompanied by the formation of free radicals[1,3] which in a number of instances are recorded by the EPR method[66].

In the oxidation of sterically hindered phenols, the formation, as final products, of compounds of the type PhO–OH and PhO–OPh[75–80], analogous to the products of the radical reaction of sterically hindered phenols with organic peroxides (see part 1 of this section), has been observed. The radical mechanism of the autoxidation of phenols was recently confirmed experimentally by the EPR method.

Adams and coworkers[81] observed the production of eight lines (1 : 1 : 3 : 3 : 3 : 3 : 1 : 1) in the EPR spectrum during the autoxidation of 2,6-di-t-butyl-4-methylphenol in alkaline medium. No explanation was put forward in the work cited for this structure of the EPR spectrum. Autoxidation was later studied in more detail[82] for the example of a number of 2,6-di-t-butyl-4-R-phenols. It was shown that the reaction leads to the formation of radical-ions of the semiquinone of the substituted pyrocatechol, recorded by the EPR method.

The autoxidation of *p*-hydroxyphenols (hydroquinones) is also accompanied by the formation of semiquinone radical-ions; this was proved as early as the nineteen-thirties by Michaelis and coworkers[83,84]:



(XV) (XVI)

The radical-ion formed in this reaction is stabilised by resonance, so that it can be observed by the EPR method. The EPR spectrum of (XV)[85,86], consisting of a quintuplet 1 : 4 : 6 : 4 : 1 (a = 2.37 Oe), is in agreement with the equivalence of all four protons of the benzene ring.

The semiquinone radical-ion has proved to be a convenient object for the study of the influence of substituents on the distribution of spin density in the ring[87], for the investigation of the inductive effect of substituents[88,89], and for the experimental verification of the theory of hyperconjugation[90].

Unlike (XV), the undissociated semiquinone (XVI) has a low stability and it has not been detected by the direct method.

Recently, Pokhodenko and Khiznhyi[91] detected uncharged semiquinone radicals in neutral medium (benzene) by the EPR method during the oxidation of hydroquinones containing bulky alkyl substituents in the *ortho*-positions. Thus in the oxidation of a solution of 2,6-di-t-butylhydroquinone in benzene with PbO_2, a triplet signal (1 : 2 : 1) is produced with splitting constant 1.75 Oe, corresponding to the uncharged semiquinone radical. The autoxidation of this compound in alkaline medium also gives a triplet signal, but with a reduced hyperfine splitting constant (1.2 Oe), assigned to the semiquinone radical-ion. The stabilities of the uncharged and charged semiquinone radicals differ considerably from one another: removal of the oxidising agent (PbO_2) in the first instance leads to the immediate disappearance of the EPR signal, whereas thorough evacuation of the oxidising agent (oxygen) in the second instance does not lead to rapid disappearance of the EPR signal.

5. Action of γ-Radiation and Ultraviolet Radiation on Phenols

It can be seen from the foregoing that most reactions leading to the formation of phenoxy-radicals are associated with the removal of hydrogen from the hydroxyl group of the phenol under the influence of oxidising agents. In recent years it has been shown that the rupture of the O–H bond in phenols with the formation of radicals may be brought about under the influence of ionising radiation. Thus the action of X-rays or ultraviolet light on 2,4,6-tri-t-butylphenol in the solid state or in benzene solution leads to the formation of a stable radical, whose EPR spectrum consists of a single line with a breadth of 3 Oe[92]. The irradiation of 2,4,6-tri-isopropylthiophenol leads to the formation of the corresponding disulphide[92], but the EPR spectrum could not be recorded, apparently due to the low stability of the radical produced. The detection of unstable radicals on irradiation is facilitated by the use of low temperatures. Thus the EPR spectra of radicals obtained by the photolysis of a number of thiophenols at 77°K [93] or by the γ-irradiation of solid bis-phenol[94] have been studied. The EPR method has been used to detect the formation of primary phenoxy-radicals when ultraviolet radiation is used for the initiation of the decomposition of t-butyl peroxide in the presence of a number of phenols at temperatures reaching −30°C.[95]

III. THE PROPERTIES OF PHENOXY-RADICALS

1. Properties of Sterically Hindered Phenols

Sterically hindered phenols, whose oxidation produces phenoxy-radicals, exhibit a number of specific properties. The presence of screening alkyl substituents in the *ortho*-positions relative to the hydroxyl group of the phenol leads to the loss of such typical properties of phenols as solubility in water and alkalis, the ability to give colour reactions with $FeCl_3$, and the ability to react with metallic Na, RMgBr, or diazomethane[96,97].

Bulky *ortho*-substituents hinder the reaction of the hydrogen of the O–H group with other molecules, and this influences reaction rates and the ability to form a hydrogen bond. The retarding action of bulky substituents on the rate of the reaction of phenols with peroxides was noted earlier. Thus in a study of the reaction of $RO_2^{\cdot}$ radicals with 2,6-dialkyl-4-methylphenols it was found that the rate of the process decreases with increase in the volume of the substituents in positions 2 and 6, in the following order: 2,6-dimethyl > 2,6-di-isopropyl > 2-t-pentyl > 2-t-octyl > > 2,6-di-t-butyl > 2,6-di-t-pentyl > 2,6-di-t-octyl > > 2-t-butyl-6-t-octyl[19,20]. An analogous influence of substituents was also noted in studies of the rates of the oxidation of phenols by lead tetra-acetate[55] and the acetylation[98] and alkylation of alkyl halides[99].

Steric hindering of the hydroxyl group of the phenol leads to a sharp decrease in its acidity, as with carboxylic acids[100–102]. Large groups hinder the solvation of the anion formed as a result of the dissociation, and hence decrease its stability. Moreover, it is possible that alkyl substituents in the phenol molecule, as in hindered acetic acids, decrease the effective dielectric constant around the OH group, increasing the electrostatic energy of the anion and hence decreasing the dissociation constant[100,101].

It is natural to assume that the steric hindering of the hydroxyl group is also responsible for the decrease in the electrical conductivity of solutions of substituted phenols. The ratio of the conductivities of the *p*-alkylphenol and its *o*-isomer in solution is equal to 14 for the cresols, 336 for the isopropylphenols, and 136 for the t-butylphenols[103].

As already noted, the hindering of the hydroxyl group by bulky substituents in the *ortho*-positions prevents the formation of associates of the substituted phenols with other molecules. A large number of studies have shown that unlike unsubstituted phenol[104–106], sterically hindered phenols show no tendency to form intermolecular hydrogen bonds[107–110]. For 2,6-di-t-butyl-4-methylphenol, the appearance in the infrared spectra of weak bands corresponding to hydrogen bonds is observed only in strongly basic solvents[111]. Groups which are less bulky than t-butyl have a smaller influence on hydrogen bond formation[109,112,113].

The study of phenol solutions by nuclear magnetic resonance (NMR) also confirms that steric factors have a decisive influence on the possibility of hydrogen bond formation[114–117]; a good correlation is observed between the magnitude of the chemical shift resulting from hydrogen bonding[117] and the displacement of the frequencies in the infrared spectra[107].

The frequencies of the stretching vibrations of the hydroxyl group in phenol are altered by the introduction of alkyl substituents in the *ortho*-positions, and the increase in frequency for 2,6-di-t-alkylphenols relative to unsubstituted phenol ($\Delta\nu = 34$ cm^{-1})[118–120] is too large to be attributed entirely to the inductive influence of the alkyl substituents.

At first sight, this increase in the frequency of the stretching vibrations of the hydroxyl group can be attributed to the breakdown of the coplanarity of the OH group and the ring, since this would lead to a decrease in conjugation and an increase in frequency. Proof of this influence of substituents on the coplanarity of individual groups of molecules has been published[121–124]. Study of the frequencies of the stretching vibrations of the OH group in 4-substituted

and 2,6-dialkyl-4-substituted phenols shows, however, that the frequencies and intensities of the bands show a good correlation with the Hammett constants σ of the substituents[108,118-120]. The slope of the straight lines is the same in both instances[118] and is equal to 13.7 cm^{-1}. On this basis it was concluded that the OH group in 2,6-dialkylphenols, as in phenols which have no substituents in the *ortho*-positions, is coplanar with the ring. Ingold[120] attributed the observed increase in frequency to the interaction of the electron clouds of the hydroxyl and *ortho*-alkyl groups. A similar explanation was used to interpret the results of a study of the chemical shifts of the NMR signal from the OH group of a number of mono- and di-ortho-substituted phenols, which showed that the screening of the hydroxyl proton increases with increase in the volume of the *ortho*-substituent[125]. Comparison of the values of ν and τ shows a correlation between these quantities, apparently indicating that the same factors are responsible for the change in these quantities. Although these results confirm the coplanarity of the OH group and the ring, the accuracy of the experiments does not exclude the possibility that there is slight rotation. The energy of conjugation of this group with the ring changes as $\cos^2\theta$ (where θ is the angle of rotation)[121,126], that is, even a fairly marked rotation of the bond under the influence of bulky substituents does not eliminate the conjugation completely. Thus for small values of θ this difference in the infrared spectra may not be detected.

The facts examined in this section indicate the highly specific nature of sterically hindered phenols, resulting from the presence of bulky alkyl substituents in the *ortho*-positions relative to the hydroxyl groups. The steric screening is also responsible for a number of the unusual properties of the radicals formed by the removal of hydrogen from the hydroxyl group of these phenols, particularly their high stability.

2. Stability of Phenoxy-radicals

The factors leading to the stabilisation of radicals have been examined in most detail for the example of the triphenylmethyl radicals formed by the dissociation of hexaphenylethane[7,127-129]:

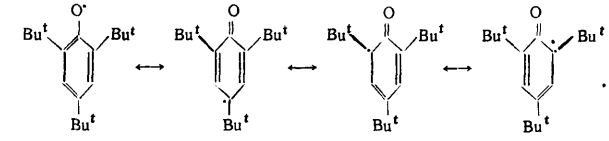
$$(C_6H_5)_3C{-}C(C_6H_5)_3 \rightleftarrows 2(C_6H_5)_3C^{\cdot}.$$

The chief factors determining the stability of free radicals are: (1) the extent of the steric hindrance of the atom formally carrying the unpaired electron; and (2) the extent of the delocalisation of the unpaired electron.

The introduction of phenyl groups into the *para*-positions of the benzene rings of the triphenylmethyl radical leads to an increase in the stability of the radical[130,131], due to the additional possibilities for delocalisation of the unpaired electron[132]. An analogous influence is observed when the phenyl rings are replaced by naphthyl rings. On the other hand, substituents in the *ortho*-positions of the phenyl rings lead to greater stabilisation of the radical than the same substituents in the *para*-position[133,134]. In the opinion of Razuvaev and coworkers[135], the stability of the radical may be due to intramolecular and intermolecular stabilisation. Study of the kinetics of the disappearance of substituted naphthoxy-radicals has shown the importance of both steric and energetic factors. Increase in the stability of radicals also takes place as a result of the formation of complexes with electron-donating solvents. The possibility of interaction between free radicals and the medium was also proved[137] by the EPR method for the example of nitrogen oxide radicals, which form a hydrogen bond with the participation of the unpaired electron with polar solvents.

Let us now consider the factors leading to the stabilisation of phenoxy-radicals.

The infrared spectra and EPR spectra‡ have shown that sterically hindered phenoxy-radicals are characterised by delocalisation of the unpaired electron[138]:



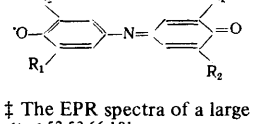
The infrared spectra of phenoxy-radicals shows a doublet band in the range 1600–1660 cm^{-1}. The presence of this band, which is characteristic of the C–O bond in 2,5-cyclodienones and substituted diphenoquinones[80,142-146], indicates that there is a marked contribution from the quinonoid structure in the overall state of the radical. This delocalisation of the unpaired electron leads to an increase in the stability of the phenoxy-radical.

When the t-butyl group in the *para*-position of the radical is replaced by a methoxy- or t-butoxy-group, the stability of the radical remains unchanged. This is apparently due to the participation of the ether oxygen in the overall conjugation, and this stabilises the radical to a sufficient extent, although the ether group in the *para*-position occupies less space than the t-butyl group[138].

The most important factor responsible for the stabilisation of phenoxy-radicals, however, is the steric hindering of the phenoxy-oxygen by bulky alkyl substituents. Thus the 2,4,6-tri-t-butylphenoxy-radical in the absence of oxygen may exist for as long a period as desired, whereas the 2,4,6-trimethylphenoxy-radical has a low stability and undergoes various changes. As already noted, the replacement of a t-butyl group in the *para*-position by the t-butoxy-group does not alter the stability of the radical. On the other hand, the replacement of an *ortho*-t-butyl group by an *ortho*-t-butoxy-group leads to a sharp decrease in stability. The gain in conjugation energy obtained due to the ether oxygen is insufficient to stabilise the sterically less hindered radical.

In recent years a number of attempts have been made to study the stability of phenoxy-radicals quantitatively. Thus Cook and coworkers[33] studied the disappearance of 2,6-di-t-butyl-4-isopropylphenoxy-, 2,6-di-t-butyl-4-cyclohexylphenoxy-, and 4-s-butyl-2,6-di-t-butylphenoxy-radicals from the change in the optical density of their solutions at 630 nm. The kinetic results obtained show that the rate of disappearance of these radicals decreases in the following order of substituents in the 4-position of the phenol: isopropyl > cyclohexyl > s-butyl. The rates of disappearance of the 2,6-di-t-butyl-4-methylphenoxy- and 2,6-di-t-butyl-4-ethylphenoxy-radicals was found to be so great that it could not be measured by the spectrophotometric method.

Extensive possibilities for the study of the stability of free radicals are provided by the EPR method. By using this method, it has been possible to determine the influence of the degree of steric hindrance of the phenoxy-oxygen of a number of indophenoxy-radicals on their stability[147]:



$R_1 = R_2 = t\text{-}C_4H_9$,	(XVII)
$R_1 = R_2 = t\text{-}C_5H_{11}$,	(XVIII)
$R_1 = R_2 = cyclo\text{-}C_6H_{11}$,	(XIX)
$R_1 = R_2 = iso\text{-}C_3H_7$,	(XX)
$R_1 = t\text{-}C_4H_9$; $R_2 = CH_3$.	(XXI)

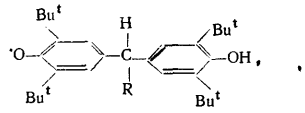
‡ The EPR spectra of a large number of phenoxy-radicals have now been studied[52,53,66,181].

It was shown that the radicals (XVII) and (XVIII), which do not contain α-hydrogen atoms in the *ortho*-substituents, have an extremely high stability; their concentrations in benzene or xylene solutions do not change to a significant extent as far as 70°C. On the other hand, the radicals (XIX), (XX), and (XXI), which contain α-hydrogen atoms in the *ortho*-substituents, have a much lower stability.

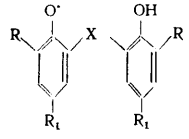
Comparison of the rate constants for the disappearance of the three indophenoxy-radicals (XIX), (XX), and (XXI) showed that their stability depends to a marked extent on the structure of the *ortho*-substituents. The ratio of the rate constants for the disappearance of the radicals studied is approximately

$$K_{XIX} : K_{XX} : K_{XXI} = 1 : 2 : 50.$$

The sharp increase in the rate of disappearance on going from the radicals (XIX) and (XX) to the radical (XXI) is due to the increase, by four orders of magnitude, in the value of the pre-exponential term, indicating that the *ortho*-substituents have a much smaller hindering effect on the reactive centre in radical (XXI) than in the radicals (XIX) and (XX). It is of interest to compare the stability of the radicals formed by the oxidation of *p*- and *o*-bis-phenols[148]. In the study of the oxidation of *p*-bis-phenols by the EPR method:



where R = H or C_6H_5, it was found that the phenoxy-radicals formed in the reaction have a high stability (for the radical with R = C_6H_5, $\tau_{1/2}^{40^\circ}$ = 1050 s). This is due to the extremely low value of the pre-exponential term ($K_0 = 3.2 \times 10^3\ s^{-1}$, $\Delta S^{\neq} = 60$ e.u.), and this in turn is due to the marked restrictions in the elementary stage of the disappearance of the phenoxy-radical. On the other hand, the phenoxy-radicals formed in the oxidation of *o*-bis-phenols have such a low stability that the authors cited[148] could not determine it quantitatively by the EPR method



X = CH_2, CH-C_6H_5, -S-;
R = t-C_4H_9, $C(CH_3)_2C_6H_5$;
R_1 = CH_3, C_2H_5, t-C_4H_9.

The reason for such a sharp decrease in stability on going from the *p*- to the *o*-bis-phenoxy-radicals is apparently the marked decrease in the steric hindering of the phenoxy oxygen by the ortho-substituents. In the *p*-bis-phenoxy-radicals studied, the oxygen is surrounded by bulky *o*-t-butyl groups, whereas in the *o*-bis-phenoxy-radicals one of the *ortho*-positions relative to oxygen is occupied by $-CH_2-$ or $-CH-C_6H_5$-groups or sulphur atoms, which have a smaller hindering effect than the *o*-t-butyl groups. Decrease in the degree of hindrance of the phenoxy-oxygen by *ortho*-substituents, as shown above for substituted indophenoxy-radicals, leads to a sharp decrease in the stability of the resulting radical.

The stability of phenoxy-radicals is also influenced to a significant extent by the degree of branching of the carbon atom of the alkyl substituent in the *para*-position.

Comparison of the rate constants of the disappearance and the transformation half-periods for 2,6-di-t-butyl-4-R-phenoxy-radicals (R = CH_3, C_2H_5,[149] or t-C_3H_7 [33]) indicates that their stability increases in the order of *para*-substituents: $CH_3 < C_2H_5 <$ iso-$C_3H_7 <$ t-C_4H_9.

An interesting feature is that the stability of the radicals formed by the oxidation of 2,6-di-t-butyl-4-alkylphenols is much less than that of the *p*-bis-phenoxy-radicals, due to the additional possibilities for delocalisation of the unpaired electron in the second instance. The 2,4,6-tri-t-butyl-phenoxy-radical, which does not contain α-hydrogen atoms in the *para*-substituent, is exceptionally stable and may exist for a prolonged period in the absence of oxygen.

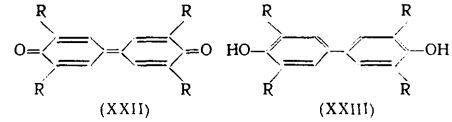
The examples considered in this section show that, as with the triphenylmethyl radicals, the chief factors responsible for the stability of phenoxy-radicals are the delocalisation of the unpaired electron and the extensive steric hindrance of the atom carrying a large proportion of the charge of the unpaired electron. These two effects explain the characteristic behaviour of phenoxy-radicals in chemical reactions. Let us consider some of these reactions.

3. Reactions of Phenoxy-radicals

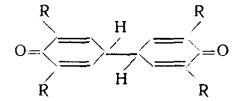
a. Recombination. As already noted, the phenoxy-radicals formed by the oxidation of 2,4,6-trialkylphenols which do not contain labile α-hydrogen atoms in their substituents are generally stable and do not undergo significant changes in the absence of oxygen. The recombination of these radicals is prevented by bulky substituents in the *ortho*- and *para*-positions. On the other hand, 2,6-di-t-alkylphenoxy-radicals with substituents in the *para*-position capable of conjugation with the unpaired electron exist in equilibrium with their dimers[53,150]. This dimer exists, for example, for the 2,6-di-t-butyl-4-cyanophenoxy-radical, whose unpaired electron is capable of conjugation with the substituent and can be found on the nitrogen atom.

The existence of a dimer has also been demonstrated[151] for the 2,4,6-triphenylphenoxy-radical, but its structure has not been determined[136,152].

The oxidation of 2,6-dialkylphenols containing a hydrogen atom in the *para*-position is accompanied by the formation of phenoxy-radicals and produces dimeric final products. Thus in the oxidation of 2,6-dimethylphenol or 6-t-butyl-2-methoxyphenol by lead dioxide[64], potassium hexacyanoferrate(III) in an alkaline medium[141,153,154,156], organic peroxides[21,22,79,157], and oxygen[62], the chief products of the reaction are the diphenoquinone (XXII) and its dihydroxy-derivative (XXIII), whose structures were confirmed from the infrared and ultraviolet spectra:



(XXII) (XXIII)



(XXIV)

The intermediate product (XXIV) is comparatively stable only in non-polar solvents and undergoes rapid isomerisation to the corresponding dihydro-derivative in polar media[64,141].

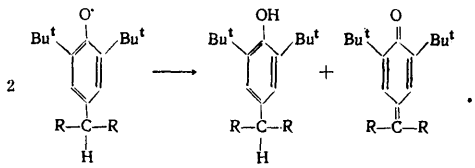
Analogous dimeric products are also formed in the oxidation of 2,6-di-t-butyl-4-chloro(bromo)phenols[36].

Study of the oxidation of phenols in which one or both *ortho*-positions were unsubstituted[21,22,60,62,71,154-156] showed that dimers joined in the *ortho*-positions are formed. These reactions involving the recombination of phenoxy-radicals show the importance of the influence of steric factors on the direction of the process. In all instances,

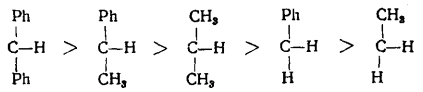
recombination takes place at the least screened position of the radical, carrying the unpaired electron.

b. Disproportionation of phenoxy-radicals. The introduction of secondary alkyl substituents into the *para*-position of 2,6-di-t-butylphenols leads to a decrease in the stability of the corresponding radicals relative to radicals whose *para*-position is occupied by tertiary alkyl substituents.

In a study of the disappearance of the blue 2,6-di-t-butyl-4-isopropylphenoxy- and 4-s-butyl-2,6-di-t-butylphenoxy-radicals, it was found that they are converted not into dimeric products but into the corresponding yellow quinone methides. Spectrophotometric study of the kinetics of this reaction showed that the rate of disappearance is described by an equation of second order with respect to the radical. On this basis, the following reaction scheme was proposed:



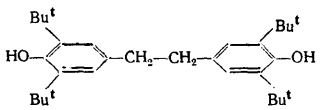
The formation of quinone methides and the original phenols was also observed in a study of the disappearance of a number of other phenoxy-radicals[158,159]. Study of the rate of disappearance of phenoxy-radicals by disproportionation has made it possible to estimate qualitatively the influence of a substituent in the *para*-position on the stability of the radicals[158,159]. It was found that the stabilities of the phenoxy-radicals decrease in the following order of substituents:



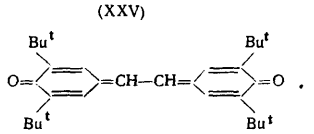
Examination of this series of substituents confirms the stabilising influence of the phenyl group on the radical.

c. Isomerisation of phenoxy-radicals. When the number of α-hydrogen atoms in the *para*-substituent of a 2,6-di-t-butylphenol is increased, the products of the oxidation of these phenols differ from those obtained from *p*-s-alkylphenols.

Thus the chief products of the oxidation of 2,6-di-t-butyl-4-methylphenol are 4,4′-ethylenebis-(2,6-di-t-butylphenol) (XXV) and 4,4′-ethanediylidenebis-(2,6-di-t-butylcyclohexa-2,5-dien-1-one) (XXVI):



(XXV)

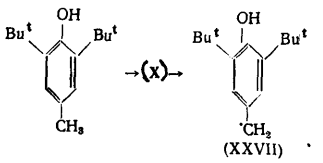


(XXVI)

The formation of these products led a number of authors[27,79,80] to suggest that the primary act in the oxidation of 2,6-di-t-butyl-4-methylphenol involves the removal of a hydrogen atom of the methyl group with the formation of the hydroxybenzyl radical (XXVII), whose dimerisation produces (XXV). Subsequent oxidation of (XXV) gives the final stilbenequinone (XXVI).

On the other hand, the formation of cyclohexadienone structures in the oxidation of 2,6-di-t-butyl-4-methylphenol by organic peroxides suggests the existence of phenoxy-radicals, whose presence in 2,6-di-t-butyl-methylphenol undergoing oxidation was later established reliably by spectroscopic methods, including the EPR method[51-52,141]. The formation of phenoxy-radicals as primary products of the oxidation of 2,6-di-t-butyl-4-methylphenol made it difficult to explain the production of the dimers (XXV) and (XXVI), since direct conversion into these compounds from the phenoxy-radical is impossible.

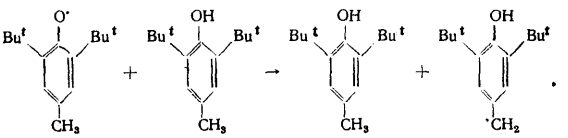
To resolve these contradictions, Cook[29] suggested that the initially formed phenoxy-radical (X) subsequently undergoes isomerisation to form the hydroxybenzyl radical, according to the scheme:



(XXVII)

The radical (XXVII) then undergoes dimerisation to 4,4′-dihydroxybibenzyl and is oxidised to the stilbenequinone.

Experimental confirmation of the isomerisation of the phenoxy-radical into the hydroxybenzyl radical was obtained by Brodskii and Pokhodenko[49,160,161], who studied the oxidation of 2,6-di-t-butyl-4-methylphenol containing deuterium in the methyl group. It was found that the oxidation of 2,6-di-t-butyl-4-methylphen[^{2}H]ol gives a dimeric product whose infrared spectrum, instead of the 2690 cm^{-1} band due to the stretching vibrations of the OD group, contains a band at 3650 cm^{-1} due to the OH group. This result shows that the primary act in the oxidation of 2,6-di-t-butyl-4-methylphenol involves the removal of hydrogen from the hydroxyl group, since the primary removal of hydrogen from the methyl group would have produced a dimer containing the OD group of the original phenol. An analogous result was obtained[161] in the oxidation of 2,6-di-t-butyl-4-perdeuteriomethylphenol. The infrared spectrum of the dimeric product was found to contain the band due to the stretching vibrations of the OD group, instead of the 3650 cm^{-1} band present in the original 2,6-di-t-butyl-4-perdeuteriomethylphenol. The results obtained in the works cited indicate isomerisation of the initially formed phenoxy-radical to produce the hydroxybenzyl radical, with transfer of hydrogen from the methyl group to the oxygen. These results also make it possible to reject the possibility of formation of benzyl radicals by the reaction of phenoxy-radicals with molecules of the original phenol according to the scheme proposed by Becconsall[51]:



The reaction of organic peroxides with trialkylphenols containing a methyl group in the *para*-position is interesting. The reaction of 2,4,6-trimethylphenol (XXVIII) and 2-t-butyl-4,6-dimethylphenol (XXIX) with peroxo-compounds gives the corresponding stilbenequinones as the final product[9]. On the other hand, the reaction of 2,6-di-t-butyl-4-methylphenol with peroxides gives cyclodienone structures of type (II)[10].

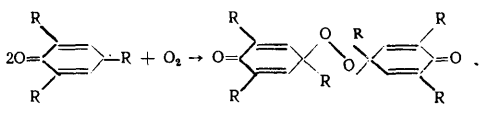
The only reaction of 2,6-di-t-butyl-4-methylphenol in which the formation of stilbenequinone is observed is that with triphenylmethyl hydroperoxide. This difference in the

behaviour of these phenols[9,10] can be explained as follows. The phenoxy-radical formed as a result of the primary attack of the peroxide residue on the phenol containing a methyl group in the *para*-position may react in two ways: in the first place, it may undergo isomerisation to an unstable hydroxybenzyl radical, whose dimerisation with subsequent oxidation of the dimeric products gives finally the stilbenequinone, or, in the second place, it may react with a new peroxide residue to give a cyclodienone derivative.

From the fact that the reaction of the phenols (XXVIII) and (XXIX) with peroxides gives stilbenequinones, it may be assumed that in this instance isomerisation takes place much more rapidly and more readily than their reaction with the peroxide residues. The phenoxy-radical formed in the oxidation of 2,6-di-t-butyl-4-methylphenol is much more stable than the phenoxy-radical formed in the oxidation of the phenols (XXVIII) and (XXIX), since both of its *ortho*-positions are occupied by bulky t-butyl groups. As a result, the rate of its isomerisation is decreased to such an extent that the main process leading to the disappearance of the radical is its reaction with the peroxide residues with the formation of cyclohexadienone structures of type (II). In the reaction with triphenylmethyl hydroperoxide, however, the rate of the reaction between the phenoxy-radical from the 2,4-di-t-butyl-4-methylphenol and the peroxide residue is decreased as a result of the marked steric hindrance of the reactive centre of the peroxide residue by the phenyl groups, and this prevents the reaction. The rate of this reaction is less than the rate of isomerisation of the phenoxy-radical to form the hydroxybenzyl radical, so that stilbenequinone is formed as the final reaction product.

The reaction of 2,6-di-t-butyl-4-methylphenol with alkyl nitrites, which readily decompose in solution to RO· and NO· radicals, leads to the corresponding quinonitrole (XXX) and hydroxybenzaldehyde (XXXI)[26]. To explain the formation of these products, a reaction mechanism which in our opinion is quite correct, was proposed[26]. The radical (X) formed as a result of the attack on the phenol molecule by the RO· radical either reacts with NO· with the subsequent formation of the quinonitrole or undergoes isomerisation to the hydroxybenzyl radical and then recombines with NO· to form the oxime of the corresponding hydroxybenzaldehyde; the oxime is readily converted into the aldehyde under the influence of the alkyl nitrite.

d. Reaction with oxygen. On contact with atmospheric oxygen, the usual bright blue or red colours of trialkylphenoxy-radicals gradually change to yellow, due to the formation of the bis-(1,3,5-trialkylcyclohexa-2,5-dienone) peroxides (XXXII)[27,28,30,46,64,65]. The formation of these peroxides is also observed in the oxidation of the phenols by PbO_2 or $K_3Fe(CN)_6$ in the presence of atmospheric oxygen:

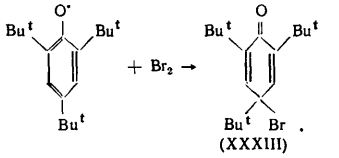


Proof of this structure for the peroxo-compounds is provided by the fact that the infrared spectra contain a doublet at 6.0 μm and 6.2 μm, corresponding to the quinonoid structure, and do not contain the band due to the hydroxyl group of the original phenols.

When the products of the reaction of phenoxy-radicals with oxygen are treated with hydriodic acid or sodium iodide in acetic acid, free iodine is liberated, indicating that they contain the peroxo-group O–O [50].

The ease of formation of bis-peroxides from phenoxy-radicals depends on the type of substituent in the *para*-position of the radical. Thus the rate of the reaction of 2,6-di-t-butylphenoxy-radicals with oxygen decreases with change in the substituents in the following order[36]: C_6H_5 > > $(C_6H_5)_3C$ > C_6H_5CO > C–N. A decrease in the rate of the reaction of phenoxy-radicals with oxygen is also observed when the t-butyl group in the *para*-position of the radical is replaced by methylphenyl or naphthyl groups, due to the additional stabilisation of the radical resulting from delocalisation of the unpaired electron[36,163]. An interesting feature is that the rate of the reaction with oxygen for the radical in which the *para*-position is occupied by the *p*-methylphenyl group is only half the rate of the reaction of the radical containing the *o*-methylphenyl group in the *para*-position[163]. This increase in reaction rate is apparently due to the decrease in the stability of the radical containing the *p*-methylphenyl group as a result of its displacement from the coplanar state, leading to the loss of conjugation energy.

e. Reaction with halogens. The addition of bromine solution to a solution of the 2,4,6-tri-t-butylphenoxy-radical in the absence of atmospheric oxygen produces a yellow crystalline precipitate[28], whose infrared spectrum[46] does not contain the band due to the hydroxyl group, but contains a double band at 6.0 μm and 6.2 μm, corresponding to the quinonoid structure (XXXIII):



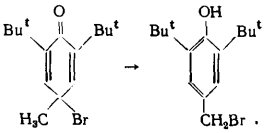
(XXXIII)

Compound (XXXIII) is also formed by the reaction of the phenol itself with bromine[164]. Study of the bromination of a number of phenols showed that in all instances the products are *p*-quinonoid structures, even when attack at the *ortho*-position is less hindered than attack at the *para*-position. This phenomenon is explained by the fact that electrophilic substitution in the phenol series takes place with a much smaller activation energy in the *para*-position than in the *ortho*-position[164].

All the quinobromides isolated have an absorption maximum in the range 248–251 nm, confirming the formation of the *p*-quinonoid structure (*o*-quinonoid structures have an absorption maximum in the range 320–360 nm [164]).

The stability of the quinobromides depends to a marked extent on the size of the substituents. Thus mesitol quinobromide exists for only 8 min at 20°C, whereas 2,6-di-t-butyl-4-methylphenol quinobromide exists for several days[162].

The instability of quinobromides with a methyl group in the *para*-position is due primarily to their spontaneous rearrangement with transfer of the bromine from the benzene ring to the methyl group



At elevated temperatures in the solid state and in non-polar solvents, this rearrangement takes place by a radical mechanism[72].

The reaction of phenoxy-radicals with (dichloroiodo)-benzene or with free chlorine gives quinochlorides similar

to the quinobromides described above. These compounds are unstable, and when heated they liberate chlorine and the original phenoxy-radicals.

f. Dehydrogenation of phenoxy-radicals. An extremely characteristic reaction of phenoxy-radicals, as of other free radicals, is the removal of hydrogen from organic compounds; the hydrogen becomes attached to the oxygen atom of the phenoxy-radical, and the radical formed from the molecule donating the hydrogen often recombines with the original phenoxy-radical with the formation of a quinol ether [165,166]. An example is the reaction of phenoxy-radicals with aromatic aldehydes [12] and with oximes of various structures [167].

The reaction of phenoxy-radicals with hydroperoxides leads to decomposition of the latter with the formation of stable products, and this is of considerable importance for processes of inhibited oxidation. The hydroperoxides in this instance cannot initiate new oxidation chains. Study of the kinetics of the disappearance of the 2,6-di-t-butyl-4-(3′,5′-di-t-butyl-4-hydroxydicyclohexa-2′,5′-dienylidenemethyl)phenoxy-radical in the presence of propene hydroperoxide [168] showed that the reaction is of first order with respect to each component. A bimolecular reaction mechanism with first-order kinetics with respect to each component was also found [169] in a study of the reaction of the 2,4,6-tri-t-butylphenoxy-radical with t-butyl hydroperoxide. The 2,4,6-tri-t-butylphenoxy-radical also removes a hydrogen atom from diethyl phosphite molecules. On the basis of kinetic data it was shown [170] that the reaction with diethyl phosphite involves the removal of hydrogen from the P–H bond of the monomeric form of the phosphite.

Stable phenoxyl radicals readily dehydrogenate phenols. An example is provided by the reaction of the 2,4,6-tri-t-butylphenoxy-radical (ArO·) with 4-t-butylphenol (PhOH) [171]. The observed ratio of the reacting components (2 moles ArO· per mole of PhOH) corresponds to the following reaction scheme:

$$\underset{\text{stable}}{ArO^{\cdot}} + PhOH \rightleftarrows ArOH + \underset{\text{unstable}}{PhO^{\cdot}}$$

$$ArO^{\cdot} + PhO^{\cdot} \underset{\text{slow}}{\overset{\text{rapid}}{\rightleftharpoons}} ArOOPh$$

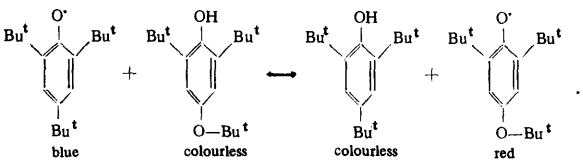
$$2ArO^{\cdot} + PhOH \rightarrow ArOH + ArOOPh$$

The formation of the quinol ether was also observed [172] in the reaction of the 2,6-di-t-butyl-4-phenylphenoxy-radical with 2-naphthol.

All the quinol ethers obtained are unstable. When heated in organic solvents they undergo reversible dissociation to the original radicals. The rate of dissociation is greater, the more marked the screening of the hydroxyl group of the phenol. Thus the quinol ether formed by diphenylnitroxide and the 2,4,6-tri-t-butylphenoxy-radical, formed by removal of a hydrogen atom at 20°C by the 2,4,6-tri-t-butylphenoxy-radical, undergoes reversible dissociation to the extent of 1%. [66]

The reaction of stable phenoxy-radicals with sterically hindered phenols in which the *para*-position is free or contains halogens, produces other reaction products [173]. For example, the reaction between the 2,4,6-tri-t-butylphenoxy-radical and 2,6-di-t-butylphenol leads to condensation of the benzene rings of the latter with subsequent dehydrogenation of the dimeric products and the formation of the corresponding diphenoquinone. The reaction of 2,6-di-t-butyl-4-methylphenol with stable radicals is analogous [143].

The reaction of stable phenoxy-radicals with phenols which also give stable radicals on dehydrogenation is an equilibrium reaction of the type:



The equilibrium constant for this reaction at 25°C is 51.7 ± 4.1, [35] that is, for the same initial concentrations of the components, the equilibrium is displaced towards the formation of the more stable alkoxyphenoxy-radical.

The same equilibrium reaction with the 2,4,6-tri-t-butylphenoxy-radical is undergone by 2,6-di-t-butyl-4-methoxyphenol [174] and 2,4,6-triphenylphenol [151].

Kreilick and Weismann [175] used the NMR method to determine the rate constant for the reaction of the 2,4,6-tri-t-butylphenoxy-radical with a molecule of the corresponding phenol, from the broadening of the signal due to the protons of the hydroxyl group. The rate constant found in this way at 30°C in CCl_4 was 300 litre mole^{-1} s^{-1}, and the value found for the activation energy was 1.0 ± 0.5 kcal mole^{-1}.

On the basis of a study of a large number of dehydrogenations, Muller and coworkers [176] suggested that the first stage in the dehydrogenation of organic compounds by phenoxy-radicals is the formation of an ion pair (A), stabilised with the formation of a new radical (B), which subsequently undergoes further transformation:

$$ArO^{\cdot} + HXR \rightleftarrows \underset{(A)}{[Ar\bar{O}\cdots H\cdots \overset{+}{X}R]} \rightleftarrows ArOH + \underset{(B)}{RX^{\cdot}}.$$

The dehydrogenation of various organic compounds by stable radicals provides a convenient method for studying the reactivity of these compounds. Kinetic studies of dehydrogenation by stable radicals make it possible to estimate the part played by energetic and steric factors in kinetics and to reach conclusions regarding the reaction mechanism. Here, promising possibilities are provided by the EPR method.

Buchachenko and coworkers [177] have used this method to study the reactivity of C–H bonds in various hydrocarbons with respect to the 2,4,6-tri-t-butylphenoxy-radical. It was found that in the hydrocarbon series n-decane–trimethylheptane and toluene–ethylbenzene–cumene, it is possible to follow the influence of methyl groups on the reactivity of the C–H bond being attacked, and in the series toluene–diphenylmethane it is possible to follow the influence of phenyl groups. The data obtained indicate that the reaction of the 2,4,6-tri-t-butylphenoxy-radical with hydrocarbons is characterised by relatively high activation energies, due to the endothermic nature of the removal of hydrogen, and that the activation energy decreases regularly with decrease in the strength of the C–H bond being attacked, from n-decane to diphenylmethane. Comparison of the activation energies in the toluene–diphenylmethane series shows that the introduction of phenyl groups has a much more marked influence on the kinetics of the process than the introduction of methyl groups. Examination of the values of the pre-exponential term (K_0) and entropy of activation ($\Delta S^{\neq}$) revealed the screening influence of the methyl and more particularly the phenyl groups, leading to a decrease in the probability of formation of the activated complex.

The 2,4,6-tri-t-butylphenoxy-radical has also been used to study the reactivity of the OH bonds in nitrophenols and the influence of solvents on this reaction[178].

The data obtained indicate that when nitro-groups are introduced into the phenol molecule, the activation energy for the removal of hydrogen from the hydroxyl group of the phenol is increased, but when several nitro-groups are introduced the effect is not additive. Measurement of the rate constants for the removal of hydrogen from *o*-nitrophenol in hexane, benzene, acetone, or methanol showed that the rate constant is independent of the nature of the medium. In the opinion of the authors cited[178], this indicates that the phenol taking part in the reaction is not solvated, apparently because of steric hindrance, in contrast to *m*-nitrophenol, which forms stable hydrogen bonds with the solvent.

As already noted, the thermal decomposition of the peroxide of the substituted cyclodienone (III) and ionol hydroperoxide (VII) is accompanied by the formation of phenoxy-radicals. It has been shown by the EPR method that these radicals are capable of removing hydrogen from the OH and NH groups of sterically hindered phenols.

The kinetics of the reaction of the stable tetra-t-butylindophenoxy-radical (XVII) with various aromatic amines and phenols were studied recently[179,180]. These compounds were chosen in order to study the influence of steric factors on the rate of hydrogen transfer, and also to study the influence of substituents and the applicability of the Hammett equation to radical reactions of this type.

Comparison of the activation energies, pre-exponential terms, and entropies of activation for the reaction of (XVII) with diphenylamine (DPA) and aniline shows that the replacement of one hydrogen atom in the NH_2 group of aniline by a phenyl group does not alter significantly the stability of the bond being attacked: the activation energy changes only slightly on going from aniline to DPA. The pre-exponential term, however, decreases by two orders of magnitude (the entropy of activation, which is a measure of the probability of formation of the active complex, decreases by 8 e.u.), indicating marked steric hindrance by the phenyl group. Thus the decrease in the rate constant for the reaction with DPA relative to the reaction with aniline is due to steric hindrance of the reactive centre of the DPA molecule by the two phenyl groups. A similar marked steric hindrance by the phenyl group was also observed[177] in a study of the removal of hydrogen from toluene and diphenylmethane by the 2,4,6-tri-t-butylphenoxy-radical.

The kinetics of the reaction of the radical (XVII) with aniline and its *para*-derivatives were studied[180] to investigate the influence of substituents on the reactivity of the NH bond in anilines. The values found for the rate constants for this reaction show that electron-donating substituents in the *para*-position of aniline increase the rate of removal of hydrogen, whereas electron-accepting substituents decrease the rate of hydrogen removal. The values of the logarithms of the reaction rate constants as functions of the corresponding values of the Hammett constants σ lie satisfactorily on a straight line, whose slope gives a value for ρ equal to 2.58. This high value of ρ indicates the importance of the polar influence of the substituents on the rate of removal of hydrogen from the NH bond of amines. A study of the rate of removal of hydrogen from DPA and aniline labelled with deuterium in the amino-group showed the existence of isotopic effects k_H/k_D, indicating that the stage determining the rate of the radical reaction of hydrogen removal is the rupture of the NH bond in the amine.

To investigate the influence of polar and steric factors on the reactivity of phenols, a study was made[179] of the reaction of the radical (XVII) with 2,6-di-t-butyl-4-R-phenols and phenols which did not contain alkyl substituents in the *ortho*-positions.

The reaction was carried out at phenol concentrations in the range 10^{-4}–10^{-3} M, in which displacement of the band due to the monomeric form of the OH group of the phenol in the infrared spectra is not observed. On this basis the results of the study were related to non-associated phenol molecules.

The data obtained show that on going from *ortho*-unsubstituted phenols to 2,6-di-t-butyl-4-R-phenols the pre-exponential term decreases by more than two orders of magnitude, corresponding to a decrease in the entropy of activation by 6 e.u. This indicates marked screening of the O–H group of the phenols by the two ortho-t-butyl groups. Despite this, the rate of transfer of hydrogen to the radical (XVII) from the 2,6-di-t-butyl-4-R-phenols is much greater than that from *ortho*-unsubstituted phenols. Comparison shows that the activation energy for the reaction of the radical (XVII) with sterically hindered phenols is only one-third of that with *ortho*-unsubstituted phenols. Thus in the reaction of the radical (XVII) with sterically hindered phenols there is a strong compensation effect, so that in spite of the marked screening action of the two *ortho*-t-butyl groups on the OH bond of the sterically hindered phenols, these groups at the same time alter the properties of the OH bond being attacked to such an extent that the transition state of the reaction is realised with a smaller expenditure of energy for 2,6-di-t-butyl-4-R-phenols than for *ortho*-unsubstituted phenols. For this reason the reactivity of sterically hindered phenols in the transfer of hydrogen to a stable radical is greater than that for *ortho*-unsubstituted phenols.

The rate of transfer of hydrogen to the radical (XVII) decreases in the order 2,6-di-t-butylphenol–2,6-di-t-butyl-4-methylphenol–2,6-di-t-butyl-4-ethylphenol, and the electron-donating properties of the substituents in the *para*-position increase in the same order.

Comparison of the rate constants for the reactions of the radical (XVII) with diphenylamine and phenols shows that the rate of the reaction with diphenylamine is less than that with phenols by a factor of 100–1000. This is due to the marked hindrance of the reactive centre in DPA and its derivatives, resulting in lower values of the pre-exponential term, compared with phenols. Similar low values of the pre-exponential terms were previously observed in the reaction of DPPH with a number of amines[66].

Practical requirements in the development of new and effective phenolic inhibitors of radical reactions should be turning the attention of research workers primarily to the study of the influence of the steric and polar properties of substituents on the stability and reactivity of the radicals formed in the oxidation of sterically hindered phenols, since detailed information in this field will open up new perspectives in the scientific selection of substances capable of retarding undesirable changes in organic compounds chiefly polymers, during their exploitation.

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Retention of Configuration in Reactions with Opening of an Epoxide Ring

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Information on the opening of an epoxide ring with retention of the initial configuration under conditions of catalytic hydrogenation and under the action of various nucleophilic reagents is examined. It is noted that when an electron-donating *p*- or π-grouping is present in the α position to the epoxide ring the retention of the initial configuration is more probable than its inversion. Bibliography of 182 references.

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I. INTRODUCTION

A large number of reactions of epoxides with various reagents has now been studied. The great mass of results that had accumulated were summarised in several exhaustive reviews[1-6], and the most recent of these also dealt with the stereochemical aspect of the transformations. In 1951 Fürst and Plattner[7] formulated the "rule for the biaxial opening of the expoxide ring", which three years later Cookson[8,9] and Angyal[10] extended its applicability from the position of conformational analysis to cyclic systems. According to these ideas, the opening of the oxide should be accompanied by inversion of the configuration of one of the carbon centres of the three-membered ring. However, at approximately the same time publications appeared showing that in several instances opening of the epoxide ring takes place with retention of the original configuration. An analysis of the constantly increasing number of experimental results shows that the so-called "sterically anomalous (*cis*-)opening of an epoxide ring" is observed among various representatives of the class of oxide compounds when various reagents act on them. The present review considers those instances which have not yet been summarised in the literature and covers information published up to July 1966.

II. SOME GENERAL FEATURES OF THE CHEMISTRY OF EPOXIDES

In the reviews mentioned above the correctness of the following general features of the chemistry of epoxides has been demonstrated convincingly.

1. The epoxide group often reacts in two ways, interacting with both electrophilic and nucleophilic agents under definite conditions. However, information on reaction with the latter predominates in the literature. The changes in the presence of electrophilic and radical reagents, and also on irradiation, lead mainly to the formation of products of various rearrangements of the oxide ring.

2. Breaking of the C–O bond of the epoxide takes place under the influence of various agents. Breaking of the C–C bond of the oxide ring is improbable and is observed only in the presence of strongly electronegative substituents, as occurs, for example, for oxides of cyclic trienes[11] and pentaenes[12], tetracyanoethylene oxide[13], etc.

3. The mechanism of the opening of the epoxide under the action of a nucleophilic reagent depends on the electronic and steric properties of the two reagents and on the reaction conditions. The results of the opening of the oxide are usually explained by schemes of the unimolecular and bimolecular substitution type. The direction of