A Thesis entitled

'Autoxidation of 2-naphthols'

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by

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CONTENTS

SUMMARY.

This thesis describes an investigation of the structural factors which influence the susceptibility of substituted 2-naphthols to autoxidation. The mechanism of these processes is discussed in detail in the light of the results obtained.

Previous workers had found that 2-naphthols containing α-branched alkyl substituents at C-1 (ethyl, isopropyl, cyclohexyl) autoxidise readily under extremely mild conditions, the overall rate being greater for those containing bulkier substituents. 2-Naphthols containing small substituents at C-1 (H, methyl, benzyl) do not autoxidise at an appreciable rate.

It is proposed that the major factor controlling the overall rate of autoxidation of substituted 2-naphthols is the degree of steric strain within the molecule, and especially the magnitude of the peri-interaction between substituents at C-1 and C-8. This peri-interaction is absent in the 1-alkyl-1-hydroperoxy-2(1H)-naphthalenones (1) produced in the autoxidation reactions. The resulting strain relief is thought to be the factor controlling the overall autoxidation rates.

I set out to prepare a range of 2-naphthols incorporating a variety of structural features which may elucidate the factors influencing the autoxidation rates, and to study the relative rates in a semi-quantitative manner. Several unknown naphthols which autoxidise rapidly under extremely mild conditions have been prepared, viz. 1-t-butyl- and 1-t-pentyl-2-naphthol, 1-methyl-3,6-di-t-butyl-2-naphthol, 1,8-dimethyl-2-naphthol, and 1-isopropyl-6-bromo-2-naphthol. Autoxidation of these compounds was found to give the corresponding hydroperoxides (1) in high yield. Several unknown naphthols which are stable to oxygen have also been prepared.

A consideration of the results obtained shows conclusively that

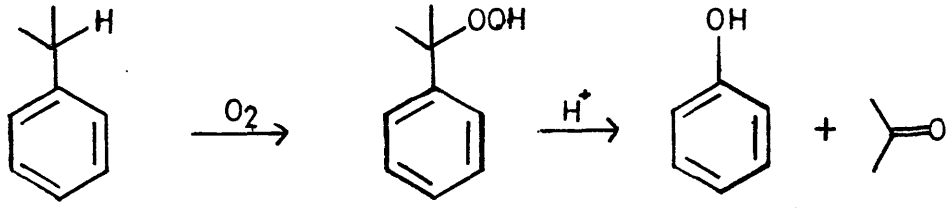
the autoxidation rates of 2-naphthols is indeed a function mainly of steric strain, electronic factors being of secondary importance. Two plausible mechanistic interpretations are proposed. It is thought that the reaction of the intermediate 2-naphthoxy radicals with molecular oxygen may be the rate-determining step, since this involves the removal of the unfavourable peri-interaction, or that the phenolic O-H bond may be weakened as a result of molecular distortions, thus facilitating the abstraction of hydrogen from the naphthol by the intermediate peroxy radical.

Some of the anomalous spectroscopic and chemical behaviour of the compounds under investigation are also related to steric compression.

INTRODUCTION

The term autoxidation is generally defined as a spontaneous radical chain reaction between ground-state (triplet) molecular oxygen and organic compounds which occurs at moderate temperatures, and at relatively slow rates. This is in contrast with the rapid process of combustion which takes place at high temperatures.

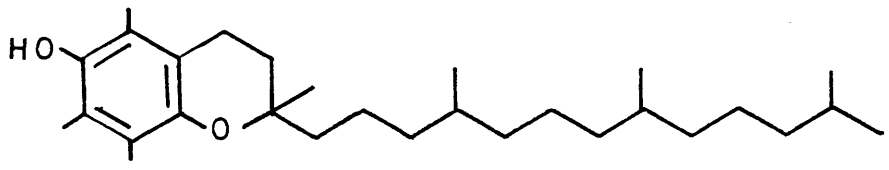
Autoxidation processes are of prime importance in the chemical and other industries. They often provide a cheap and easy method of producing bulk organic chemicals. Particularly important is the production of cumyl hydroperoxide, acid catalysed decomposition of which provides phenol and acetone.



The effects of autoxidation are often highly undesirable. The oxidative deterioration of both natural and synthetic organic materials such as edible oils, rubber, and petroleum products can be inhibited by the addition of suitable additives. The course and rate of autoxidation of many organic substrates can be drastically altered by the addition of traces of impurities. This phenomenon has stimulated extensive studies in the application of both antioxidants and catalysts designed on one hand to retard or prevent autoxidation processes, and on the other to accelerate them.

Autoxidation is believed to have an important role in some biological transformations but the detailed mechanism of the processes taking place is not often understood. The presence of unsaturated compounds in edible oils and fats renders them liable to oxidative

deterioration. That this does not occur to a significant extent in many biological systems suggests that antioxidants are present to prevent it. Tocopherols (vitamin E) are distributed widely throughout the tissues of man and animals, and the absence of this from their diet has been claimed to induce many disorders such as diabetes, and the formation of blood clots. These conditions have been found to respond to other antioxidants such as 2,6-di-t-butyl-4-methoxyphenol.



α-tocopherol

It is believed that singlet molecular oxygen is involved in the majority of oxygenation reactions which occur in nature.

Owing to the technological importance of autoxidation processes and to their complex nature, a great amount of research effort has been expended in investigating the fate of organic materials in autoxidation reactions, the factors influencing the occurrence of these reactions, and the kinetics of the radical processes involved.

Several recent reviews[1] cover this subject comprehensively. This review attempts to outline the important advances in recent years. Studies of photosensitised oxygenation of organic molecules involving singlet molecular oxygen are mentioned only when they are considered pertinent to the discussion.

Autoxidation processes are normally investigated in the homogeneous liquid phase with or without solvent at temperatures below 200° on rigorously purified samples, or on samples containing known quantities of impurities. This reaction almost invariably results in the formation of hydroperoxides, which frequently undergo further decomposition.

Mechanism of autoxidation.

The mechanism of the free-radical chain process can be described by the following series of steps[1].

Initiation: Production of free radicals $R^{\bullet}$ (a)

Propagation: $R^{\bullet} + O_2 \longrightarrow ROO^{\bullet}$ (b)

$ROO^{\bullet} + RH \longrightarrow ROOH + R^{\bullet}$ (c)

Termination: $\left.\begin{matrix} R^{\bullet} \\ ROO^{\bullet} \end{matrix}\right\} \longrightarrow$ non-radical products (d)

Initiation can be achieved in several ways, and often more than one mechanism operates.

Thermal initiation is not well understood owing to the possible complications caused by trace impurities, wall effects, photoinitiation, etc.. Direct thermal initiation has been studied by Bromberg and Muszket[2], in the presence of high concentrations of the radical scavenger 2,6-di-t-butyl-4-methylphenol (IH). This simplifies the kinetics, as the normal chain process is intercepted,

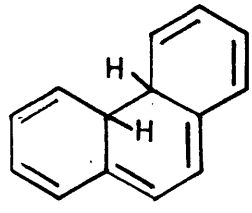
$$ROO^{\bullet} + IH \longrightarrow ROOH + I^{\bullet} .$$

$I^{\bullet}$ is a radical which is assumed to be incapable of propagating the chain, so that the chain length is reduced, in theory, to 1. It was found that the self initiation of 4a,4b-dihydrophenanthrene (1) (PH_2) under these conditions obeyed the kinetic expression

$$-\frac{d}{dt}(O_2) = k_i (PH_2)(O_2)$$

which implies that the initiation process is bimolecular.

$$PH_2 + O_2 \longrightarrow PH^{\bullet} + {}^{\circ}OOH$$



(1)

However, other workers suggest a termolecular mechanism,

$$2RH + O_2 \longrightarrow 2R^{\bullet} + H_2O_2$$

as being more feasible, since this process is much less endothermic for most organic molecules, and indeed the self initiation of tetralin and indene were found to obey the kinetic expression,

$$R_i = k_i (RH)^2(O_2)$$

where R_i is the rate of initiation[3].

Self initiation by the reaction of substrate directly with oxygen to give radicals becomes a relatively unimportant process as soon as a small amount of hydroperoxide has been formed, since hydroperoxide decomposition is a much more energetically favourable process. Self initiated autoxidations are frequently subject to long induction periods while the concentration of hydroperoxide builds up. This phenomenon is known as autocatalysis, and is attributed to the decomposition processes

$$ROOH \longrightarrow RO^{\bullet} + {}^{\bullet}OH$$

at low concentrations of hydroperoxide, and

$$\overset{H}{\underset{|}{ROO}}\text{- - - }HOOR \longrightarrow RO^{\bullet} + H_2O + ROO^{\bullet}$$

at high concentrations of hydroperoxide, where a hydrogen bonded dimer is involved, and can be detected by i.r. spectroscopy[10, 4].

The majority of autoxidation reactions are catalysed by light. This can be due to photolysis of the substrate or of a substrate-oxygen complex to give free radicals, as well as photolytic decomposition of the products of autoxidation,

$$ROOH \xrightarrow{h\nu} RO^{\bullet} + {}^{\bullet}OH,$$

the latter process predominating once the reaction is under way. This process is distinct from photosensitised oxygenations involving singlet oxygen.

Because of autocatalysis, self initiated autoxidations are usually unsuitable for kinetic studies, the initiation rates being irreproducible. Reproducible rates of initiation can be achieved using free radical

initiators such as α,α'-azobisisobutyronitrile which decompose unimolecularly either thermally or photochemically in a well defined manner.

$$In_2 \xrightarrow{k_i} 2In^{\bullet}$$

Alternatively, the salts of heavy metals such as Co, Cu, Fe, etc. can be used to catalyse initiations.

$$RH + M^{(n+1)} \longrightarrow R^{\bullet} + H^{+} + M^{n+}$$

However, this reaction is soon overshadowed by reactions between hydroperoxide and metal ions such as[1(a)]

$$M^{(n+1)+} + ROOH \longrightarrow M^{n+} + ROO^{\bullet} + H^{+}$$

and,

$$M^{n+} + ROOH \longrightarrow M^{(n+1)+} + RO^{\bullet} + OH^{-} .$$

Of the propagation steps, the reaction of the substrate radical with oxygen (step (b)) is normally considered to be fast and non-rate determining, with low activation energies. This would be expected to be a facile reaction as it is essentially a radical coupling process, oxygen being a diradical in the ground state. Thus, at moderate pressures, the overall rate of autoxidation is normally found to be independent of oxygen pressures.

For particularly stable radicals such as triphenylmethyl however, the rate of reaction has been shown to be dependent upon oxygen pressures, and the reaction

$$Ph_3C^{\bullet} + O_2 \rightleftharpoons Ph_3COO^{\bullet}$$

is known to be reversible. This equilibrium is a reflection of the steric crowding in both the triphenylmethyl and the triphenylmethylperoxy radicals[5].

The rate determining propagation step for the majority of organic substrates is the reaction between the peroxy radical and substrate, (step (c)). This is normally a hydrogen atom abstraction,

$$ROO^{\bullet} + RH \longrightarrow ROOH + R^{\bullet} ,$$

or, in the case of unsaturated substrates, an addition reaction,

$$ROO^{\bullet} + \rangle C{=}C\langle \longrightarrow ROOC\text{-}C^{\bullet}\langle$$

The overall rate of autoxidations is normally found to be proportional to the concentration of the substrate, RH, which is consistent with this reaction being rate determining.

In the case of the hydrogen atom abstraction reaction, the rate is very susceptible to the chemical environment of the hydrogen being abstracted, although polar and steric factors can also have some influence. The effect of substrate structure on autoxidation rates will be discussed below.

The autoxidation of terminal olefins has been studied by Mayo and co-workers, and has been found to produce alternating 1 : 1 copolymers of oxygen and substrate by the propagating reactions[6],

$$-CH_2\underset{H}{\overset{R}{C}}OO^{\bullet} + CH_2{=}\underset{H}{\overset{R}{C}} \longrightarrow -CH_2\underset{H}{\overset{R}{C}}OOCH_2\underset{H}{\overset{R}{C}}{}^{\bullet}$$

$$-CH_2\underset{H}{\overset{R}{C}}OOCH_2\underset{H}{\overset{R}{C}}{}^{\bullet} + O_2 \longrightarrow -CH_2\underset{H}{\overset{R}{C}}OOCH_2\underset{H}{\overset{R}{C}}OO^{\bullet} \quad .$$

The effect of structure on the rate can be considered mainly in terms of the stability of the resulting β-peroxyalkyl radical from the addition reaction, polar and steric effects being of relatively low importance. For example, styrene reacts about twenty times faster than vinyl acetate, but only about one third as fast as p-methoxystyrene[7], in accord with the resonance stabilisation of

$$-CH_2\overset{H}{C}{}^{\bullet}{}_{Ph} \quad .$$

The only <u>termination</u> reaction which normally need be considered at moderate oxygen pressures is

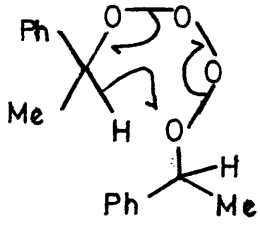
$$RO_2^{\bullet} + RO_2^{\bullet} \longrightarrow \text{products.}$$

as the concentration of $R^{\bullet}$ is so much lower than that of $RO_2^{\bullet}$, except

when R$^{\bullet}$ is particularly stable[5]. E.s.r. studies have shown that, at low temperatures, peroxy radicals combine to form tetroxides,

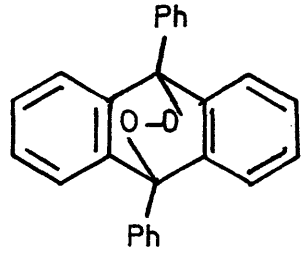
ROO—OOR

and at higher temperatures self termination proceeds <u>via</u> irreversible decomposition of these tetroxides[8]. Russell proposed a cyclic transition state for the decomposition of the 1-phenylethylperoxy dimer which has found general acceptance for primary and secondary alkylhydroperoxides[9].



$\longrightarrow$ PhCOMe + $^1O_2$ + PhCH(OH)Me

This was confirmed by deuterium labelling studies, and by trapping the resultant singlet oxygen demanded by the Wigner spin-conversion rule, using 9,10-diphenylanthracene to give the transannular peroxide (2)[10].



(2)

In cases where singlet oxygen has not been detected, weak luminescence has been observed, and has been attributed to the decay of triplet ketone to the singlet ground state[1(a)].

Employing the usual steady-state assumptions that the rate of chain initiation, R_i, is equal to the rate of chain termination, and that the rate of the two propagation steps is the same, the overall rate of autoxidation of an organic substrate, RH, is given by the expression,

$$-\frac{d}{dt}(O_2) = -\frac{d}{dt}(RH) = \frac{d}{dt}(RO_2H) = k_p \frac{(RH)R_i^{\frac{1}{2}}}{(2k_t)^{\frac{1}{2}}} ,$$

where k_p is the rate constant for the rate determining propagation step (c), and $2k_t$ is the rate constant for the termination step,

$$2RO_2^{\bullet} \longrightarrow \text{molecules.}$$

The overall rate of autoxidation therefore depends upon the rate of initiation and the absolute values of k_p and $2k_t$. These are normally measured in independent experiments using either radical scavengers or initiators, and carrying out the reactions to low conversion (often $< 1\%$), in order to simplify the kinetics and minimise the complicating effects of products.

Structural influences upon autoxidation reactions.

Attempts to relate structural changes to substrate reactivity in autoxidations are complicated by the possibility of differing reactivity of the chain carrying peroxy radicals, and by differing termination rates. Ingold and co-workers[11] overcame this problem by comparing the rates of reaction of series of closely related substrates (RH), in the presence of the same hydroperoxide, for example t-butyl hydroperoxide. The propagation and termination steps can then be assumed to involve the same peroxy radical by virtue of a chain transfer mechanism.

Chain transfer: $ROO^{\bullet} + {}^{t}BuOOH \longrightarrow ROOH + {}^{t}BuOO^{\bullet}$

Propagation: $^{t}BuOO^{\bullet} + RH \longrightarrow {}^{t}BuOOH + R^{\bullet}$

$R^{\bullet} + O_2 \longrightarrow ROO^{\bullet}$

Termination: $2\,{}^{t}BuOO^{\bullet} \longrightarrow$ molecular products.

In this manner, meaningful comparisons of the rates of autoxidation of different substrates can be made. For example, isopropyl alcohol is ca. fifteen times more reactive towards the t-butyl peroxy radical than isopropyl chloride, but only about one fifth as reactive as diisopropyl ether (per active hydrogen). The relative reactivities of toluene, ethyl benzene and benzyl ether are found to be in the ratio 1 : 10 : 30

respectively (per active hydrogen) towards the same peroxy radical.

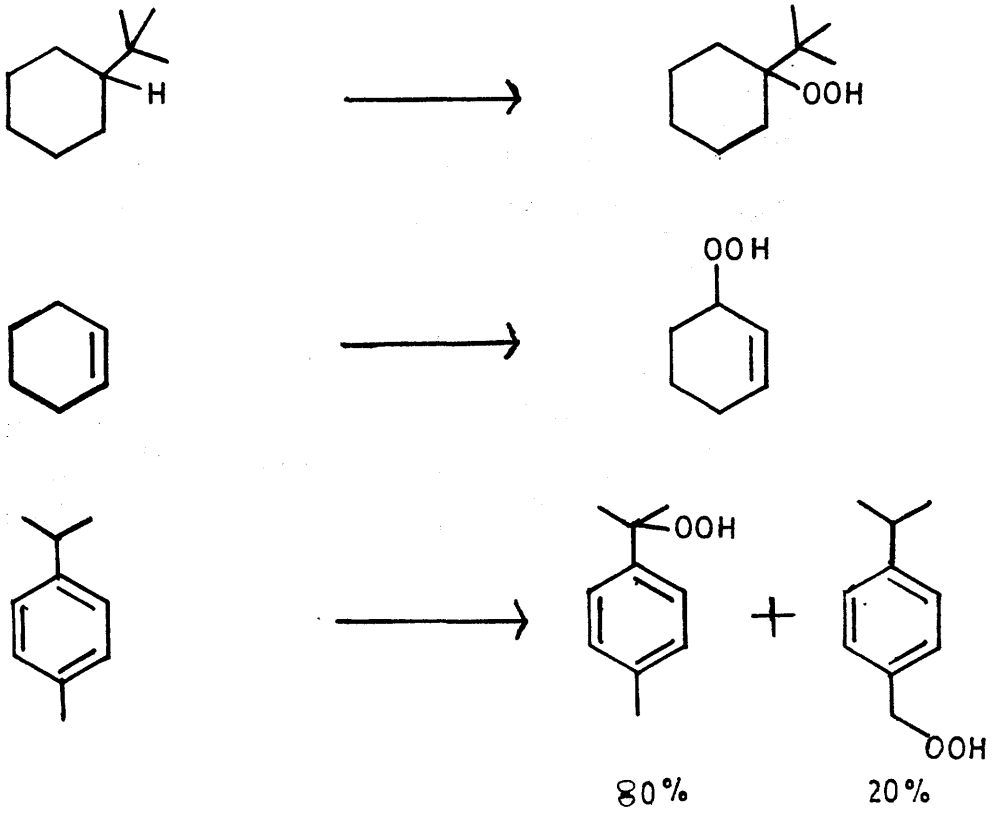
Employing the same technique, the relative reactivities of alkylperoxy radicals have been investigated. The reactivity of the isomeric butylperoxy radicals to hydrogen atom abstraction are in the order

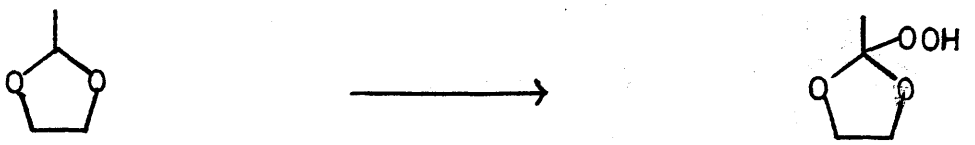
n-butyl > isobutyl > t-butyl.

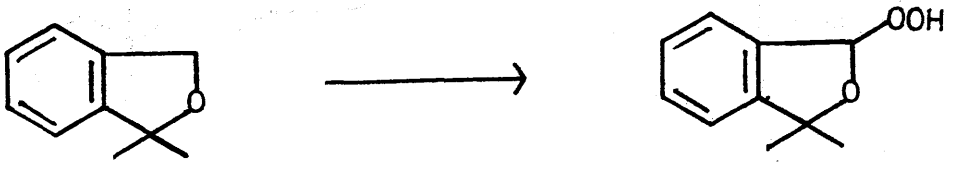
However, this work shows that the differences in reactivity of alkylperoxy radicals are small, any variations being attributable to the degree of α-branching in the carbon chain, so that steric accessibility is probably the major criterion for peroxy radical reactivity. It could therfore be considered justifiable to assume that peroxy radicals of similar structure have similar reactivities when comparing autoxidation rates for a series of closely related substrates[11].

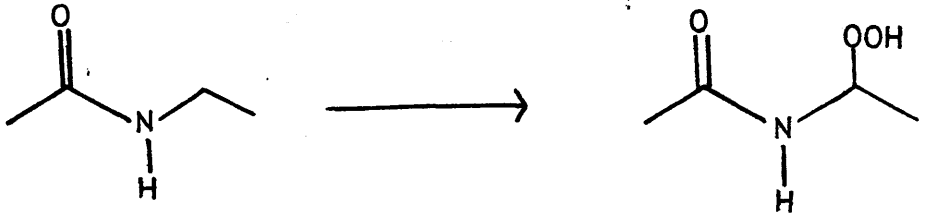
The range of organic compounds which react with oxygen is too extensive to be adequately covered here. In many cases, the initially formed hydroperoxide decomposes <u>in situ</u> and is never isolated.

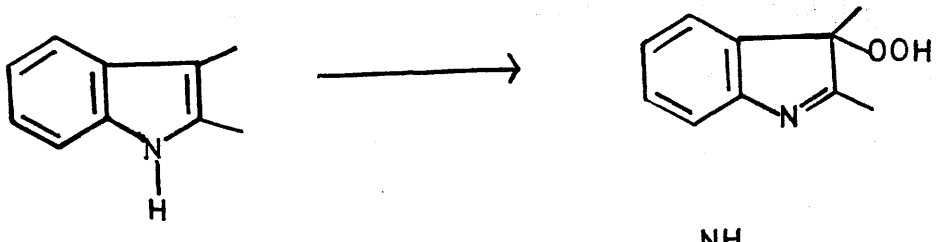
The following examples indicate the generality of this reaction. In each case, only the major products of autoxidation are indicated[12].

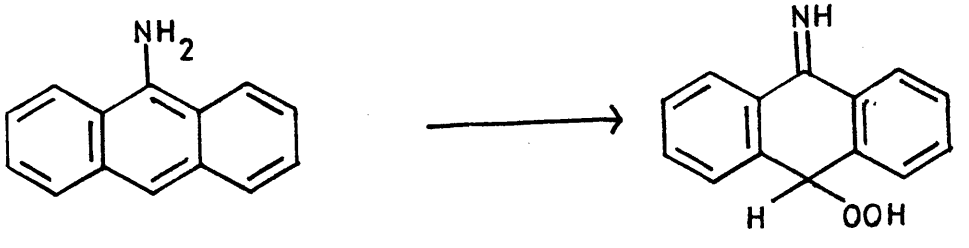


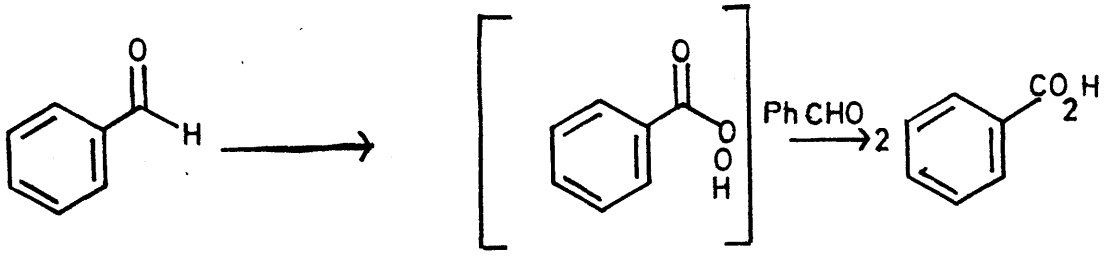


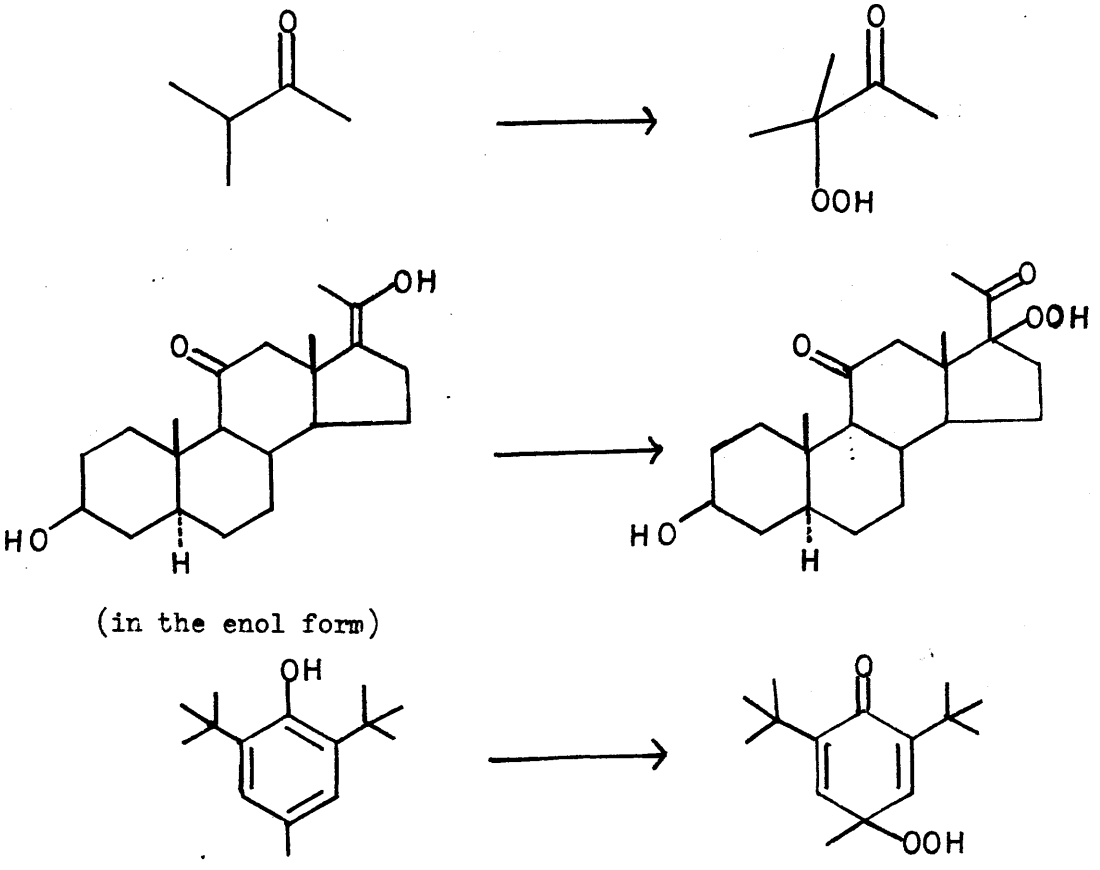












The most striking feature of these examples is the high degree of selectivity displayed by organic substrates in their reactions with oxygen. This is a direct consequence of the relatively low reactivity of the perexy radical to hydrogen abstraction from the majority of organic substrates. The strength of the ROO-H bond has been estimated to be ca. 88 kcal. mole^{-1},[13] which means that this bond is only slightly stronger than the enolic or phenolic O-H bond (76-85 kcal. mole^{-1}),[27] and allylic (ca. 85-88 kcal. mole^{-1}) or benzylic C-H bond (84 kcal. mole^{-1}), and weaker than the C-H bonds in saturated hydrocarbons (tertiary C-H ca.93 kcal. mole^{-1}, secondary C-H ca. 95 kcal. mole^{-1}, primary C-H ca. 104 kcal. mole^{-1})[1(a)]. This is also reflected in the rates of autoxidation. Alkanes, olefins, aliphatic ketones etc. normally autoxidise very slowly, and reasonable yields of hydroperoxides are normally obtained only by the use of catalysts or by employing high temperatures or pressures. In the cases where the bonds to be cleaved are weaker, such as for enamines, enols and phenols, uncatalysed autoxidation can

often reach completion in several hours or less.

Large deuterium isotope effects have been measured for the hydrogen abstraction step. For the reaction of the t-butyl peroxy radical with tetralin, the deuterium isotope effect was estimated to be in the order of 16[14]. This indicates a high degree of bond breaking in the transition state leading to products, and, according to Hammond's postulate, this transition state should therefore resemble products[15],

ROO : H • R .

The stability of the incipient radical, R•, should therefore be a major factor in determining the rate of this reaction.

Factors influencing free radical stability.

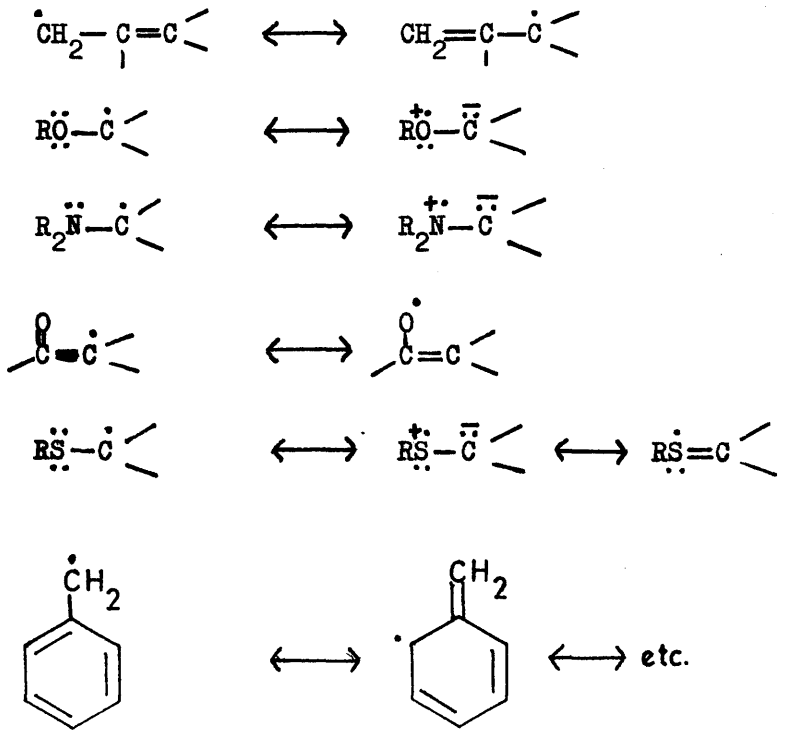
The stability of free radicals is influenced by the groups attached to the radical centre, and especially by the ability of these groups to delocalise the unpaired electron.

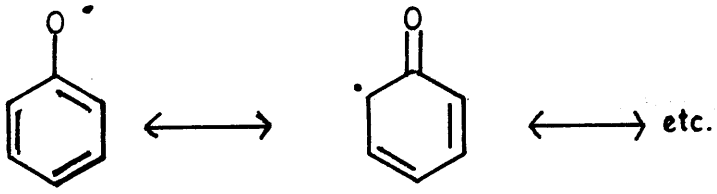
For alkyl radicals, the order of stability is

tertiary > secondary > primary.

This order can be attributed mainly to hyperconjugation.

Much greater stability is introduced by resonance delocalisation,





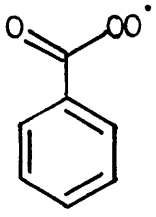
While these effects predominate in determining the stability of a free radical, polar effects have been shown to exert some influence upon autoxidation rates, as well as on other free radical reactions. This has been attributed to the dipolar nature of the transition state

$$ROO^{\delta-} : H \cdot^{\delta+}R$$

which is thought to be important in the rate determining hydrogen abstraction step. Thus, groups which increase the electron density at the radical centre facilitate the reaction, the peroxy radical being electrophilic in nature. In phenol autoxidations, the use of the Hammett equation employing σ^+ substitution constants leads to a ρ^+ value of -1.5 for hydrogen abstraction by peroxy radicals in accord with the development of considerable positive charge in R in the transition state[16].

However, these effects are easily overshadowed by changes in substitution on the α-carbon, so that oxidation of benzyl phenyl ethers is insensitive to substitution on the benzyl or phenyl group, owing to the powerful electron supplying effect of the ether oxygen atom[16].

Electron withdrawing α-substituents on the attacking peroxy radical increase the electrophilicity of this species, so that the benzoyl peroxy radical (3) was estimated to be <u>ca</u>. 40,000 times more reactive towards benzaldehyde than the t-butyl peroxy radical[17].



(3)

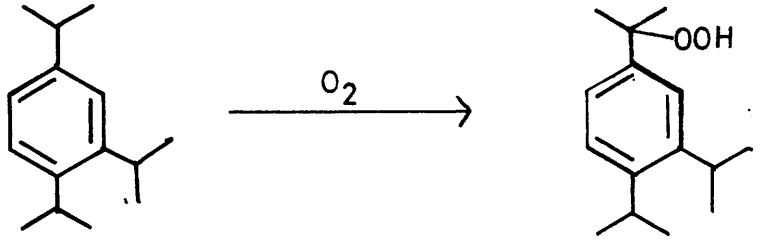
Steric and conformational influences.

The third factor which can influence the rate of the hydrogen abstraction reaction in autoxidations is the steric requirement. Steric hindrance can have a dramatic effect on the ease of hydrogen abstraction from many organic substrates. However, attack by molecular oxygen is not normally subject to steric influences, except in extreme cases. For example, the triphenylmethyl radical reacts slowly with oxygen, and the perchlorotriphenylmethyl radical not at all[18].

The difference in reactivity of alkyl peroxy radicals to hydrogen abstraction has been attributed mainly to steric factors, so that an increase in the degree of branching in the α-carbon results in a decrease in reactivity[1(a)],

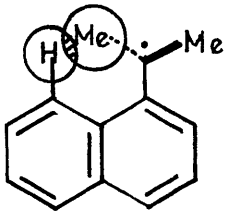
$$MeOO^{\cdot} > EtOO^{\cdot} > {}^{i}PrOO^{\cdot} > {}^{t}BuOO^{\cdot} .$$

The most dramatic effects of steric environment are seen in the substrate reactivities, where the accessibility of the hydrogen atom to be abstracted can be important. α,α'-Dimethylbenzyl ether is one fifteenth as reactive as benzyl ether towards t-butyl peroxy radicals[19]. o-Substituted alkyl benzenes autoxidise much more slowly than the p-isomers, and 1,2,4-triisopropyl benzene autoxidises only in the four position[20].



This effect has been related to a decrease in σ-π conjugation of the C-H bonds in o-dialkylbenzenes, both in the ground state, and in the transition state leading to products. This can be correlated directly with shifts to shorter wavelength and a diminution in absorption intensities in the u.v. spectra of these compounds.

A similar effect in 1-alkylnaphthalenes compared with 2-alkylnaphthalenes has been related to the steric effect of the peri-hydrogen. This interaction may force the adjacent C-aryl - C-alkyl bond out of the plane of the naphthalene nucleus. This would result in a breakdown of σ-π conjugation of the ring with the α-C-H bond of the alkyl group in the transition state. Thus 1-isopropylnaphthalene is more stable to autoxidation than 2-isopropylnaphthalene, possibly as a result of the decreased stability of the radical (4), or of the transition state leading to this radical[20].



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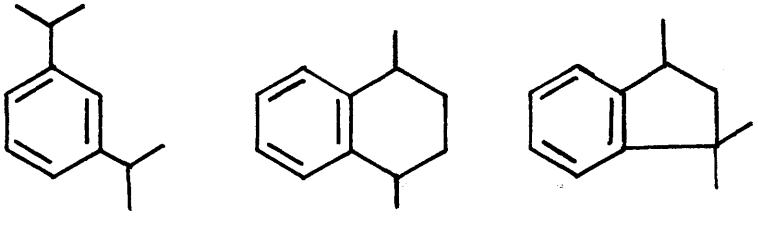
An interesting contrast to this phenomenon can be found in the autoxidation of substituted indanes and tetrahydronaphthalenes, as displayed by the following examples.



Relative rate: 2 9 10

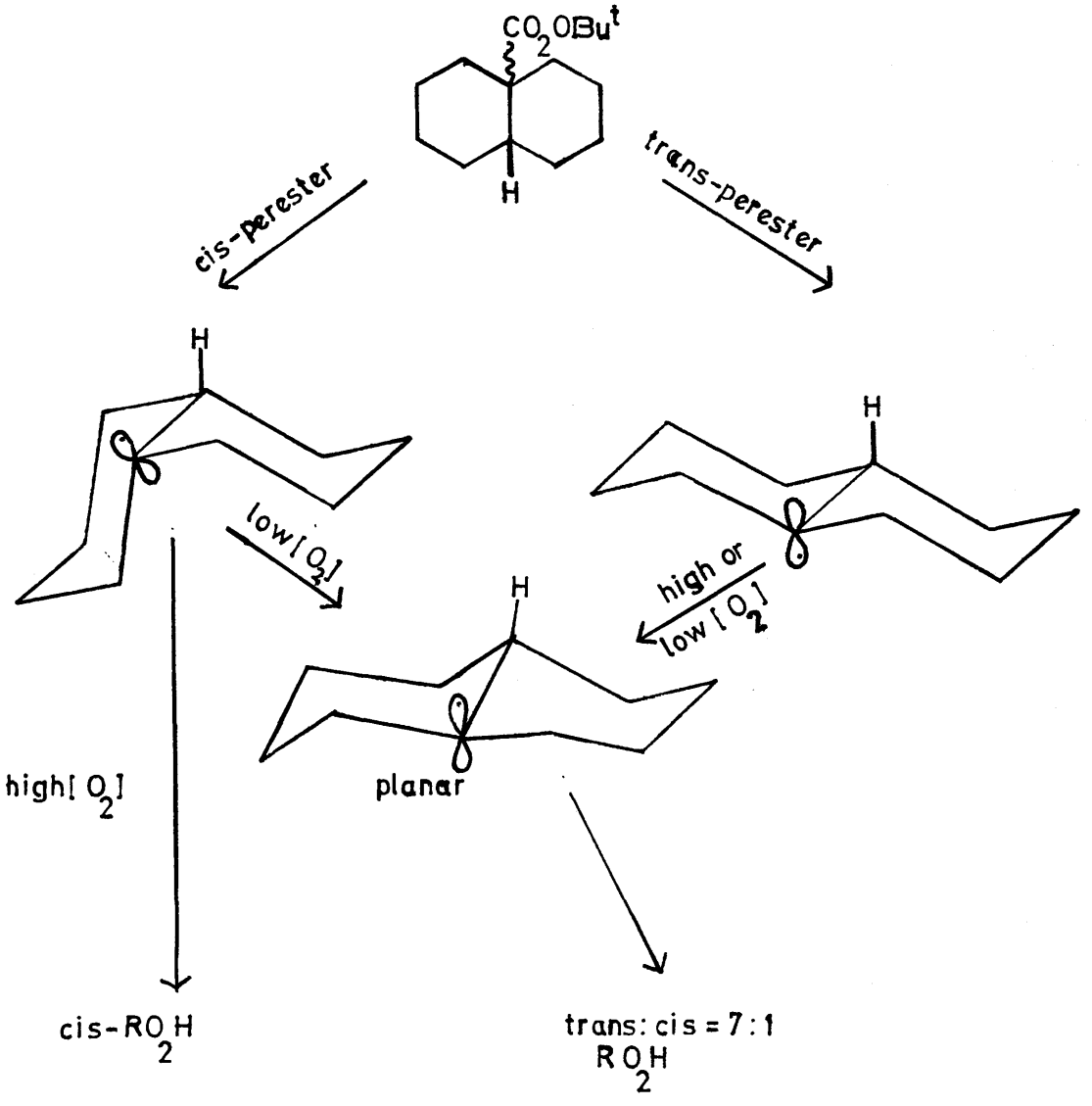
This can be explained if one considers the rigid nature of the indane and tetrahydronaphthalene skeletons relative to alkylbenzenes. The incipient radicals involved in the hydrogen abstraction step must be planar, and in the plane of the aromatic nucleus, for maximum stabilisation. In the alicyclic molecules, the axial α-hydrogen to be abstracted is already close to the conformation required in the

transition state, whereas such a conformation constitutes only a small proportion of the possible conformers of the non-rigid alkylbenzenes[20].

Shapes of free radicals.

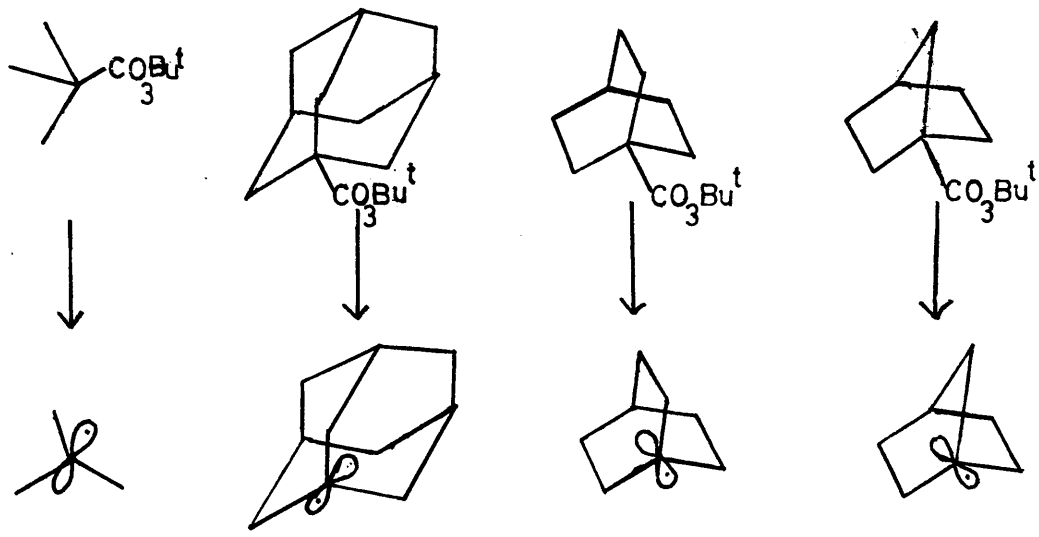
It has been shown that free radicals have a preference for a planar geometry, although this has been a matter of controversy in the past[21]. Results from theoretical calculations were inconclusive, but they did indicate that the energy difference between a pyramidal geometry and a planar geometry is much smaller than for carbonium ions. Recent e.s.r. studies and extensive chemical evidence indicate that the planar conformation is preferred where possible.

The product ratio in the autoxidation of the cis-9-decalyl radical is dependent upon oxygen pressures, whereas that of the trans-9-decalyl radical is insensitive.



At high oxygen concentrations, an excess of the cis-hydroperoxide is formed from the cis-perester. These results indicate that the cis-radical, which requires a 'ring inversion' to attain a planar geometry, prefers to do so if oxygen concentrations are sufficiently low to allow time for this process to occur. The trans-radical, which requires only a slight flexing of its structure to achieve planarity, shows no dependency upon oxygen concentration. This is a clear indication that a planar conformation is preferred[21].

However, there is considerable evidence that non-planar radicals do exist, and are relatively more stable than their carbonium ion counterparts. Bridgehead radicals, which have a non-planar configuration, are found to be less stable than those which can achieve planarity, but are considerably more stable than corresponding bridgehead carbonium ions. For example, the relative ease of decomposition of peresters indicates the relative stabilities of the corresponding radicals.

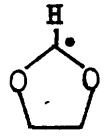


1·0 0·3 0·03 0·0016

Relative rates:
(corrected for differences in inductive effects)

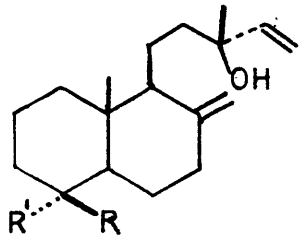
These results indicate that strain decreases the stability of radicals, but to a much smaller extent than in the corresponding

carbonium ions[21]. Recent investigations of the ^{13}C hyperfine splittings in the e.s.r. of oxygen- and halogen-containing radicals indicate that they are non-planar, for example[22],

$\dot{C}H_2OH$, $\dot{C}Me_2OH$,  , $\dot{C}H_2F$.

Steric effects are almost invariably used to explain decreases in autoxidation rates, and this is normally due to difficulty of access of the peroxy radical to the active C-H bond.

An interesting example of a case where steric factors are thought to facilitate the autoxidation of terpenic aldehydes has recently been reported.



(5a) R = CHO, R' = CH_3

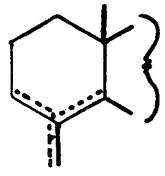
(5b) R = CH_3, R' = OOH

(5c) R = OOH, R' = CH_3

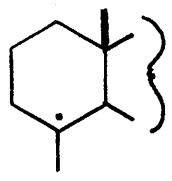
(5d) R = CO_2H, R' = CH_3

(5e) R = OH, R' = CH_3

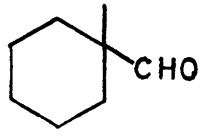
(5f) R = CH_3, R' = OH



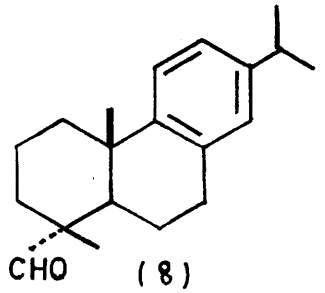
(6)



(7)



(9)



(8)

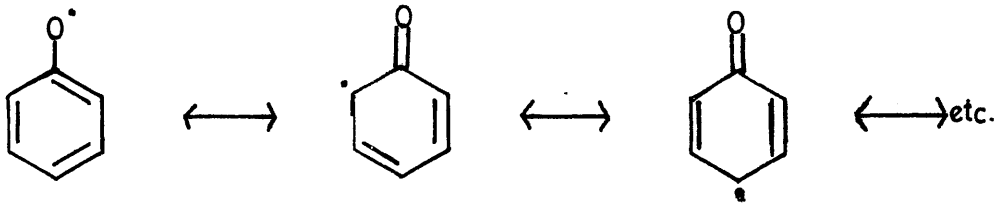
It was found that autoxidation of torulosal (5a) gave, as well as the expected acid (5d), the nor-compounds (5b, 5c, 5e, 5f) and the isomeric olefins (6). These are thought to have arisen from

decarbonylation of the initially formed acyl radical to give the radical (7), which can then react with oxygen, and abstract an aldehydic hydrogen atom from another molecule to give the hydroperoxides (5b, 5c). Reduction of these and subsequent dehydration can account for the other products. It is proposed that the major factor responsible for this anomalous behaviour is the unfavourable 1,3-diaxial interaction between the formyl group and the angular methyl group, so that the formation of the planar radical (7) leads to a relief of strain within the molecule. It was found that dehydroabietic aldehyde (8), where the formyl group is equaterial, was much more stable than torulosal to autoxidation, and a much lower proportion of the anomalous products was found. In this case, it is assumed that the 1,3-diaxial interaction is less serious than in the case of telurosal, although it may well be that deformylation of axial aldehydes is a more facile process for other reasons. It was found that conformationally non-rigid tertiary aldehydes such as (9) gave much smaller proportions of the decarbonylated products, the major product being the derived carboxylic acid[23].

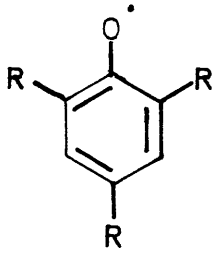
Autoxidation of phenols and related systems.

The autoxidation of phenols in neutral and basic media, and with or without the use of catalysts, has been extensively investigated. Great interest has also been shown by both physical and organic chemists in the properties and coupling reactions of phenoxy radicals, many of which display great stability[24]. The radical coupling of phenols has been shown to be involved in many biosynthetic pathways[25].

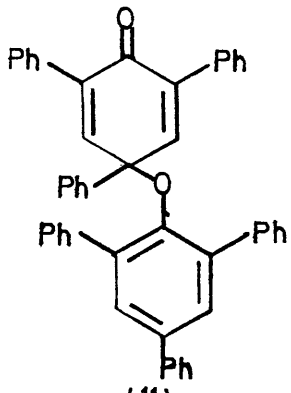
The phenoxy radical is stabilised by delocalisation of the unpaired electron throughout the aromatic system.



Phenoxy radicals readily couple to form O-C and C-C dimers, unless steric hindrance prevents or retards such dimerisation processes. For this reason, the behaviour and properties of 2,4,6-trisubstituted phenoxy radicals (10) are of special interest, since many of these exist as stable monomers in the absence of oxygen for long periods. This stability is attributed mainly to the steric strain which would be present in the dimer. For example, 2,4,6-tri-t-butylphenoxy (10, R = ^{t}Bu) is completely monomeric both in solution and in the solid state.



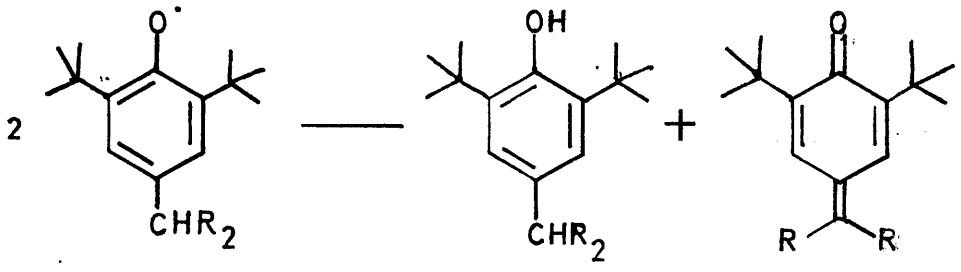
(10)



(11)

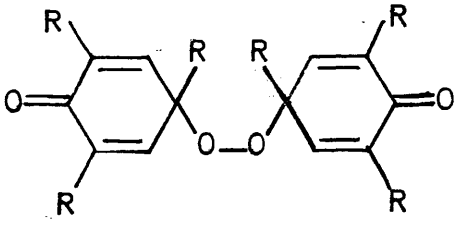
2,4,6-Triphenylphenoxy is also monomeric in solution, but exists as a dimer (11) in the solid state. The greater tendency of the latter to dimerise is attributed to the smaller steric requirement of the phenyl group.

The stability of 2,6-di-t-butyl-4-substituted phenoxy radicals is markedly reduced if the substituent at the 4-position contains an α-hydrogen, owing to the ease with which disproportionation can occur to give a quinone methide and a phenol.



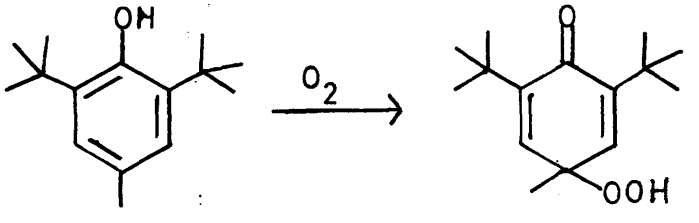
These sterically hindered radicals have been termed stable, but in fact the majority of phenoxy radicals react rapidly with molecular

oxygen, which has very little steric requirement. Thus 2,4,6-tri-t-butylphenoxy is decolorised by oxygen in ca. thirty minutes, while 2,6-di-t-butyl-4-phenylphenoxy requires eight hours, and 2,4,6-triphenylphenoxy is inert to oxygen. Electron withdrawing substituents, or those which increase the conjugation, reduce the tendency of the radical to react with oxygen. The products of these reactions are normally peroxides of the type (12), although ortho-ortho- and ortho-para-coupled peroxides are formed in some cases[24].



(12)

Hydroperoxides have also been isolated from these reactions, for example[26],



It is interesting to note that, in the case of phenols, the reaction with oxygen is not always a fast step, and indeed, in some cases, does not occur at an appreciable rate. This is in contrast with the vast majority of autoxidation reactions.

Much of the interest in phenol autoxidation stems from their antioxidant properties[1]. Aromatic amines show similar activity, but they have not been so extensively investigated. The main feature of antioxidants is that they have readily abstractable hydrogens and give stable radicals so that they interrupt the propagating chain

reaction in autoxidation reactions.

$$ROO^{\bullet} + ArOH \longrightarrow ROOH + ArO^{\bullet}$$

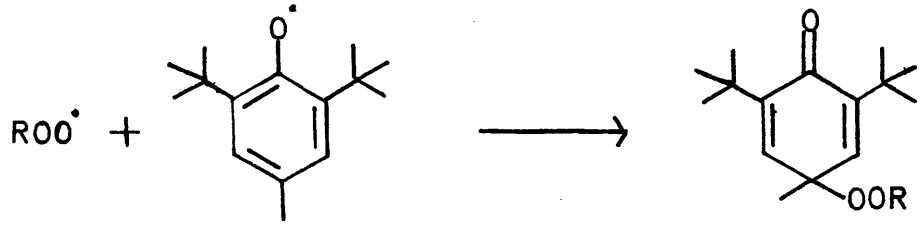
$$ArO^{\bullet} + RH \not\longrightarrow ArOH + R^{\bullet}$$

Termination then occurs by one of the steps

$$RO_2^{\bullet} + ArO^{\bullet} \longrightarrow \text{molecular products}$$

$$ArO^{\bullet} + ArO^{\bullet} \longrightarrow \text{molecular products.}$$

For example,

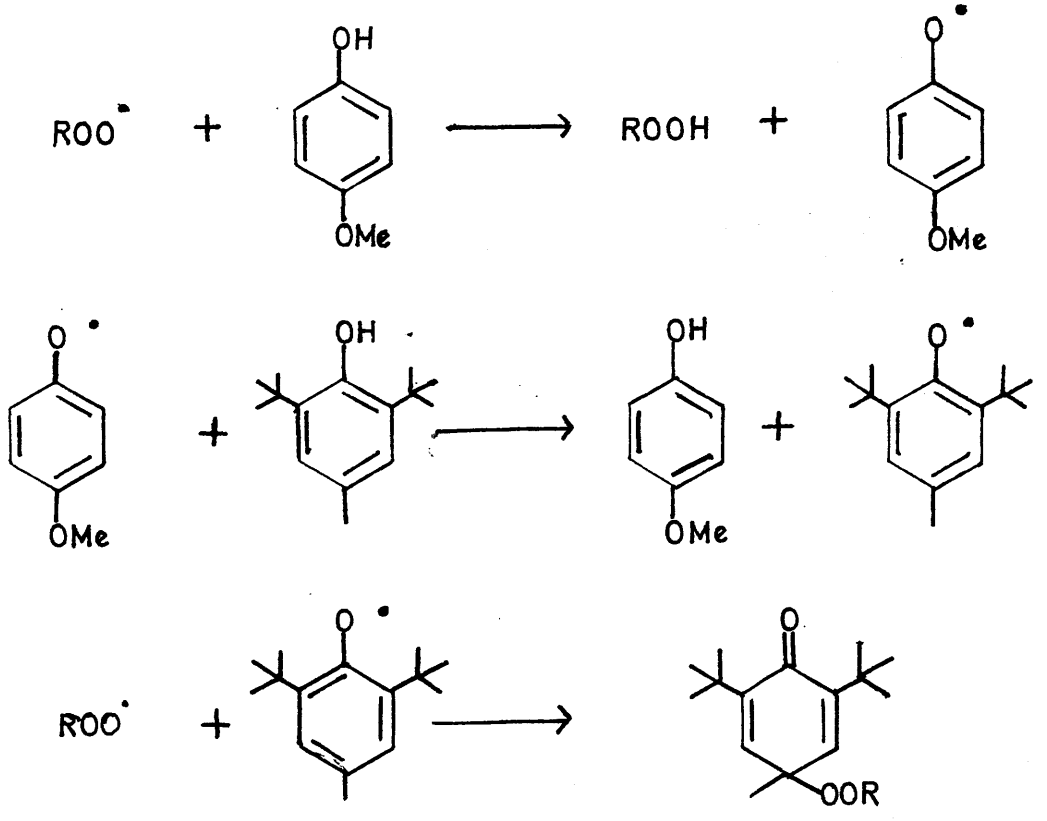


In cases where the phenol has either or both ortho-positions free, the resulting radical may be sufficiently reactive to continue the autoxidation process, possibly at a slower rate.

Howard and Ingold were able to show that 2,6-di-t-butyl-4-methylphenol-OD is about one tenth as efficient an inhibitor of styrene autoxidation as the undeuteriated phenol.[1(a)] Thus, the O-H bond of the phenol must be cleaved in the slow step of the chain transfer process. A series of meta- and para-substituted phenols were correlated using σ^+ constants, and the values of ρ^+ were estimated to be in the order of -1.5, indicating that electron releasing substituents in the phenol accelerate the hydrogen abstraction process (cf. page 13). This is not surprising owing to the known electrophilicity of peroxy radicals, but does indicate that the transition state does have some polar character.

The phenomenon of synergism, whereby the addition of two or more antioxidants is more effective than the sum of their individual effects, has often been used to advantage, especially in overcoming the disadvantages of 2,6-disubstituted phenols, which often react too slowly,

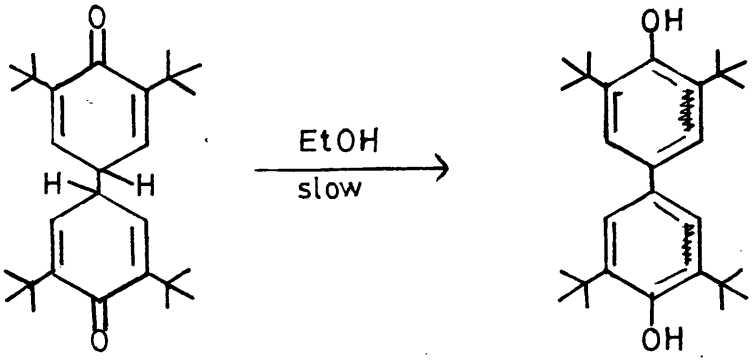
and those of phenols unsubstituted in the ortho-positions, which are normally too reactive to be completely effective. This is exemplified by the following scheme[1]



The influence of steric factors in the properties of hindered phenols has been the subject of investigation for many years. Evidence for a departure from planarity in these molecules is accumulating. This includes anomalies in i.r., u.v. and n.m.r. spectra[27]. It is thought that for 2,6-di-t-butylphenols, steric compression results in a weakening of the O-H bond. Estimates of 76±3 kcal. mole^{-1} for the dissociation energy of the O-H bond in hindered phenols imply that this bond is considerably weakened compared to the value of 85 kcal. mole^{-1} for normal phenols. This lower value would facilitate homolysis of the O-H bond in autoxidation of these molecules[27].

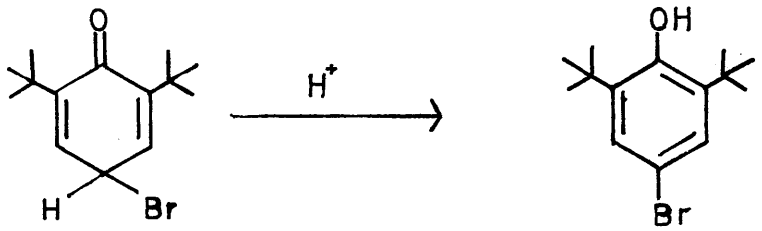
Steric crowding would also account for the tendency shown by

heavily substituted phenols to form 4,4-disubstituted-cyclohexadienones in many reactions including autoxidations, especially when this relieves buttressing effects within the molecule. This occurs even when aromatisation would be possible. Kharasch and Joshi isolated the keto-tautomer (13) of the diphenol (14) by base catalysed ferricyanide oxidation of 2,6-di-t-butylphenol[28].



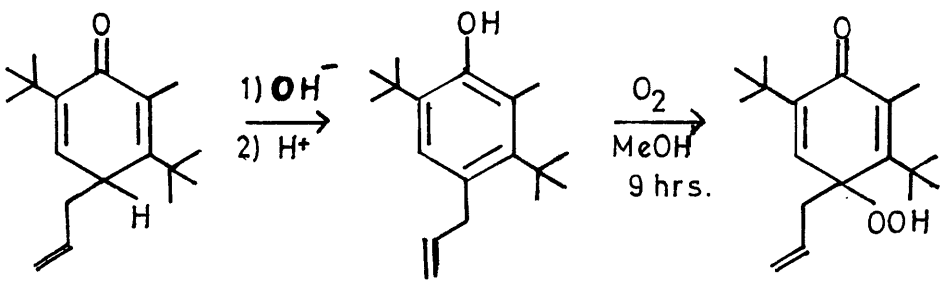
(13) (14)

Bromination of 2,6-di-t-butylphenol gives the stable keto-tautomer (15), which isomerises to the phenol (16) only in acidic media[29].



(15) (16)

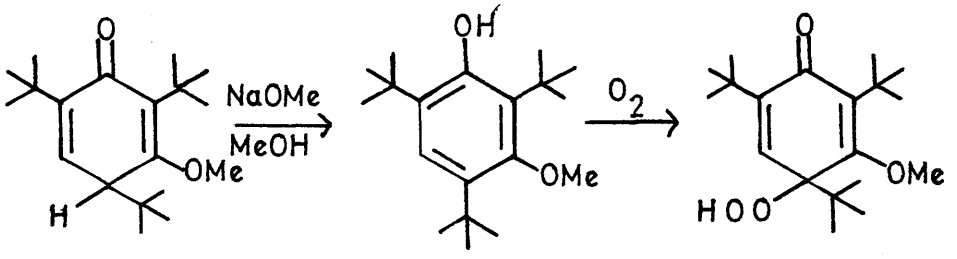
This phenomenon can be interpreted as evidence of strain within these molecules, and has been found to be accompanied by ready autoxidation in some cases. Miller found that the cyclohexadienone (17) is stable over prolonged periods, and inert to atmospheric oxygen. However, the phenolic tautomer (18) is converted to the hydroperoxide (19) in several hours.



(17) (18) (19)

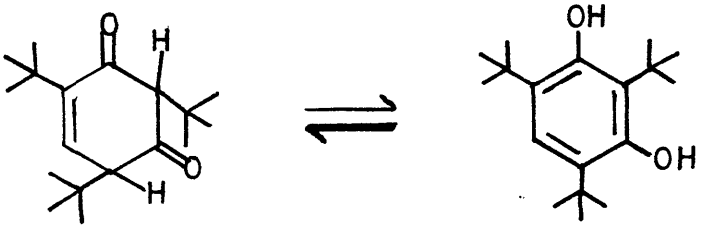
The author points out that the buttressing effects of three adjacent substituents in (18) introduces severe strain into the molecule, which is not present in the structures (17) and (19). This is one of the rare cases where steric effects have been associated with acceleration of an autoxidation process[30].

A similar argument could be used to account for the stability of the keto-tautomer (20), and the facile autoxidation of the phenol (21) to the hydroperoxide (22)[31].



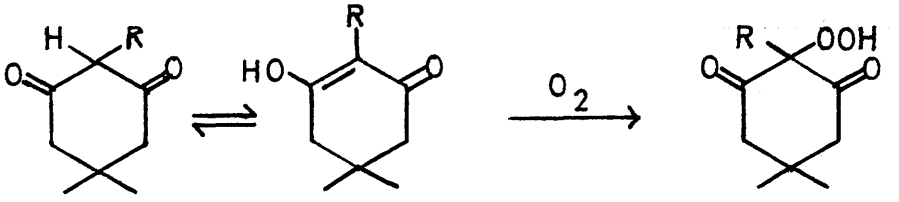
(20) (21) (22)

The tri-t-butyldione (23) is present in excess even in basic media, and does not tautomerise to the phenol in weak acid[32].



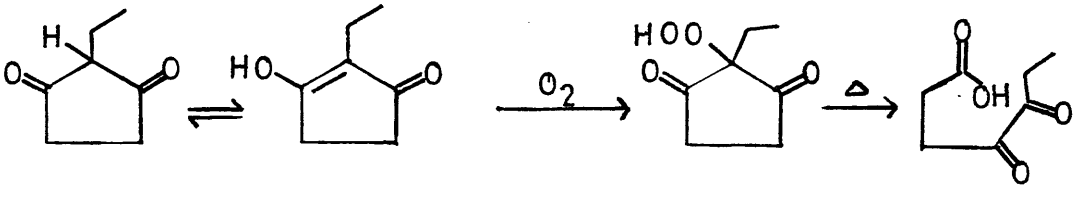
(23)

The stability of the keto-tautomers of phenols to oxygen is not surprising, since ketones autoxidise very slowly, if at all. However, several reports of facile autoxidation of readily enolisable ketones have been reported. Bredereck and Bauer found that benzene solutions of the substituted dimedones (24), (R = Me, Et, ^{i}Pr, ^{i}Bu, -CH_2Ph, Ph), were autoxidised to the unstable hydroperoxides (25) in 12-14 hours[33].



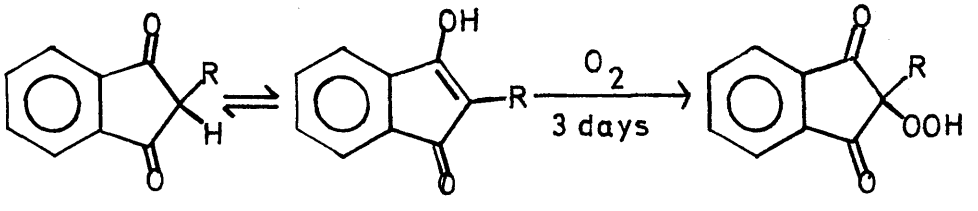
(24) (25)

The cyclopentandione (26) was converted to the diketo acid (28) via the hydroperoxide (27), on exposure of benzene solutions to oxygen, in virtually quantitative yield over a period of days[34].



(26) (27) (28)

The indandiones (29), (R = Et, nPr, nBu, $-CH_2Ar$), behave in a similar manner[33, 35].

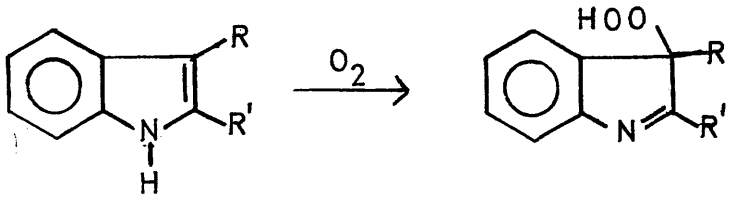


(29)

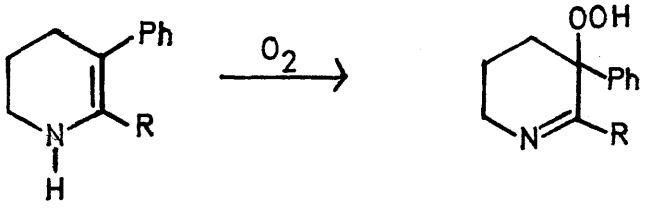
It was suggested that the facile reaction of such compounds is due to the acidity of the doubly activated α-hydrogen, but this seems unlikely in view of the stability of the keto-tautomers of phenols to oxygen. A possible explanation is that the steric compression caused by the alkyl substituents in the planar enol form of these β-diketones is relieved in the autoxidation reaction, thus accelerating this process.

Wojack found that the alkylindandiones (29) were increasingly unstable to oxygen as the bulk of the alkyl group was increased, although he did not identify the initial products of autoxidation[35]. The methyl hydroperoxide from the dione (29, R = Me) was characterised recently[33].

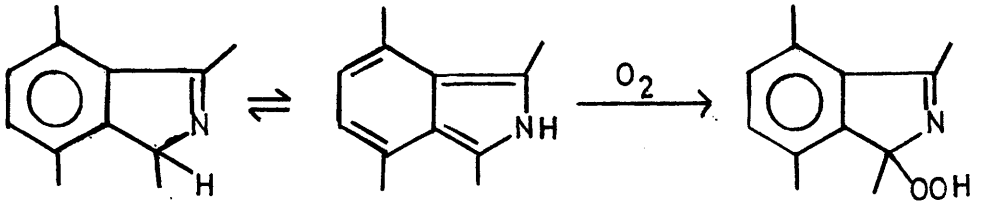
A similar behaviour is exhibited by substituted enamines and aromatic amines. A selection of such compounds which autoxidise to hydroperoxides is given below[12].

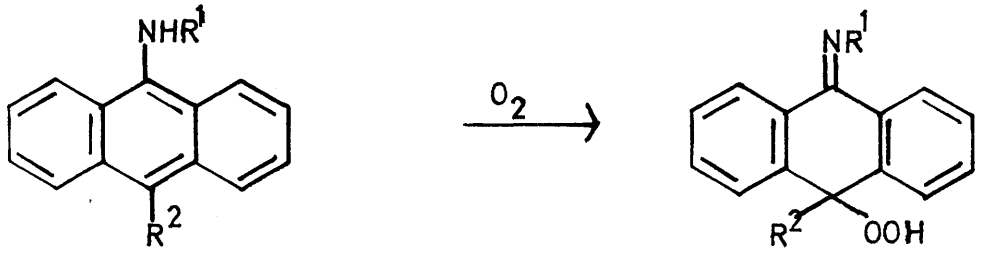


R = R' = Me ; R = Me,R' = ^{i}Pr ; R = Me,R' = Ph ; R,R' = -$(CH_2)_4$-.

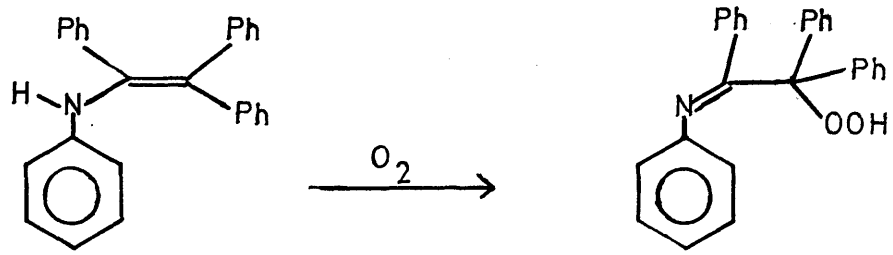


R = Me, CH_2Ph.



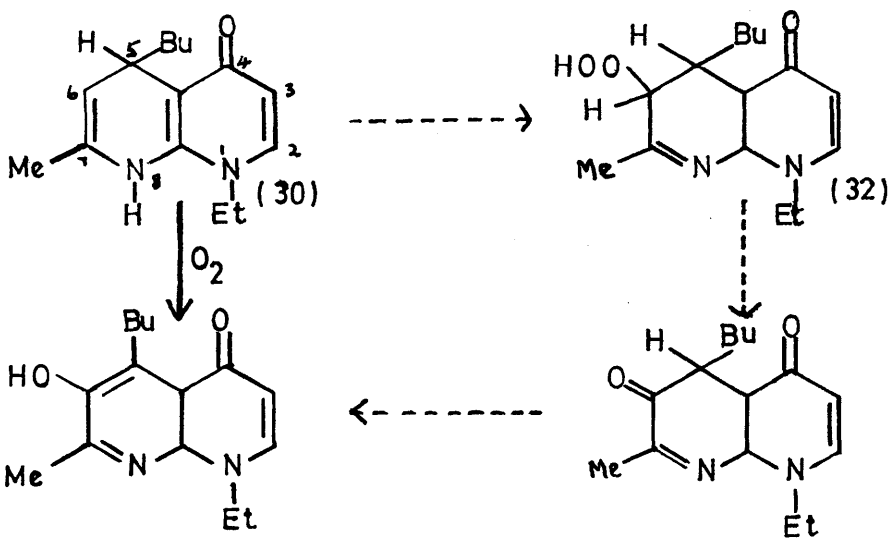


R^1, R^2 = H ; R^1 = H,R^2 = Ph ; R^1 = p-$MeOC_6H_4$-, R^2 = Ph .



In all of these examples one could postulate that the formation of hydroperoxide results in a release of strain within the molecule.

The recent report of the autoxidation of enamine (30) to the hydroxylated naphthyridine (31) may proceed *via* dehydration and subsequent tautomerisation of the ketone (32), although the authors propose an alternative pathway involving hydroperoxide formation at the 5-position[36].

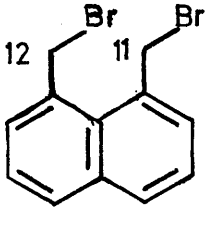


Peri-interactions in fused aromatic systems.

Condensed aromatic systems such as naphthalenes and anthracenes have a unique steric interaction due to the proximity of substituents in the peri-positions. This is the subject of a comprehensive review[37]. A large amount of physical evidence has been accumulated in support of this interaction.

The strain due to congestion between the peri-substituents in 1,8-dimethylnaphthalene has been estimated at about 8 kcal. mole^{-1}, and is evident from the distorted bond angles revealed in X-ray studies of both this compound and the related 3-bromo-1,8-dimethylnaphthalene. Predictions of geometry based on strain minimisation calculations are in excellent agreement with the X-ray results, the most marked distortions being in the plane of the naphthalene nucleus, although in other systems, severe buckling of the naphthalene nucleus has been observed[38]. The rotation barrier for the methyl groups in 1,8-dimethylnaphthalene has been estimated, using n.m.r. Fourier transform techniques, at 3 kcal. mole^{-1} compared with the normal value of 2 kcal. mole^{-1} for isolated methyl groups[39].

A recent X-ray study of 1,8-di(bromomethyl)naphthalene (33) indicates that, while the major deformations are in the plane of the molecule by virtue of in-plane bending of the C_1-C_{11} and C_8-C_{12} bonds, there are also out-of-plane deformations throughout the molecule. This study revealed considerable distortions of both bond angles and bond lengths in the naphthalene nucleus. For example, the C_1-C_2 and C_7-C_8 bonds are almost 2% longer than the C_3-C_4 and C_5-C_6 bonds. Such distortions could explain the anomalous reactivity displayed by such compounds.



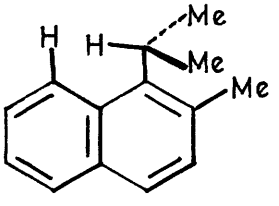
(33)

Low temperature n.m.r. studies of the dibromide (33) and a series of related compounds indicated that the barrier to rotation about the peri-bonds in these molecules is too low to be estimated by this method[40].

The substantial downfield shift of the peri-proton signal in the

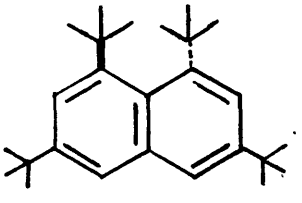
n.m.r. of 1-alkylnaphthalenes observed by many groups has been attributed to peri-interactions. This effect is maximised in 1-t-butylnaphthalenes and 1,4-di-t-butylnaphthalenes. A smaller downfield shift of the t-butyl signals relative to 2-t-butylnaphthalene has been attributed to the same interaction[41].

Low temperature n.m.r. studies of 1-isopropyl- 2-methylnaphthalene indicate a very high barrier to rotation of ca. 13 kcal. mole^{-1}, in contrast with t-butylnaphthalenes, where the barrier to rotation has been found to be lower than expected[42]. This can be explained by postulating a low energy conformation (34) for this molecule, whereas for 1-t-butylnaphthalenes all conformations are strained.



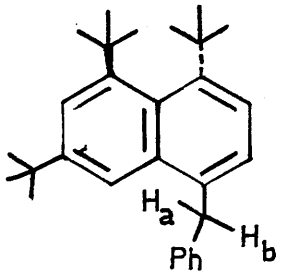
(34)

In the extreme case of 1,3,6,8-tetra-t-butylnaphthalene (35), Franck and co-workers have found that the peri-substituents lie on opposite sides of the mean plane of the naphthalene ring, the barrier to interconversion to the mirror-image conformation being greater than 24 kcal. mole^{-1}.



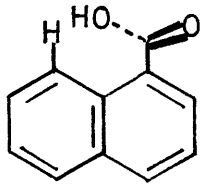
(35)

The non-equivalence of the benzylic protons in (36) at elevated temperatures is taken as further proof of the high barrier to interconversion between the mirror-image conformations[43].



(36)

Further physical evidence of the severity of the peri-interaction include anomalous u.v. and i.r. spectra, dielectric measurements, and enhanced acidities of 1-naphthoic acids compared to 2-naphthoic acids. This last effect is rationalised as a destabilisation of the free acid (37) due to steric inhibition of resonance[37].

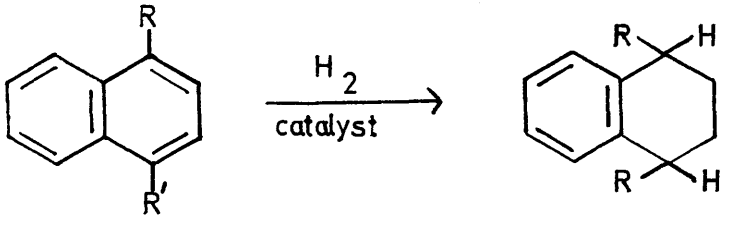


(37)

In molecules such as 1,8-diphenylnaphthalene, it was recently reported that there is no extension of conjugation, as peri-interactions prevent coplanarity of the phenyl groups and the naphthalene system[44]. A recent report on the fluorescence of methyl substituted naphthalenes suggests that high rates of intersystem crossing in 1,8-dimethylnaphthalene and 1,4,4,8-tetramethylnaphthalene are caused by lack of planarity in these molecules as a result of peri-interactions[45].

The influence of peri-interactions upon the chemical reactivity of substituted naphthalene and anthracene derivations is often striking. The relative ease of acid-catalysed isomerisation of 1,8-dimethylnaphthalene to the 1,7-isomer compared to other dimethyl naphthalenes has been attributed to the relief of strain in the transition state leading to the C-1 protonated derivative[37]. In the majority of cases, anomalous behaviour of substrates which are subject to peri-interactions

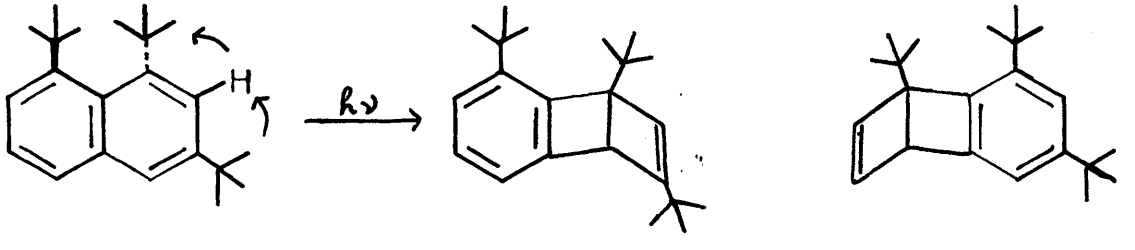
involves the removal of this interaction in the transition state, in the products, or in both by loss of aromaticity in one ring, leading to tetrahedral geometry at one of the peri-positions. The rapid rate of hydrogenation of α-t-butylnaphthalenes, and the high degree of selectivity displayed in the reaction has been attributed to steric strain release in the transition state.



R = ^{t}Bu, R' = H ; R = R' = ^{t}Bu .

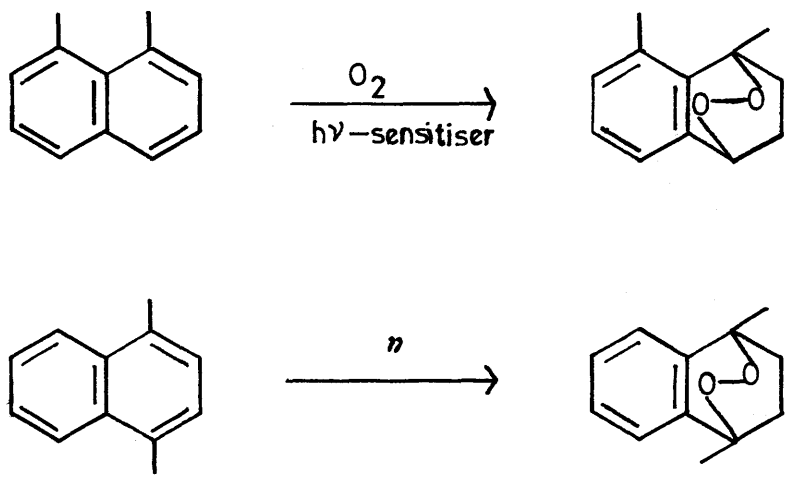
1,4-Di-t-butylnaphthalene is hydrogenated ca. thirteen times more rapidly than naphthalene itself[41].

The photochemical isomerisation of 1,8-di-t-butylnaphthalenes to their Dewar isomers is unique. The exclusive formation of the tri-t-butyl Dewar isomer (38) can be accounted for by postulating the existence of a buttressing effect between the meta-t-butyl groups. None of the isomer (39) was detected[46].



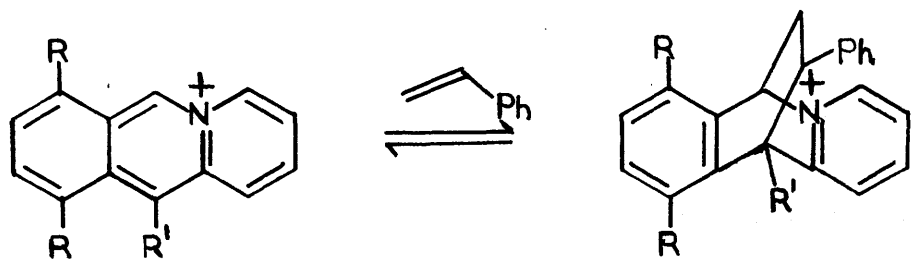
(38) (39)

Peri-dimethylnaphthalenes readily undergo cycloaddition reactions with singlet oxygen to give transannular peroxides. 1,4-Dimethyl-naphthalenes react exclusively in the substituted ring.



1-Methylnaphthalene and 1,5-dimethylnaphthalene are inert under these conditions[47].

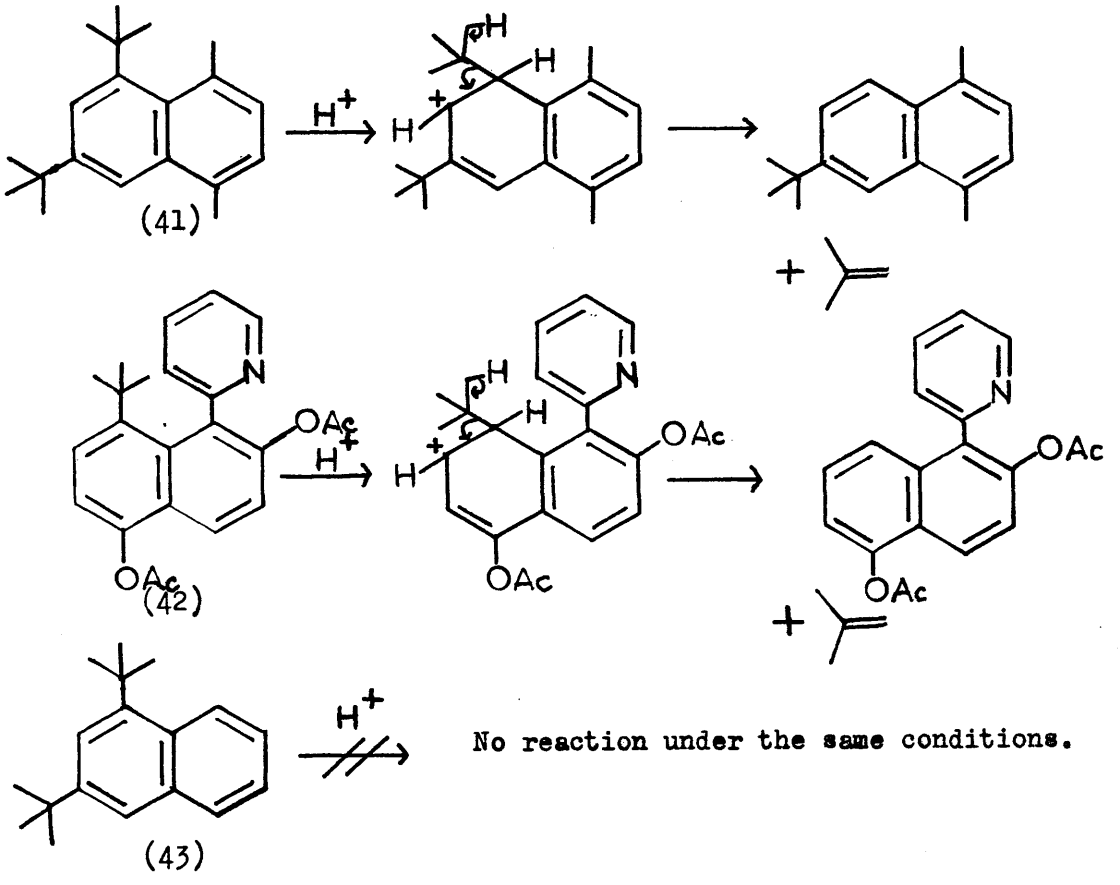
The substituted acridizinium ions (40) undergo cycloaddition reactions with styrene, and the increase in rate for the methyl substituted cases can be correlated qualitatively with increases in peri-interactions within the molecule. A similar trend is followed by substituted anthracene derivatives[48].



(40)

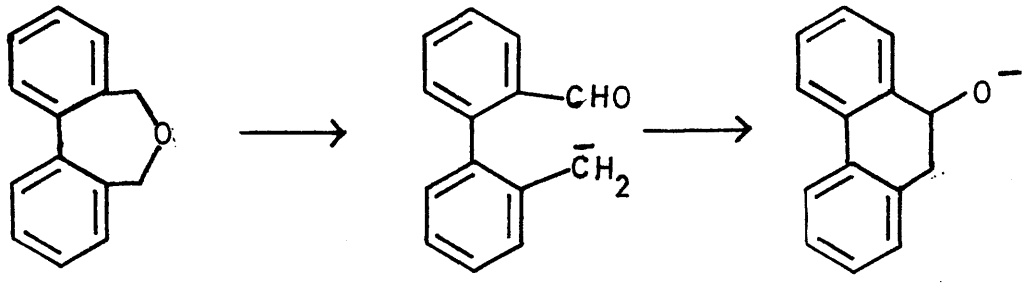
R = R' = H ;	R = H, R' = Me ;	R = R' = Me .
Relative rate:-		
1 :	13 :	130 .

The facile de-t-butylation of the strained naphthalenes (41) and (42) relative to the di-t-butylnaphthalene (43) may be due to a relief of strain in the C_1-protonated intermediates[43, 49].

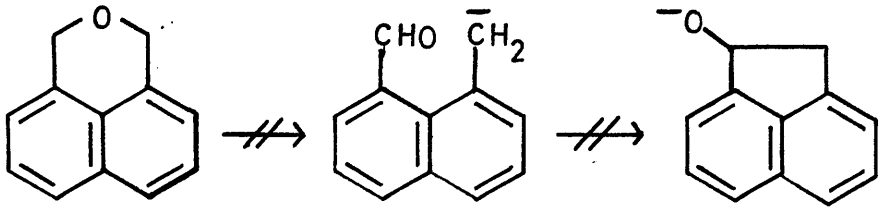


1-Trityl-2-naphthol is converted to 2-naphthol and triphenyl carbinol rapidly in dilute hydrochloric acid[50].

The failure of the naphthopyran (45) to undergo a similar reaction to diphenan (44) on treatment with potassium amide in liquid ammonia has been accounted for by postulating the suppression of resonance stabilisation in the carbanion (46) due to steric compression[37].



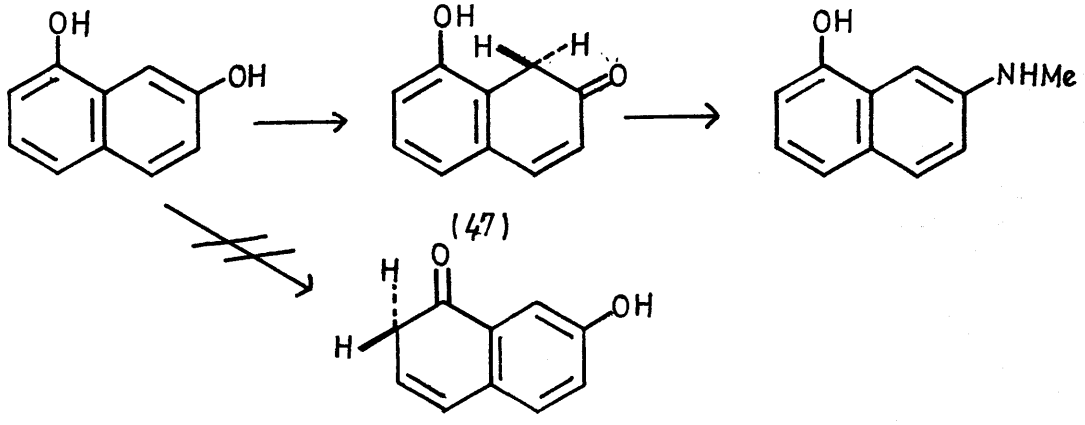
(44)



(45) (46)

Peri-effects in naphthols.

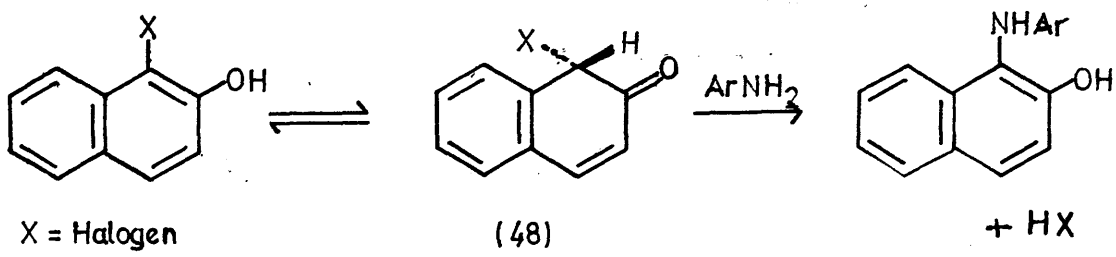
The chemistry of strained naphthols might be expected to resemble that of the strained phenols mentioned above. Some evidence for the existence of keto-tautomers of strained naphthols is available. The exclusive formation of 7-methylamino-1-naphthol from the Bucherer reaction on 1,7-naphthalenediol has been taken as evidence for the preferential formation of the 2-keto-tautomer (47) in the initial step, the major influence being the greater relief of strain in this intermediate[37].



(47)

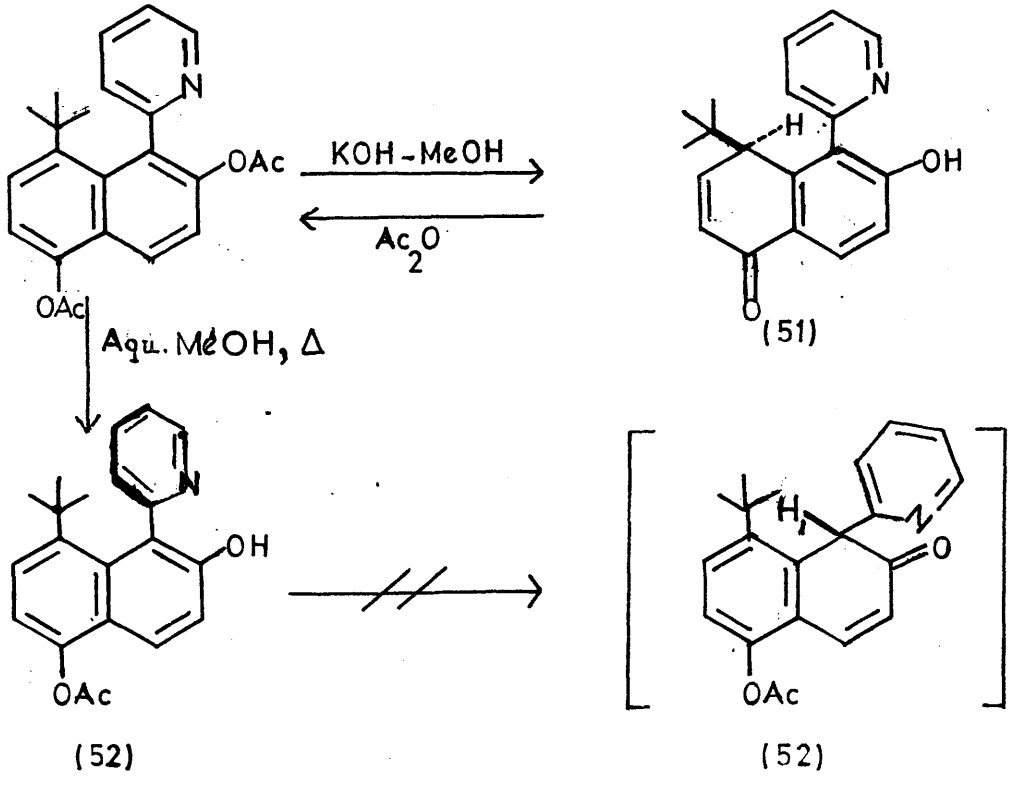
1-Halogeno-2-naphthols are found to be anomalously reactive to substitution by anilines. This was related to the presence of the keto-tautomer (48), which can readily undergo nucleophilic substitution. This type of reaction is normally activated by the presence of strong electron-withdrawing substituents placed in a position conjugated with the carbon atom carrying halogen, but operates via a different mechanism

in these cases.



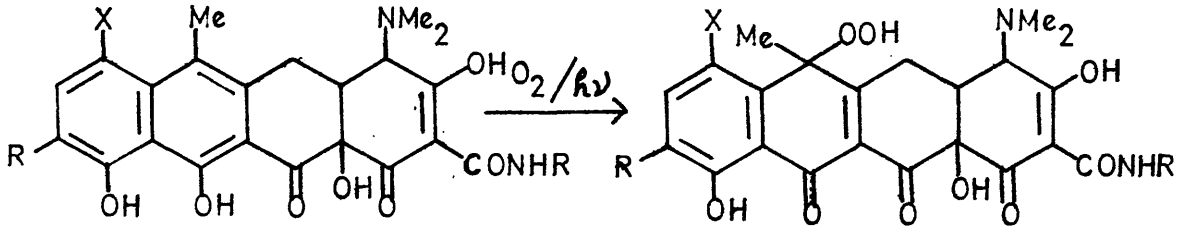
The failure of the 1-halogeno-2-naphthoxide ion, and 1-halogeno-2-methoxynaphthalenes to undergo this reaction support this hypothesis.[51]

The naphthol (51) has been shown to exist entirely in the keto-form, but the isomeric naphthol (52) does not tautomerise to any measurable extent.



Examination of models indicates that the keto-tautomer of (52) has a serious steric interaction between the t-butyl group and H-1, whereas the structure (51) is completely free of unfavourable steric interactions. This implies that the loss of aromatic resonance stabilisation in the keto-tautomer (51) relative to the phenolic tautomer is outbalanced by the decrease in energy as a result of the relief of steric strain[49].

The tetracyclines (49) react with oxygen in the presence of light to give the hydroperoxides (50) when the substituent at the 7-position is chlorine or bromine, but not when it is hydrogen. The compound containing the larger bromine substituent reacts more quickly[52]. It is likely that singlet oxygen is involved in these reactions, since they do not proceed in the absence of light, and may involve the intermediacy of a transannular peroxide (cf. dimethylnaphthalenes, page 32).



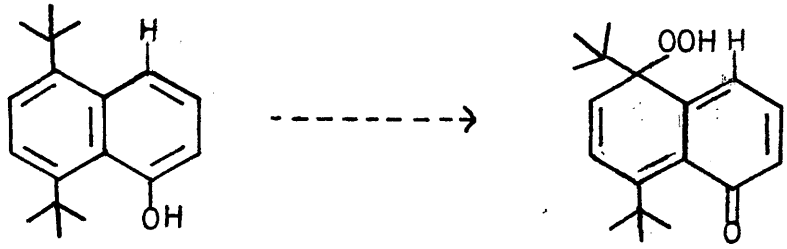
(49) (50)

R = H, ^{t}Bu ; X = H,Cl,Br .

Autoxidation of naphthols.

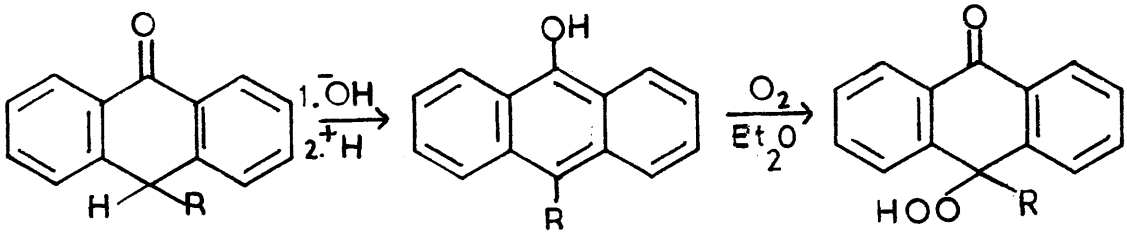
It was noted earlier that some hindered phenols which displayed keto-enol tautomerism were also found to autoxidise readily. Miller has suggested that this behaviour is associated with a relief of steric strain in the resulting hydroperoxide (see page 24).

Franck found that the strained naphthol (53) is extremely sensitive to air, but did not identify the products of autoxidation. It was suggested that this phenol may also exhibit keto-enol tautomerism, but no evidence for this has been presented[53]. In this case, formation of a hydroperoxide such as (54) would result in loss of aromaticity in both rings.



(53) (54)

A series of 9-substituted-10-anthranols (55), (R = Me, Et, $-CH_2Ph$, Ph, vinyl), were found to autoxidise spontaneously in ether in several hours, giving the hydroperoxides (56) as the sole primary products of autoxidation. In some cases, the stable keto-tautomers (57) were prepared, and found to be relatively inert to oxygen[54]. Anthranol is itself known to exhibit keto-enol tautomerism, and autoxidises in neutral or alkaline conditions to anthraquinone[55].

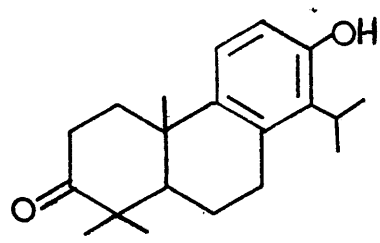


R = Me, Ph

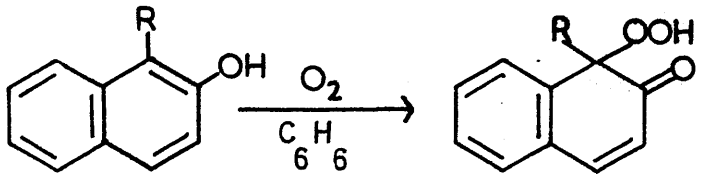
(57) (55) (56)

Similar behaviour is displayed by a series of 9-substituted-10-amino-anthracenes (see page 27)[54, 12]. In these cases, the 9-substituent is subject to peri-interactions from both sides, which implies a greater degree of steric strain than in the analogous naphthalenes, and the loss of aromatic resonance stabilisation energy is also considerably less. No attempt was made to correlate relative rates of autoxidation with the size of the substituent in the 9-position .

When 1-isopropyl-2-naphthol was first synthesised as an intermediate in the attempted synthesis of totarolone (58) it was discovered that it readily took up one mole of oxygen to give a hydroperoxide[56]. The investigation of this phenomenon was later extended to other 1-alkyl-2-naphthols (59), and the products were unambiguously identified as the 1-hydroperoxy-1-alkyl-2(1H)-naphthalenones (60)[57, 58].



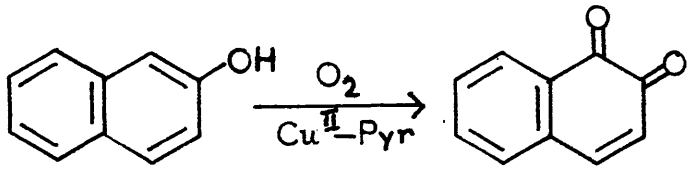
(58)



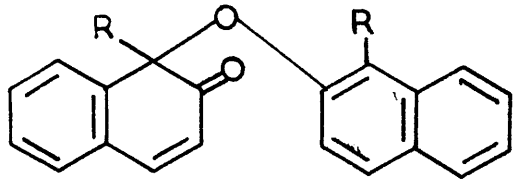
(59) (60)

R = ^{i}Pr, c-hexyl, ^{s}Bu .

2-Naphthol itself is stable in air over prolonged periods, although it can be oxygenated using copper II-pyridine complexes as catalysts[59].



1-Methyl-2-naphthol is reported to autoxidise very slowly to 1-hydroxy-1-methyl-2(1H)-naphthalenone, traces of this compound being observed after a benzene solution of the naphthol had ben exposed to air for four weeks[60]. A re-investigation of this reaction indicated that it is extremely slow, and is not catalysed by common radical initiators, Treatment with alkaline ferricyanide in an oxygen atmosphere gave only the radical dimer (61, R = CH_3)[57].



(61)

Benzene solutions of 1-ethyl-2-naphthol were found to autoxidise in diffuse sunlight to a mixture of the hydroperoxide (60, R = Et), and the dimer (61, R = Et) over a period of days[57].

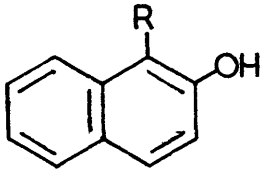
In general, the susceptibility of 1-alkyl-2-naphthols was found

to correlate qualitatively with the degree of α-branching in the alkyl substituent. It was proposed that this phenomenon is related to the degree of peri-strain within these molecules.

The work described in this thesis extends the range of substituted 2-naphthols and attempts to relate the degree of strain to the overall rate of autoxidation in a semi-quantitative manner.

DISCUSSION.

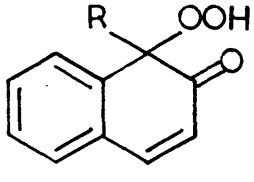
In order to investigate the factors influencing the autoxidation of 2-naphthols in a systematic manner, it was necessary to prepare a range of these compounds employing a variety of synthetic routes. A literature survey uncovered reported preparations of the following 2-naphthols, which are relevant to the present study.



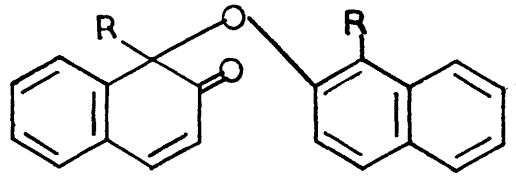
(1)

R = Methyl[1,2], ethyl[2,3], n-propyl[4], isopropyl[4,5,6], isopropenyl[4,5], n-butyl[7,8], sec-butyl[2], n-pentyl[8], isopentyl[2], n-hexyl[8], isohexyl[9], cyclohexyl[6,10], allyl[11], 3,3-dimethylallyl[2,14], benzyl[2,12], triphenylmethyl[13], phenyl[15], 2-hydroxy-1-naphthyl[16], 1-methylallyl[17].

It was already known that 1-ethyl-2-naphthol decomposes in air[3(b)], although the products of this reaction were not identified until recently. Autoxidation of a benzene solution of this naphthol was found to give the hydroperoxide (2, R = Et), and the naphthoxy radical dimer (3, R = Et)[2].



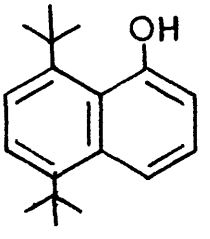
(2)



(3)

1-Methyl-2-naphthol did not react with oxygen to a significant extent in eight days, even in the presence of potential initiators such as cobalt III acetylacetonate, or the hydroperoxide (2, R = ^{i}Pr)[6]. Treatment with aqueous alkaline potassium ferricyanide in the presence

of oxygen produces only the radical dimer (3, R = Me). The naphthols (1, R = ^{i}Pr,c-hexyl,sec-butyl) were found to react rapidly with oxygen to produce virtually quantitative yields of the hydroperoxides (2, R = ^{i}Pr,c-hexyl,sec-butyl)[2, 6]. 1-Benzyl-2-naphthol was found to be inert to oxygen over prolonged periods[2]. A literature survey did not reveal any further reports of instability of 2-naphthols to oxygen. 5,8-Di-t-butyl-1-naphthol (4) is reported to react rapidly with oxygen, but the autoxidation products have not been characterised[18].



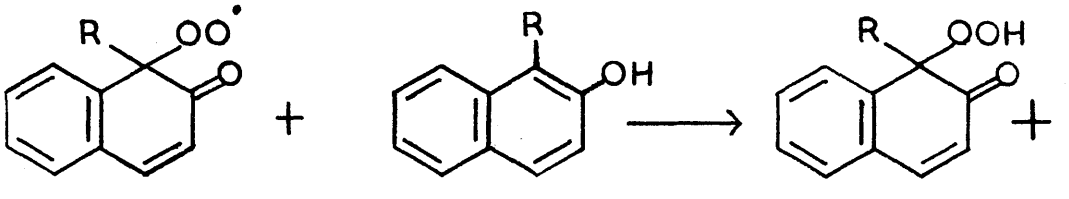
(4)

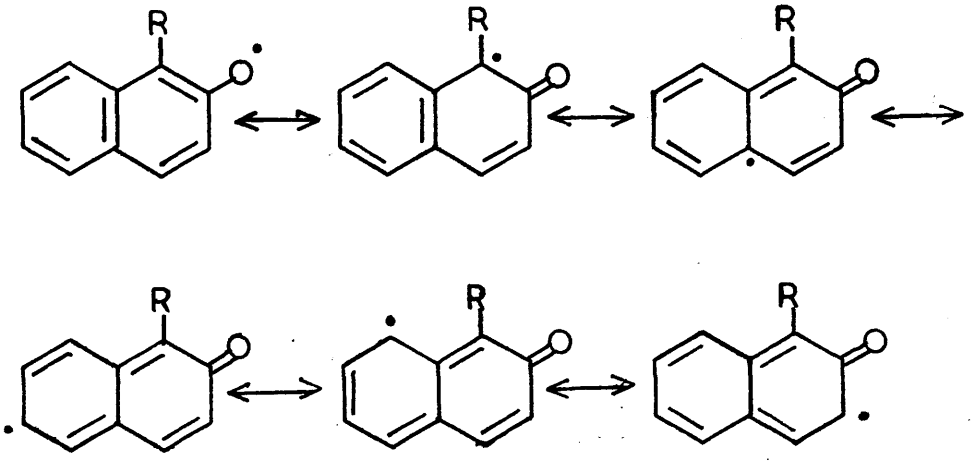
The order of reactivity of the 2-naphthols (1) known to autoxidise was found to be,

$$R = Me \ll Et \ll \text{c-hexyl, sec-butyl} < {}^{i}Pr ,$$

which correlates with the degree of strain which would be expected due to peri-interactions. The 1-naphthol (4) would also be expected to be subject to severe peri-strain.

Another plausible explanation for this order of reactivity would be an increase in inductive stabilisation of the intermediate phenoxy radical by the branched alkyl groups in the more reactive members of the series, thus increasing the rate of the hydrogen abstraction step in the autoxidation process.





Such an inductive release would increase electron density on the oxygen atom of the naphthol, and would thus favour abstraction of a hydrogen atom by the electron deficient peroxy radical. However, hyperconjugative stabilisation of the naphthoxy radical would be expected to increase in the opposite order, the methyl naphthoxy radical gaining the maximum degree of stabilisation.

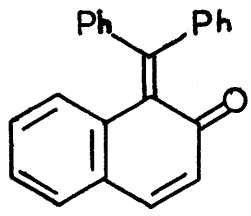
In order to evaluate the factors influencing the susceptibility of 2-naphthols to autoxidation, it was necessary to extend the range of these compounds, special emphasis being placed upon the degree of steric strain in the molecule.

Synthesis of substituted 2-naphthols.

The most obvious method of increasing the degree of peri-strain in the series discussed above is to introduce a substituent into the 1-position which contains a tertiary α-carbon, viz. t-butyl, t-pentyl, etc.

The only reported naphthols of this type are 1-triphenylmethyl-2-naphthol[13], and a substance assigned the structure 1,6-di-t-butyl-2-naphthol[19]. The former compound was prepared by the action of phenylmagnesium bromide on the known o-naphthofuchsone (5). Examination of models indicated that this molecule may be subject to considerably less strain than 1-t-butyl-2-naphthol since the phenyl groups can adopt a propellor-like conformation, thus avoiding severe

interactions with H-8.



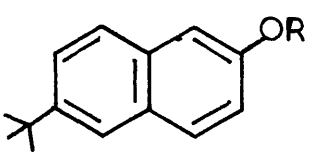
(5)

Friedel-Crafts t-butylation of 2-naphthol and 2-methoxynaphthalene.

Buu-Hoi and co-workers[19] reported that the product of the Friedel-Crafts reaction of 2-naphthol with t-butyl chloride produced a mono-t-butyl derivative, m.p. 120°, and a di-t-butyl derivative, m.p. 139°. It was proved that the monoalkyl derivative is 6-t-butyl-2-naphthol (6, R = H) by synthesising this compound independently, and that the dialkyl derivative can be made from the monoalkyl derivative by further t-butylation. This helped to clarify the extremely confused literature of this reaction, in which many erroneous structural assignments had been made.

The di-t-butyl derivative was assigned the structure 1,6-di-t-butyl-2-naphthol (7, R = H), on the basis of analogous reactions of 2-naphthol with smaller alkyl groups, and the cryptophenolic nature of this compound (insoluble in aqueous sodium hydroxide). This structural assignment was supported by the failure of the compound to couple with diazonium salts, but this is not conclusive, since the compound does not give the naphthoxide ion in aqueous media, and cannot couple for that reason.

This structural assignment was supported by later workers on the basis of the long half-life of a derived radical[20, 21].



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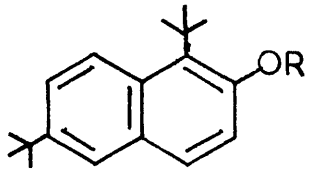

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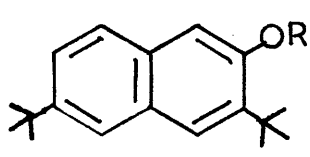


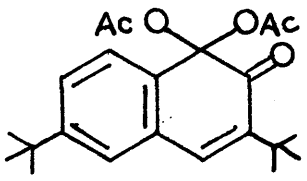
(8)

The course of Friedel-Crafts t-butylation of 2-methoxynaphthalene has also been unclear. Ferris and Hamer have claimed the preparation of 1-t-butyl-2-methoxynaphthalene as a sharply melting solid by this method[22].

Investigations in this laboratory[2] revealed that the di-t-butylnaphthol obtained from the t-butylation of 2-naphthol autoxidises very slowly, traces of a red compound being detected after a benzene solution of the di-t-butylnaphthol had been shaken in an oxygen atmosphere for several days.

In view of the unexpected stability of the di-t-butylnaphthol to oxygen, and the reported[22] preparation of 1-t-butyl-2-methoxynaphthalene by Friedel-Crafts t-butylation of 2-methoxynaphthalene, it was decided to reinvestigate these reactions[23].

Lead tetraacetate oxidation of the di-t-butylnaphthol was found to produce a mixture containing the red compound previously obtained by autoxidation of the di-t-butylnaphthol, and a second compound which could be obtained as colourless needles, m.p. 146-148° (lit.[2] 147-149°) by fractional crystallisation. The latter compound was assigned the structure 1,1-diacetoxy-3,6-di-t-butyl-2(1H)-naphthalenone (9) on the basis of its spectral characteristics. Mild hydrolysis of this compound gave a quantitative yield of the red compound previously obtained from the autoxidation reaction of the di-t-butylnaphthol. This was assigned the structure 3,6-di-t-butyl-1,2-naphthaquinone (10) on the basis of the following spectral characteristics. The ultraviolet spectrum (u.v.) ($\lambda_{max.}$ (EtOH) 225, 260, 348 nm.) bore a striking resemblance to that of 1,2-naphthaquinone ($\lambda_{max.}$ (EtOH) 224, 250, 340 nm.), as did the infrared spectrum (i.r.) ($\nu_{max.}$ (Nujol) 1690, 1660 cm.$^{-1}$ cf. 1,2-naphthaquinone $\nu_{max.}$ (Nujol) 1690, 1660 cm.$^{-1}$). The nuclear magnetic resonance spectrum (n.m.r.) lacked the high field doublet characteristic of the olefinic proton at C-3 of 1,2-naphthaquinone.



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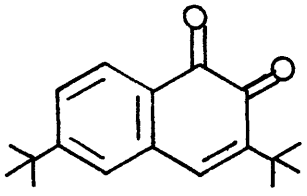

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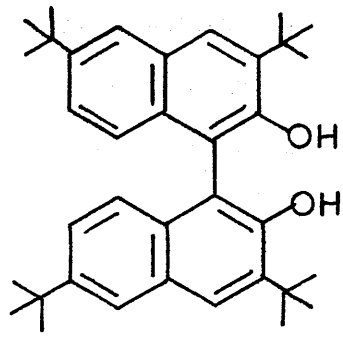


(11)

Treatment of the di-t-butylnaphthol obtained by Friedel-Crafts alkylation of 2-naphthol with alkaline potassium ferricyanide or cobalt III acetylacetonate gave a dimer, m.p. 331-333°, M^+ 510, whose spectral characteristics were extremely similar to the starting naphthol. The m.p. was identical to that reported by other workers[20] for the product of alkaline ferricyanide oxidation of the di-t-butylnaphthol. The same product was obtained in low yield when 1-iodo-3,6-di-t-butyl-2-naphthol was photolysed in benzene (reported below). This can be assigned the structure (11) on the basis of its spectral characteristics. In particular, the n.m.r. lacked the low field signal characteristic of the peri-proton in 1-t-butylnaphthalenes (see introduction ref. 41).

The di-t-butylnaphthol can therefore be assigned the structure 3,6-di-t-butyl-2-naphthol (8, R = H). This assignment is supported by the n.m.r. spectra of the phenol, which show one aromatic proton at high field (τ 3.15 in $CDCl_3$) as a broad singlet. This signal is preferentially shielded relative to other aromatic protons when the spectrum is measured in C_6D_6 (compared to CCl_4) or in dimethylsulphoxide (dmso) containing sodium hydride (compared to dmso).

This indicates the presence of one isolated aromatic proton ortho to the hydroxyl group[23].

Friedel-Crafts t-butylation of 2-methoxynaphthalene with t-butyl chloride and aluminium chloride gave a mixture of a mono-t-butyl derivative, m.p. 75.5-76.5°, and a di-t-butyl derivative, m.p. 81-82°. These were identified by comparison with authentic samples of 6-t-butyl-2-methoxynaphthalene (6, R = Me), and 3,6-di-t-butyl-2-methoxy-naphthalene (8, R = Me), made by methylating the parent phenols using sodium hydride in dmso followed by methyl iodide, or dimethyl sulphate in aqueous sodium hydroxide. The melting point found by Buu-Hoi[19] for the mono-t-butyl methyl ether (6, R = Me) of 95° could not be reproduced for analytically pure samples[23].

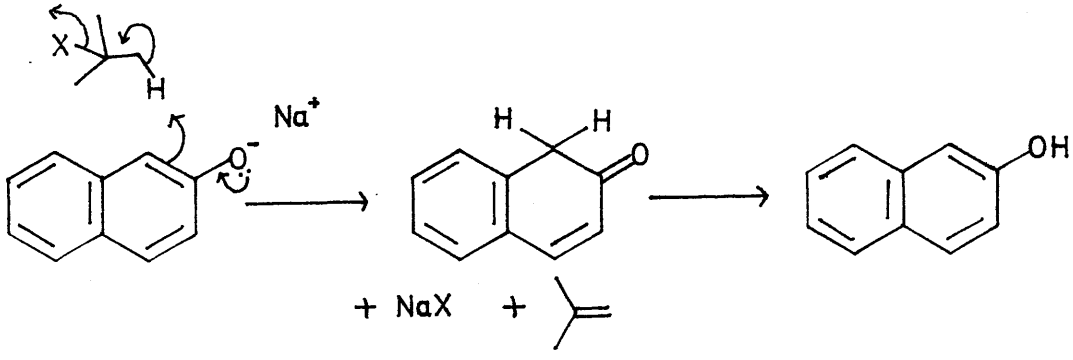
The order of reactivity of the positions in 2-naphthol on electronic grounds is 1 > 6 > 3 > 8. The order of steric accessibility is found from inspection of models to be 6 > 3 > 8 > 1. It must be concluded that with bulky reagent complexes, steric factors are of greater importance than electronic ones, and that the former is more important in this case. All attempts to obtain a tri-t-butyl derivative by Friedel-Crafts reaction upon 2-naphthol or 2-methoxy-naphthalene by prolonging the reaction time, increasing the ratio of reagent to substrate etc. failed completely. The mono-t-butyl derivatives (6, R = H,Me) on further alkylation gave only the di-t-butyl derivatives (8, R = H,Me).

The Friedel-Crafts t-butylation of 2-hydroxy and 2-methoxy naphthalenes therefore gives 6- and 3,6-substituted derivatives only. The slow autoxidation of 3,6-di-t-butyl-2-naphthol is not surprising. Other more elaborate methods must be used to introduce a t-butyl group into the 1-position in 2-naphthol.

Attempted preparation of 1-t-butyl-2-naphthol.

(a) By direct methods.

Several methods are commonly used to introduce alkyl substituents into the 1-position of 2-naphthol. Friedel-Crafts alkylation has been shown to be unsuccessful for the introduction of bulky groups such as t-butyl and triphenylmethyl[13]. The treatment of the 2-naphthoxide ion with alkyl halides is also unsuccessful for the introduction of the t-butyl group, since this results in the elimination of HX from the alkyl halide, RX[5].



The treatment of 1-bromo-2-methoxynaphthalene with t-butylmagnesium bromide under a variety of conditions gave a quantitative yield of 2-methoxynaphthalene, no t-butylated material being detected. The addition of copper halides did not alter the course of this reaction[24].

Treatment of 3,6-di-t-butyl-1,2-naphthaquinone (10) with t-butylmagnesium chloride even under forcing conditions gave only the starting quinone.

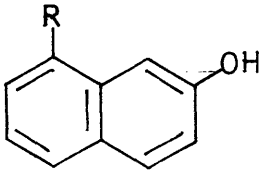
It was therefore concluded that direct methods of preparing 1-t-butyl-2-naphthol would not be successful. This difficulty has been experienced by many workers in the synthesis of 1-t-butylnaphthalenes, no direct route to these compounds having been found.

(b) <u>By indirect methods</u>.

(1) <u>From 1-tetralone</u>.

Illingworth and Peters[25] synthesised 1-t-butylnaphthalene from 1-tetralone using t-butyl Grignard reagent in an overall yield of 2%. A similar route has been employed in the synthesis of 1-cyclohexyl-

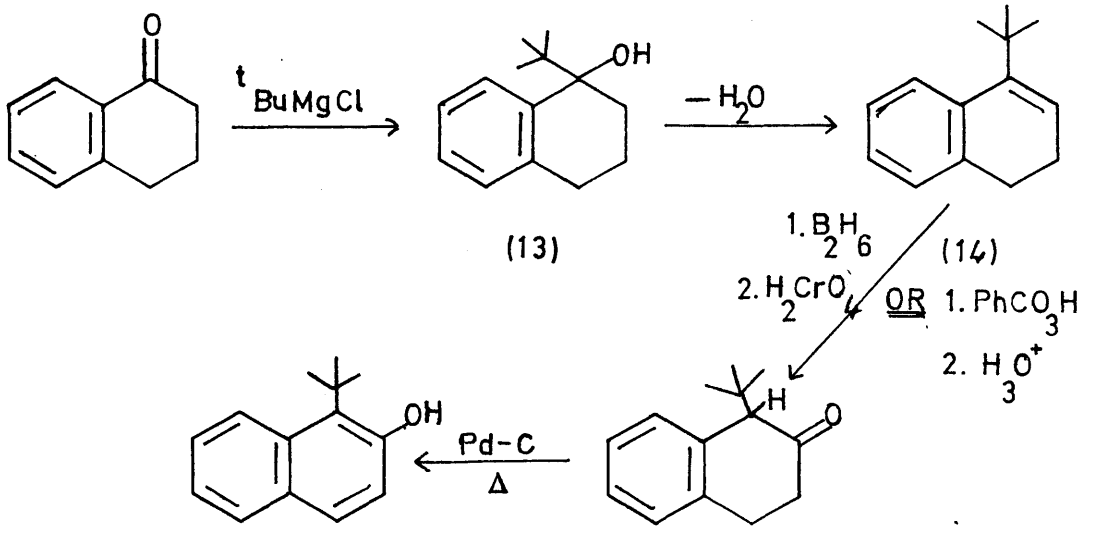
naphthalene[26], and 1-phenyl-2-naphthol[15(a)]. The major problem in this approach is proton abstraction from the substrate, leading to eventual recovery of starting material. Kadesch associated this phenomenon with steric hindrance to attack at the carbonyl group in substituted 1-tetralones[27]. Snyckers and Zollinger synthesised a series of 8-alkyl-2-naphthols (12, R = Me,Et, ^{i}Pr,Ph) from 7-methoxy-1-tetralone by Grignard addition and subsequent aromatisation and demethylation in reasonable yields. The attempted synthesis of 8-t-butyl-2-naphthol by this route was unsuccessful[28].



(12)

When the substrate or the reagent is sterically hindered, competition to the addition reaction arises from enolate formation, or from reduction of the substrate to the corresponding alcohol by transfer of hydride ion from the β-position of the Grignard reagent[29].

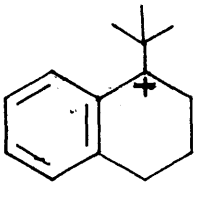
Despite these possible drawbacks it was decided to attempt the preparation of 1-t-butyl-2-naphthol by the indirect route shown below.



Perbenzoic acid has been employed to prepare 1-phenyl-2-tetralone from 3,4-dihydro-1-phenylnaphthalene[15(a)]. The hydroboration reaction followed by oxidative hydrolysis was pioneered by Brown[30].

The Grignard reaction was attempted on many occasions under a variety of conditions. It was found that the tertiary alcohol (13) was partially dehydrated to the dihydronaphthalene (14) during the mild work-up. Treatment of the product mixture with thionyl chloride in anhydrous pyridine gave a mixture of 1,2-dihydronaphthalene, 1-tetralone, and the desired 1-t-butyl-3,4,-dihydronaphthalene (14) (analysed by comparative g.l.c. and n.m.r.). The maximum yield of the t-butylated product (14) was estimated to be ca. 20%. All attempts to improve this yield by altering the proportions of reactants or the rate of addition of 1-tetralone, or by changing the conditions of the reaction failed. The addition of anhydrous magnesium bromide[29], which can increase the proportion of addition product in some cases, did not increase the yield of the desired product in this case.

Attempts to remove the starting material using Girard 'T' reagent were unsuccessful. Preparative chromatography on silica, or on silica coated with silver nitrate gave samples of the t-butyl-dihydronaphthalene (14) containing a large proportion of 1,2-dihydronaphthalene. A great deal of material was lost by this process, possibly as a result of rearrangement via the stabilised carbonium ion (15).



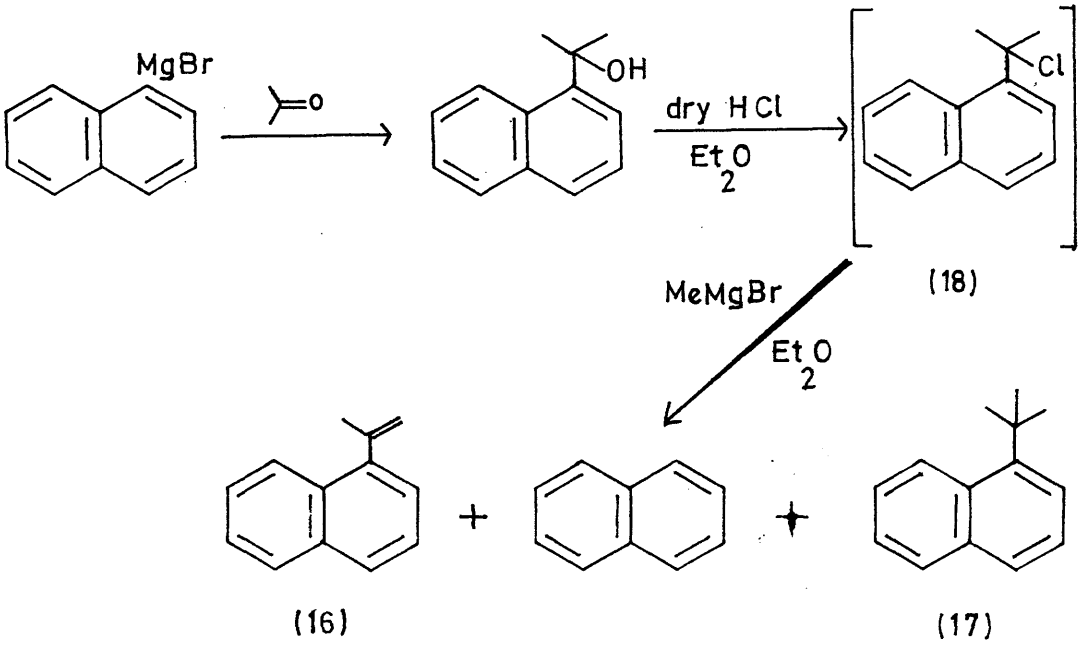
(15)

Vacuum distillation of the mixture resulted in extensive decomposition, the only pure compound isolated being 1,2-dihydro-

naphthalene. Owing to the low yield of t-butylated products, and the difficulty of isolating these, this route was abandoned.

(2) By oxidative coupling of 1-bromo-2-naphthol with methyl Grignard reagent.

The reported[31] synthesis of 1-t-butylnaphthalene by the route shown prompted us to investigate the generality of the coupling reaction between benzylic tertiary halides and methyl Grignard reagents.

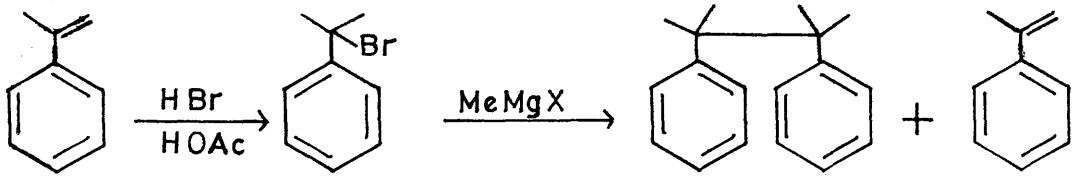


The isolated yield of the t-butyl derivative (17) from this reaction was 29%, and the isopropenyl derivative (16) could be recycled by addition of hydrogen chloride and subsequent treatment with methyl Grignard reagent. The tertiary chloride (18) was never isolated, owing to the ease with which hydrogen chloride is eliminated to give 1-isopropenylnaphthalene (16).

In order to gain experience of this reaction, a model experiment was attempted using cumyl bromide as the substrate. It was hoped that this reaction could be used to find conditions which would optimise the yield of t-butylated product.

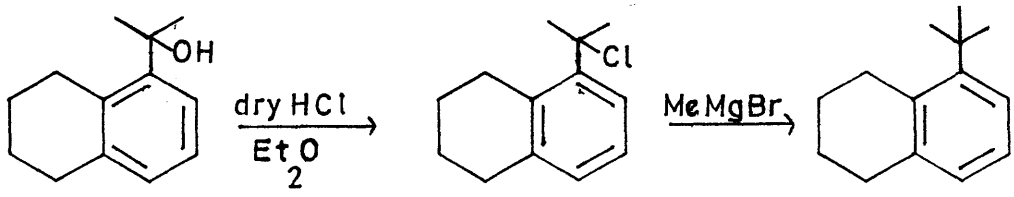
Treatment of 1-methylstyrene with a saturated solution of hydrogen bromide in glacial acetic acid followed by a cold, aqueous work-up

gave an ethereal solution of cumyl bromide. This could not be isolated in a pure state for characterisation owing to the facile elimination of hydrogen bromide, but could be analysed by n.m.r. Treatment of anhydrous solutions of cumyl bromide with ethereal methyl magnesium iodide or bromide under a variety of conditions invariably produced a mixture of 1-methylstyrene and the cumyl radical dimer (19). Cumyl radicals are known to dimerise readily[32].



(19)

None of the desired t-butylbenzene was detected on n.m.r. The reaction was attempted in the presence of anhydrous cuprous iodide[24], but the product distribution under several conditions of temperature and reaction time was virtually unaltered. The exclusive formation of the symmetrically coupled product in this case is not easy to account for, in view of the reported[33] preparation of the analagous 1-t-butyl-5,6,7,8,-tetrahydronaphthalene (20) in ca. 30% yield by a similar method to that used to prepare 1-t-butyl-naphthalene (17)[31].

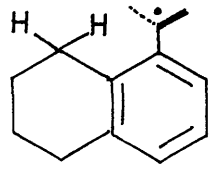


(20)

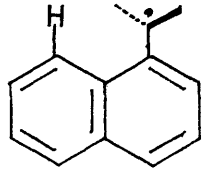
Symmetrically coupled dimers were not reported in these cases.

A possible explanation for the failure of the radicals (21) and (22) to dimerise is the steric compression which would be present in the dimers. These radicals may also be less stable than the cumyl

radical due to steric inhibition to resonance delocalisation as a result of non-planarity. 1-Isopropylnaphthalene is thought to autoxidise more slowly than the 2-isopropyl isomer because of the lower stability of the radical (22) (see introduction p.15).



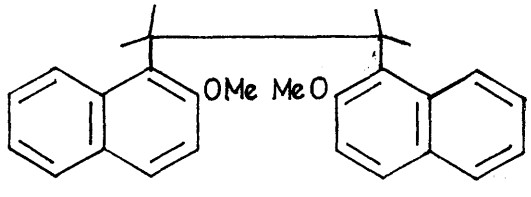
(21)



(22)

The syntheses of the t-butyl derivatives (17) and (20) were carried out using t-chlorides. It is possible that, by using cumyl chloride instead of cumyl bromide, the synthesis of t-butylbenzene may be successful.

In view of these conflicting results,,it was decided to investigate the preparation of 1-t-butyl-2-methoxynaphthalene by this method. The possible formation of the radical dimer (23) would also be of interest in the present study, as this would provide a preparation of a 1-t-alkyl-2-naphthol by demethylation of this compound.

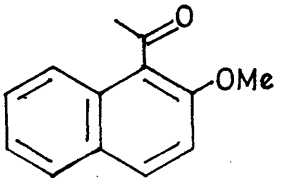


(23)

2-(2-Methoxy-1-naphthyl)-propan-2-ol (25) was prepared by treating 1-acetyl-2-methoxynaphthalene (24) with methylmagnesium iodide.

The 1-acetyl derivative (24) was obtained by methylation of 1-acetyl-2-naphthol, which was prepared by the Fries rearrangement of 2-naphthyl acetate[34] (reported below). It was found however, that the tertiary alcohol (25) readily dehydrated to 1-isopropenyl-2-methoxy

naphthalene (26) on standing. Treatment with dilute mineral acid resulted in quantitative conversion to the isopropenyl compound (26). This was converted to the tertiary chloride by treatment with dry hydrogen chloride in anhydrous ether at 0°. The chloride could not be isolated in a pure state owing to extremely facile dehydrochlorination to give the isopropenyl derivative (26).



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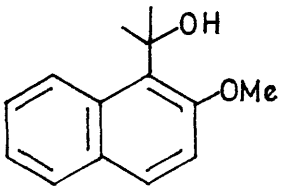
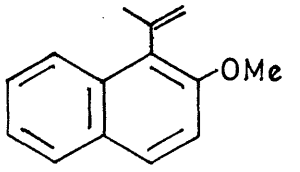


(25)



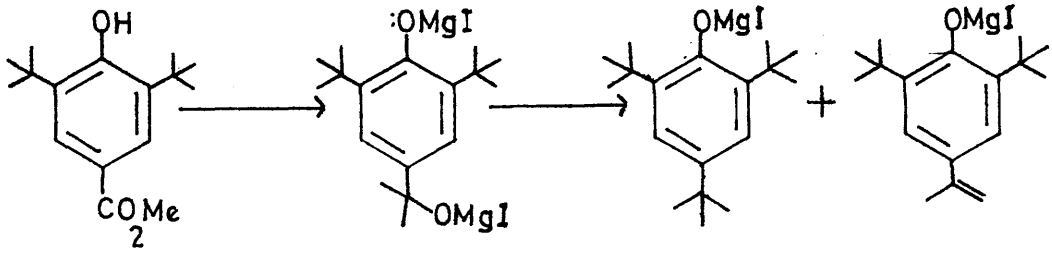
(26)

The Grignard reaction was carried out in the manner reported by Van Bekkum and co-workers[31]. G.l.c. and n.m.r. analysis of the product mixture indicated that only two products had been formed. These were the isopropenyl derivative (26), (ca. 94%), and 1-t-butyl-2-methoxynaphthalene (ca. 6%). The latter compound was identified by comparison with an authentic sample of this compound from another source (see below).

In view of the low yield of the desired product, and the difficulties involved in separating it from the major product (26), a problem which will be discussed fully later, this route to 1-t-butyl-2-naphthol was not pursued further. The overwhelming preference for elimination by Grignard reagent in this reaction relative to the analagous reaction with 2-chloro-2-(1-naphthyl)propane (18) can be interpreted either as evidence for greater steric congestion at the 1-position of 2-methoxynaphthalene relative to naphthalene, or as the result of resonance stabilisation of positive charge in the transition state by the methoxyl group.

(3) Preparation of 1-t-butyl-2-naphthol by permethylation of methyl 2-hydroxy-1-naphthoate.

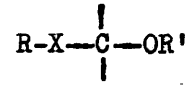
The anomalous reactivity of methyl 3,5-di-t-butyl-4-hydroxybenzoate (27) to methylmagnesium iodide at elevated temperatures to give 2,4,6-tri-t-butylphenolate (29) has been rationalised by postulating a strong activating effect of the metallated hydroxy group in the para-position of the intermediate (28).



(27) (28) (29) (30)

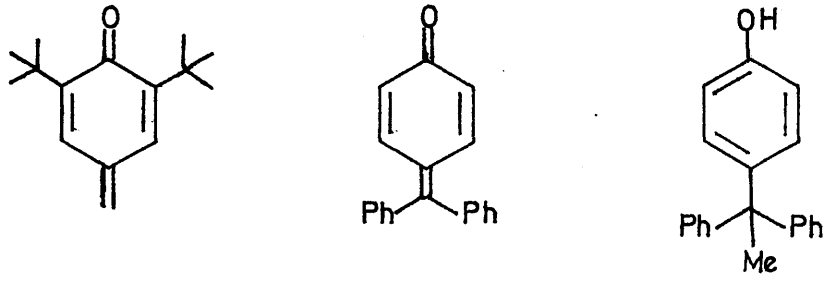
The expected isepropenyl phenolate (30) was also formed in this reaction.

Several other examples of this type of reaction are known, all of which are characterised by a general intermediate of the type,



where the group R-X-has a strong +M effect which can facilitate nucleophilic displacement of OR' by the alkyl or aryl group from a Grignard reagent[35].

A possible intermediate in the reaction of the ester (27) is the p-quinone methide (31).

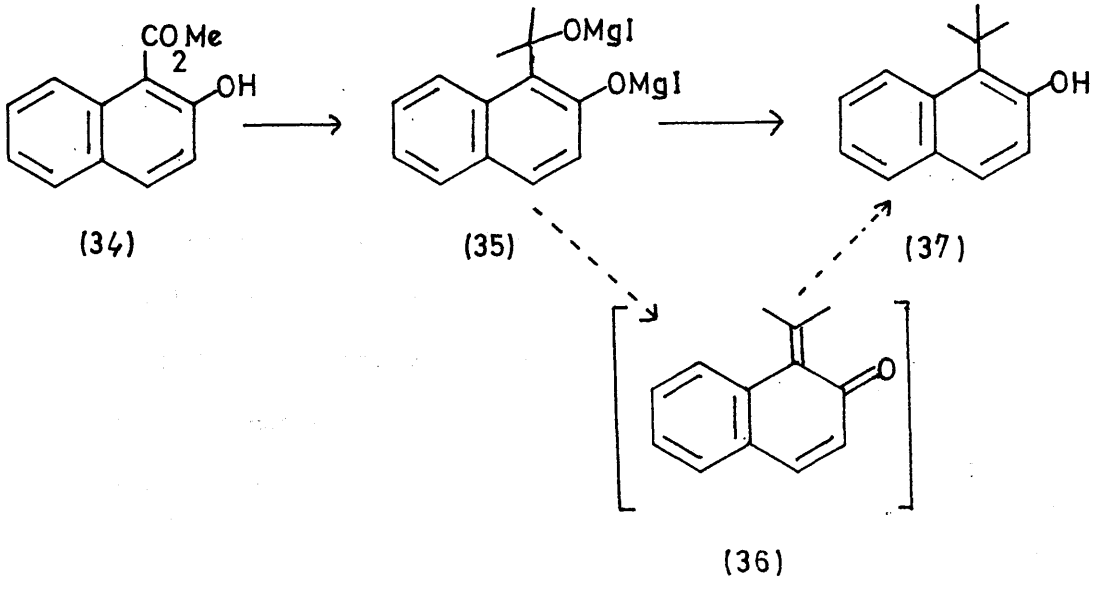


(31) (32) (33)

It is known that 1,6-addition of methyl Grignard reagent to the diphenyl quinone methide (32) gives the phenol (33)[36]. A much more general method of exhaustive alkylation of oxygenated substrates is the use of trimethylaluminium at elevated temperatures, with or without solvent. This reaction is facilitated by the presence of α-aryl groups, but this feature is not essential. 1-Naphthoic acid was successfully permethylated in this way giving a 75% yield of 1-t-butylnaphthalene, the other product being 1-isopropenylnaphthalene[37]. These represent two of the most direct methods of geminal alkylation of the carbonyl group[38].

Methyl 2-hydroxy-1-naphthoate (34) is a readily available starting material[39] for the attempted preparation of 1-t-butyl-2-naphthol (37) by one of these methods. Trimethylaluminium was not available in suitable quantities, and, owing to its extremely pyrophoric nature, requires to be handled using specialised apparatus. There is also a possibility that the phenolic group may not be stable to the extreme conditions required, in view of the known ability of aluminium compounds, to cleave the aryl-oxygen bond in phenols and methoxyaryl compounds[40].

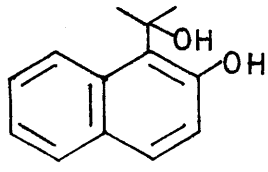
(see page105)



(34) (35) (37)

(36)

The α-arylmagnesium alkoxide (35) could be formed in ca. 75% yield by refluxing an ethereal solution of the magnesium salt of the naphthol (34), in the presence of an excess of methylmagnesium iodide for twelve hours. The reaction could be worked up at this stage with saturated aqueous ammonium chloride to give the tertiary alcohol (38), and 1-acetyl-2-naphthol.



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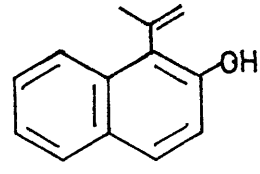

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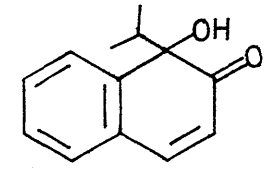
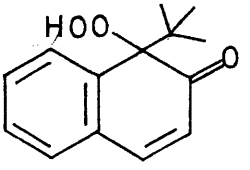


(40)

If the reaction was worked up using dilute mineral acid, 1-isopropenyl-2-naphthol (39) was isolated in 75% yield. The alcohol (38) dehydrated to the isopropenyl compound (39) on standing, or on treatment with dilute acid. All attempts to obtain a sample of the isopropenylnaphthol (39) suitable for analysis failed[5]. This compound readily decomposed on silica and during distillation, possibly due to polymerisation or autoxidation, or *via* reaction of the isomeric ortho-quinone methide (36). However, the failure of 1-isopropyl-1-hydroxy-2(1H)-naphthalenone (40) to dehydrate to this o-quinone methide may indicate that the *peri*-strain which would be present in this species does not favour its formation[2].

In the earlier attempts to carry out the exhaustive methylation reaction, sufficient time was not allowed for complete conversion of the ester (34) to the tertiary alcoholate (35), before raising the temperature and removing solvent. In a typical run, the ethereal reaction mixture was refluxed for 2-6 hours, before distilling off the solvent, and heating the solid residue at 90-130° for 17-22 hours under an atmosphere of dry nitrogen.

The reaction was worked up using saturated aqueous ammonium chloride, and the product mixture analysed by n.m.r. It was found that the n.m.r. of the mixture changed dramatically within minutes on exposure to oxygen. Fractional crystallisation of the oxygenated mixture from benzene-light petroleum gave pale yellow prisms, a purified sample of which melted with decomposition at 134-137°. This compound was unambiguously identified as 1-t-butyl-1-hydroperoxy-2(1H)-naphthalenone (41), on the basis of its spectral characteristics, and by comparison with the spectral characteristics of the known 1-alkyl-1-hydroperoxy-2(1H)-naphthalenones(2, R = ^{i}Pr,c-hexyl)[6].

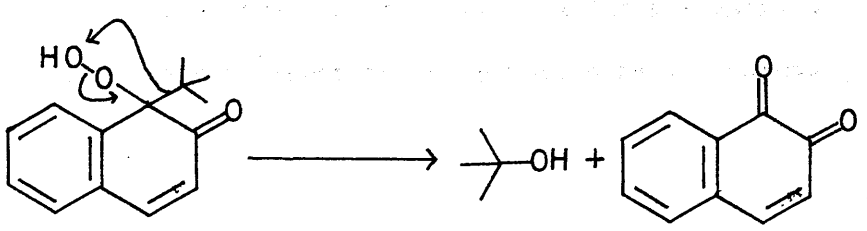


(41)

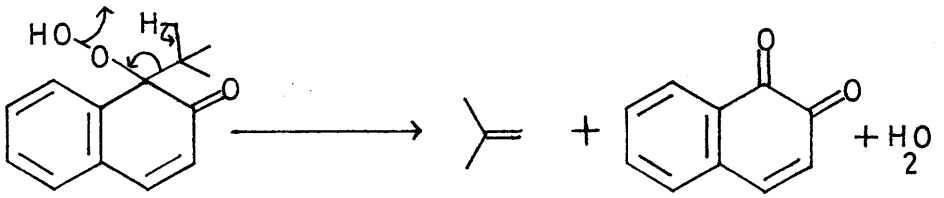
The behaviour of this hydroperoxide is discussed prior to continued discussion of the t-butyl naphthol which must be its immediate precursor.

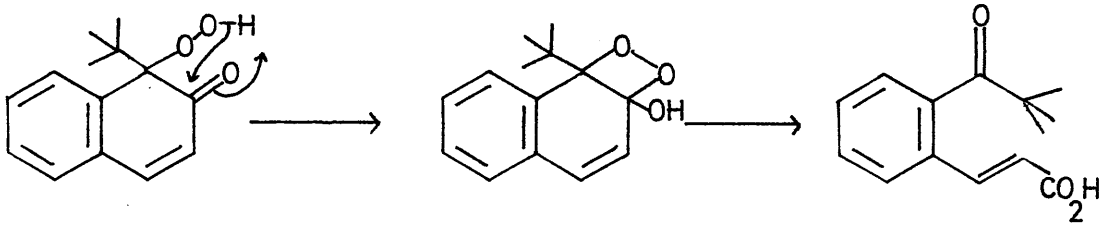
Decomposition of the hydroperoxide (41).

The t-butyl hydroperoxide (41) was found to be thermally extremely unstable. Samples stored in a freezer, in the absence of light, had partially decomposed in several days. A sample stored in benzene under nitrogen at room temperature in diffuse light had almost completely decomposed in three days. T.l.c. indicated that at least ten components were present in the solution other than unchanged hydroperoxide (41). After many attempts to isolate these decomposition products in a pure state by chromatography, the only material which could be completely characterised was 1,2-naphthaquinone, which could be compared with an authentic specimen. This quinone can arise by a migration of the t-butyl group to oxygen, to give t-butanol and the quinone, a process which very often occurs with α-ketohydroperoxides[41].

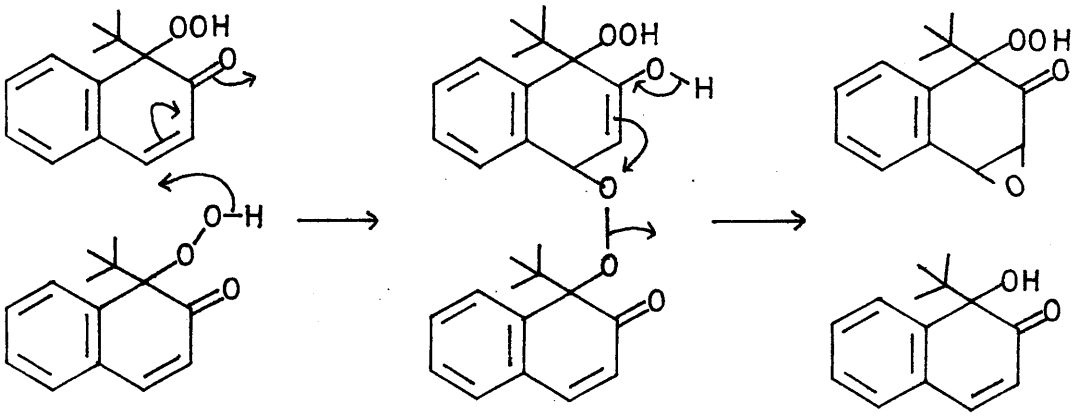


Analyses of n.m.r. spectra of the mixture did not reveal any peaks corresponding to t-butanol, however. Alternative pathways for the breakdown of this compound are outlined below.





Many intermolecular reactions could also be postulated, for example,

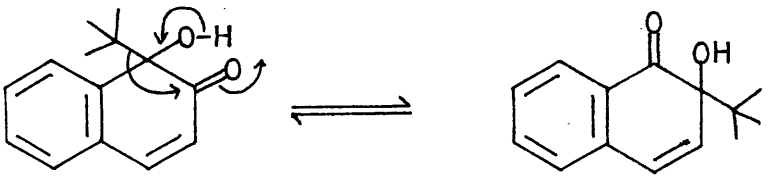


(42)

The isopropyl hydroperoxide (2, R = ^{i}Pr) undergoes analogous reactions in basic media[42], and is known to be converted to 1,2-naphthaquinone in mildly acidic media[43].

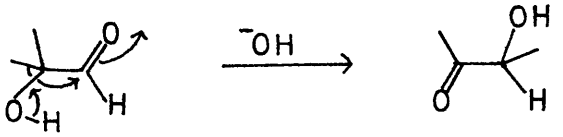
The other components which were taken from preparative chromatographic plates decomposed further before they could be characterised. One of these bands isolated from the decomposition of the hydroperoxide (41) had similar spectral characteristics to mixtures of the isomers (42) and (43), but also contained traces of at least one other compound whose structure was not determined.

The hydroxy ketone (42) could be prepared by treatment of the hydroperoxide (41) with dimethylsulphide in ether at room temperature. However, it could not be isolated in a pure state, owing to the facile ketol rearrangement to the hydroxyacetophenone (43).



(42) (43)

The analogous isopropyl compound (40) undergoes this rearrangement in basic media[42]. The conversion of α-hydroxybutyraldehyde (44) to acetoin (45) proceeds by migration of a methyl group[44].



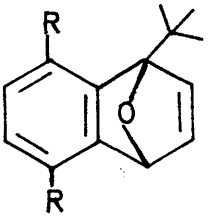
(44) (45)

Neither of the isomeric ketones (42) and (43) could be obtained in a pure state, as they equilibrate even in neutral media. The addition of acid or base rapidly produces an approximately 1 : 1 mixture of the two isomers (estimated by n.m.r.). The spectral

characteristics of the mixture (i.r., n.m.r., u.v., m.s.) can be accounted for by the two structures proposed.

The facile interconversion of the compounds (42) and (43) compared to the analogous isopropyl compounds can be rationalised in two ways. (1) The t-butyl group will migrate more easily than the isopropyl group, owing to the greater stability of the t-butyl carbonium ion. (2) The greater steric congestion at C_1 in (42) will favour rearrangement to (43).

The restricted rotation of the t-butyl group in (46), detected by low temperature n.m.r. studies, would seem to support this postulate[45].



R = Cl,-OMe. (46)

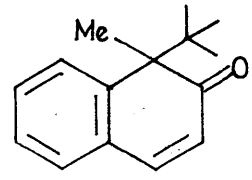
No further investigation of the processes involved in the decomposition of the t-butyl hydroperoxide (41) were carried out.

Methylation of the products of the high temperature Grignard reaction.

Owing to the extreme instability of 1-t-butyl-2-naphthol, which was assumed to be the precursor of the hydroperoxide (42), it was necessary to isolate this compound in the form of a stable derivative. One can predict that the majority of derivatives of the t-butyl naphthol (37) and the isopropenyl naphthol (39) will be of similar polarity, so that the choice of protecting group is limited. It was decided that the methyl ethers of these naphthols were most likely to be susceptible to separation by physical methods.

The mixture of naphthols produced in the high temperature Grignard reaction could be methylated readily by taking up the reaction mixture in anhydrous dimethylsulphoxide (dmso), and adding excess methyl iodide, until the bright colour of the naphthoxide ions had been dispersed.

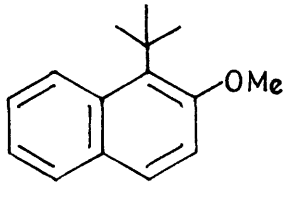
The choice of solvent in this reaction is important, as C-alkylation to give compounds such as (47) is expected to be favoured with resulting release of peri-strain (see introduction).



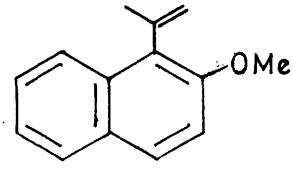
(47)

Solvents of high dielectric constant such as dmso normally result in exclusive o-alkylation[46].

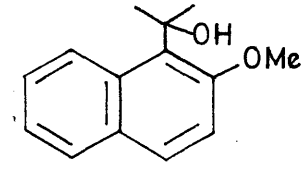
The spectral and t.l.c. characteristics of the resulting material from this reaction indicated that no phenolic material remained. The separation of 1-t-butyl-2-methoxynaphthalene (48) from the mixture was achieved by column chromatography on silica coated with 10% by weight of silver nitrate, followed by preparative t.l.c. on silica plates coated with silver nitrate. In this manner, isolated yields of ca. 25% of the desired 1-t-butyl-2-methoxynaphthalene (48) which gave one peak on g.l.c. could be obtained. Samples suitable for analysis could be prepared by vacuum distillation. The mixture of compounds (48) and (26) could not be separated by fractional distillation, since the latter polymerises on heating.



(48)



(26)



(25)

The other products of this reaction, viz. 1-acetyl-2-methoxynaphthalene, 2-(2-methoxy-1-naphthyl)-propan-2-ol (25), and 1-isopropenyl-2-methoxynaphthalene (26) were isolated, and could be characterised

by comparison with samples of these compounds prepared independently. The major product in all of the runs was the isopropenyl derivative (26), which indicates that elimination by the attacking Grignard reagent on the intermediate alcoholate (35) is favoured over substitution. Dehydration of the tertiary alcohol (25) did not occur during the mild work-up, since this product could be obtained in high yield from the reaction of 1-acetyl-2-methoxynaphthalene with methylmagnesium iodide in refluxing ether, followed by mild work-up.

A summary of the proportions of identifiable product under different reaction conditions is laid out in Table 2 (Appendix).

The use of the high boiling solvent, di-n-butyl-ether, drastically reduced the yield of t-butylated material.

At temperatures higher than 110°, polymerisation becomes significant, although this does not alter the relative proportions of isolable materials significantly .

The use of lower temperatures decreased the yield of t-butylated material substantially.

The use of 1-acetyl-2-methoxynaphthalene as a substrate resulted in the formation of a virtually identical mixture as was produced using methyl 2-hydroxy-1-naphthoate. Demethylation of aromatic methyl ethers by methyl Grignard reagent is a well known reaction (see below).

The addition of aluminium chloride as a potential ligand for the intermediate alcoholate (35) which may catalyse the substitution reaction (*cf.* trimethylaluminium) did not improve the yield of t-butylated material and increased the degree of polymerisation.

The extension of reaction time beyond *ca.* 20 hours also resulted in extensive polymerisation.

Summarising, the best isolated yields of 1-t-butyl-2-methoxy-naphthalene were obtained as follows.

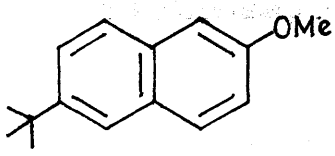
Methyl 2-hydroxy-1-naphthoate was dissolved in ether and added dropwise to a stirred solution of methylmagnesium iodide (or bromide) (5-11 molar excess), and the mixture was refluxed under dry nitrogen for 12-24 hours. The ether solvent was then distilled off, and the residue heated at 110-115° for 18-20 hours. The cooled reaction mixture was taked up in dmso, and excess methyliodide added dropwise until the brilliant colour of naphthoxide ions had been discharged. The reaction was worked up using saturated ammonium chloride solution. Preparative chromatography was carried out on silica coated with 10% silver nitrate. The material can be purified to analytical standards by vacuum distillation (purity assessed by g.l.c. and n.m.r.).

The products from this reaction were also isolated as a mixture of their acetates by treatment with acetic anhydride in dmso, but all attempts to separate 1-t-butyl-2-acetoxynaphthalene from 1-isopropenyl-2-acetoxynaphthalene were unsuccessful.

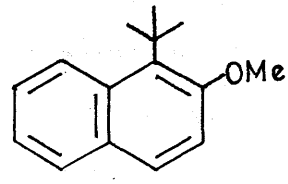
Investigations of the chemical and physical properties of 1-t-butyl-2-methoxynaphthalene (48).

The title compound (48) was a colourless oil at room temperature, which crystallised as colourless needles below ca. 5°. Many of the physical properties of this compound reflect the strain inherent in its structure.

A comparison of the u.v. spectra of the isomeric t-butyl-2-methoxynaphthalenes(6), and (48) shows considerable bathochromic and hyperchromic shifts in the longer wavelength absorption bands for the 1-t-butyl derivative, as well as some loss of fine structure for this derivative.



(6)



(48)

$\lambda_{max.}$ (EtOH):		250 (sh)	303(sh)		274(sh)		
(n.m.)	229	259.5(3.63)	316(3.13)	232	282(3.74)	323(3.24)	
		269 (3.61)	330(3.31)		291(sh)	335(sh)	

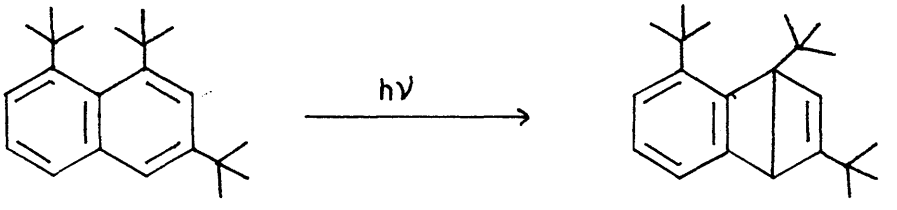
These effects have been noted by other workers[47, 51] when strained t-butylated derivatives have been compared with unstrained analogues. The changes in the u.v. spectra of strained compounds could not be accounted for by substituent effects alone. This has been attributed to a convergence of ground state and excited state energy levels as a result of destabilisation of the ground state, caused by severe distortions in the strained molecules[51] (see introduction reference 37). In 1-t-butyl-2-methoxynaphthalene, considerable distortions may arise as a result of the peri-interaction, and the buttressing effect of the 2-methoxyl group.

In the n.m.r. of (48), the peri-proton is seen at τ 1.54, and is considerably deshielded compared to the other aromatic protons, as is expected for sterically compressed peri-protons in t-butylnaphthalenes[18, 31, 47, 51]. The integrated intensity of the H-8 signal suffered an increase of 20±5% when the t-butyl signal was doubly irradiated. A nuclear Overhauser enhancement of comparable magnitude (15%) was observed between t-butyl and peri-H in n.m.r. studies of 1,4-di-t-butylnaphthalene[18]. The t-butyl signal in the n.m.r. spectrum of (48) (τ 8.27) was somewhat deshielded relative to the corresponding signal in the spectrum of (6) (τ 8.60). This effect was also observed in the t-butylnaphthalene series, and has been attributed to the

peri-interaction[18, 31].

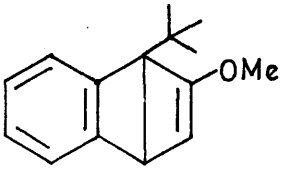
In an attempt to estimate the barrier to rotation in (48), low temperature n.m.r. studies were undertaken[48]. There was no observable change in the t-butyl signal on cooling to -150°. This indicates a particularly low barrier to rotation of the t-butyl group in this molecule. Franck et al.[49] recorded extremely low barriers to rotation (6.5 kcal. mole^{-1} or less) in 1-t-butyl- and 1-8-di-t-butylnaphthalenes. This phenomenon was associated with peri-interactions, the explanation being that the ground state conformations are all of unusually high energy, and that no conformation of relatively low energy is available to these molecules.

A report[50] that 1,3,8,-tri-t-butylnaphthalene (49) undergoes photoisomerisation to the Dewar structure (50) prompted us to investigate the photolysis of 1-t-butyl-2-methoxynaphthalene (48).



(49) (50)

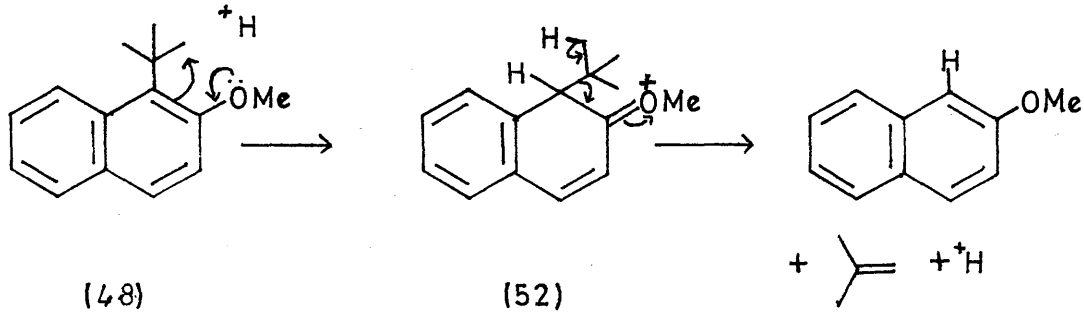
It was thought that the combined compression effects of the 2-methoxy group and the 1-t-butyl group may favour isomerisation to the Dewar isomer (51), resulting in steric decongestion within the molecule.



(51)

In the event, photolysis of a hexane solution of (48) for twenty hours employing a medium-pressure mercury lamp resulted in recovery of unchanged starting material which had partially decomposed. No other species was present in sufficient quantity to be characterised.

Extreme care was taken in preparing and isolating the t-butyl compound (48) to avoid contact with acids, as it was thought that de-t-butylation may be a facile reaction, even under mild conditions. This process would result in a decrease in strain in the transition state leading to the C-1 protonated intermediate (52).

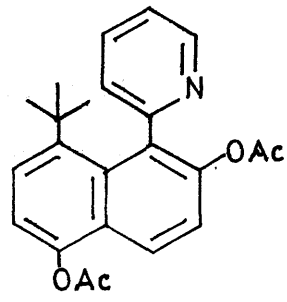


(48) (52)

Several reports of facile de-t-butylation of strained t-butylnaphthalenes have been made[47, 51]. In this case, the activating effect of the ortho-methoxyl group should facilitate this process, quite apart from the increased strain arising from steric compression due to this group.

Treatment of (48) with dilute hydrochloric acid in methanol at room temperature resulted in complete conversion to 2-methoxynaphthalene within eighteen hours. Similar treatment of 6-t-butyl-2-methoxynaphthalene (6, R = Me) and 3,6-di-t-butyl-2-methoxynaphthalene (8, R = Me) for several days resulted in quantitative recovery of unchanged starting material.

The t-butyl compound (53) is reported[51] to undergo quantitative de-t-butylation within thirty minutes in refluxing dilute hydrochloric acid.



(53)

Preparation and autoxidation of 1-t-butyl-2-naphthol (37).

In view of the instability of the methylated derivative (48) to acid conditions, a high yield, non-acidic method for the demethylation of this compound was sought.

Many of the reported basic methods of demethylation of aromatic methyl ethers are associated with severe conditions, poor yields, long reaction times, protic solvents, or isolation problems. All of these methods involve a nucleophilic displacement reaction of the type[52]

$$^{-}Y: \curvearrowright CH_3 - \overset{\curvearrowright}{O} - Ar \longrightarrow Y - CH_3 + {}^{-}OAr ,$$

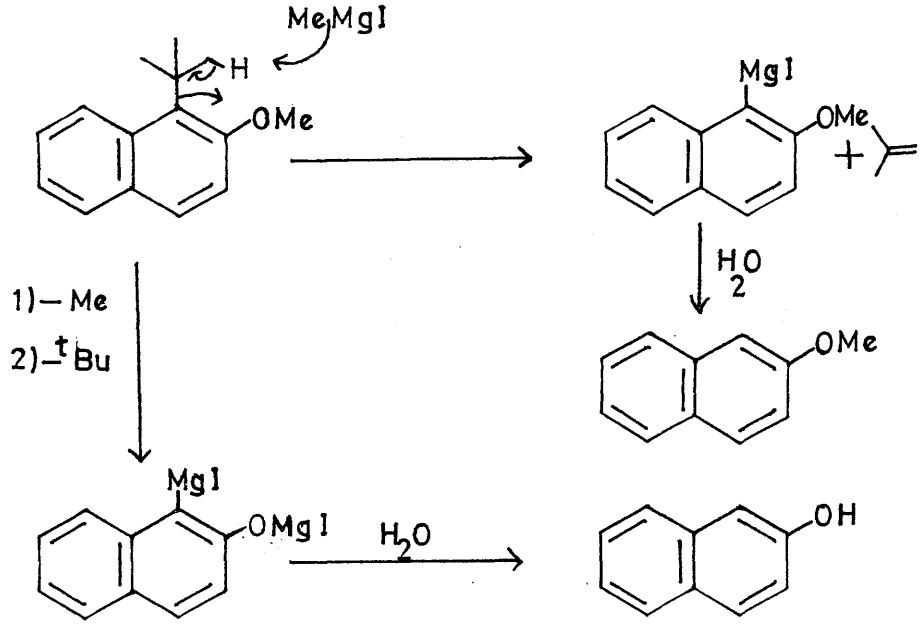
where ^{-}Y = ^{-}OH, ^{-}OR, ^{-}OAr, ^{-}SR, ^{-}SAr, $^{-}NH_2$, $^{-}PPh_2$, ^{-}I, '^{-}Me' .

The method chosen for initial investigation was the use of methylmagnesium iodide at elevated temperatures[53], since it was already known that the products of the high-temperature Grignard reaction on 1-acetyl-2-methoxynaphthalene were completely demethylated (see Table 2).

Repeated attempts to obtain a clean product from this reaction by altering the reaction conditions were unsuccessful, mainly as a result of polymerisation due to the prolonged reaction times required for complete demethylation. The usual method of base extraction followed by neutralisation and further extraction with organic solvents were not satisfactory. Owing to the cryptophenolic nature of the phenol (37), Claisen's alkali had to be employed in this process, and it was found that solutions of the naphthoxide could not be sufficiently protected to prevent extensive autoxidation and decomposition of the resulting hydroperoxide.

Exposure of benzene solutions of the impure product for ca.thirty minutes resulted in the complete autoxidation of the naphthol (37), and the formation of the hydroperoxide (41) (monitored by n.m.r.). However, the isolated yields of the hydroperoxide (41), obtained by fractional crystallisation, were low, and on occasion, zero.

Exposure of the methoxy derivative (48) to methylmagnesium iodide at 175° for thirty minutes[53] produced, as well as unreacted starting material and the desired naphthol (37), a substantial quantity of 2-methoxynaphthalene, and traces of 2-naphthol. This can be rationalised by the following reaction scheme.

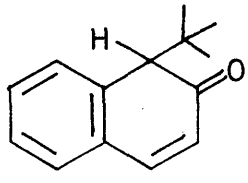


This provides supporting evidence of steric congestion in the t-butyl derivative (48).

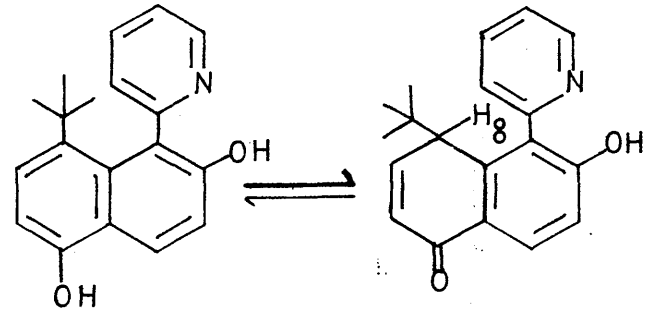
In a model reaction, demethylation of 3,6-di-t-butyl-2-methoxy-naphthalene (a sterically hindered analogue of 1-t-butyl-2-methoxy-naphthalene) using sodium thioethoxide in refluxing dimethylformamide[52] gave a quantitative yield of 3,6-di-t-butyl-2-naphthol.

Quantitative yields of 1-t-butyl-2-naphthol were obtained by this method, the reaction being worked up under extremely mild conditions.

The spectral characteristics of this compound showed a close resemblance to those of 1-t-butyl-2-methoxynaphthalene, which have been discussed in detail. A crystalline sample could not be obtained, although this compound would be expected to be a solid at room temperature. No evidence of the existence of the keto-tautomer (54) was obtained from the spectra of 1-t-butyl-2-naphthol. Readily autoxidisable sterically congested phenols are often found to form stable keto-tautomers, which are subject to less strain (see introduction, pp. 24, 25). Fields and Regan[51] have shown that the strained naphthol (55) exists in the keto form (56) in solution. The tertiary hydrogen at the 8-position in (56) does not readily undergo deuterium exchange with D_2O.



(54)



(55) (56)

The failure of 1-t-butyl-2-naphthol to tautomerise to (54) may indicate that the degree of strain in the phenolic tautomer relative to the keto-tautomer is less than the difference in resonance stabilisation between these forms.

A quantitative yield of 1-t-butyl-2-acetoxynaphthalene could be obtained by the addition of acetic anhydride to the reaction mixture of the demethylation experiment above, but this compound could not be induced to crystallise (a crystalline derivative was being sought for X-ray analysis).

Oxygenation of pure samples of 1-t-butyl-2-naphthol with pure oxygen gave high yields of 1-t-butyl-1-hydroperoxy-2(1H)-naphthalenone (41), m.p. 134-137°, which was identical in all respects to samples

obtained previously. This reaction was subject to an inhibition period (10 minutes-1 hour) when no uptake of oxygen was recorded.

When benzene solutions of the naphthol (37) were allowed to react slowly with atmospheric oxygen with or without stirring, the time taken for the complete disappearance of starting material was much longer in some cases (up to three hours), and the isolated yield of the hydroperoxide (41) considerably lower. T.l.c. indicated that two major components were present in the oxygenated mixtures other than hydroperoxide. One of these could be isolated by chromatography, and unambiguously identified as 1,2-naphthaquinone. The other component which was isolated by chromatography gave a deep red solution in benzene when exposed to sunlight or u.v. light (350nm.). This red colour disappeared when the sample was stored in the dark, or when methanol was added. When this component was chromatographed in the presence of light, a red, polar spot was detected on silica plates, which was decolourised in the dark. The addition of a drop of alkaline ferricyanide to a solution of this component intensified the red colouration initially, and eventually dispersed this colour completely, giving an intractible mixture of components which no longer exhibited this behaviour.

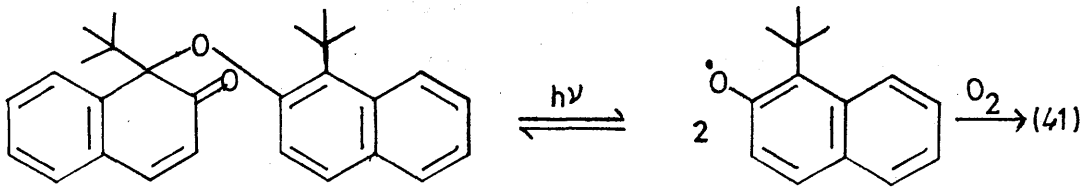
This species exhibits the characteristics of a dimer containing a weak bond which can be readily cleaved homolytically to give free radicals. It exhibits the following spectral characteristics

$\lambda_{max.}$(hexane) 286(sh), 297, 312(sh), 320(sh), 500 nm.

$\nu_{max.}$(CCl_4) 1680, 1615, 1385, 1360, 1258, 1100 $cm.^{-1}$.

m/e 398, 199.

Sufficient material for n.m.r. was not obtained. These spectral characteristics can be accounted for by the structure (57), which may be formed in a termination step by reaction between 1-t-butyl-2-naphthoxy radicals (<u>cf.</u> autoxidation of 1-ethyl-2-naphthol, page 41).



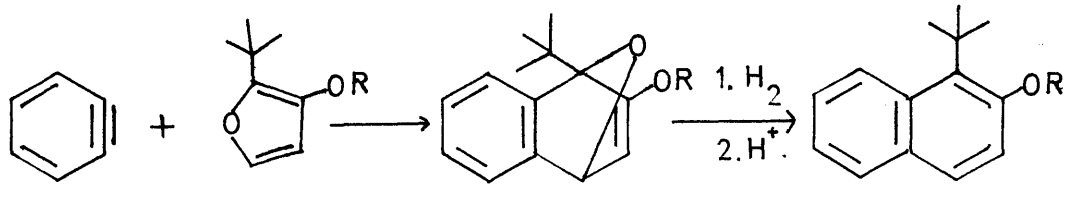
(57)

The long wavelength band (500 nm.) in the u.v. is typical of phenoxy radicals[54]. The bands at 1258 and 1100 cm.$^{-1}$ in the i.r. are indicative of a quinol ether.

That this product is not formed when 1-t-butyl-2-naphthol is oxygenated in pure oxygen with rapid stirring is not surprising. The reaction of the naphthoxy radical with oxygen is expected to be favoured, since steric hindrance to dimerisation will be severe (cf. stable hindered phenoxy radicals[54]). Prolonged exposure of a sample of this compound to air resulted in the formation of a trace of the hydroperoxide (41).

Treatment of 1-t-butyl-2-naphthol with alkaline potassium ferricyanide in the absence of oxygen may give a high yield of (57). This experiment has not yet been carried out. However, addition of a drop of alkaline potassium ferricyanide to an ethanolic solution of 1-t-butyl-2-naphthol in a u.v. cell produced a red solution with an identical u.v. spectrum to the compound assigned the structure (57). Further investigation of these processes would seem to be desirable.

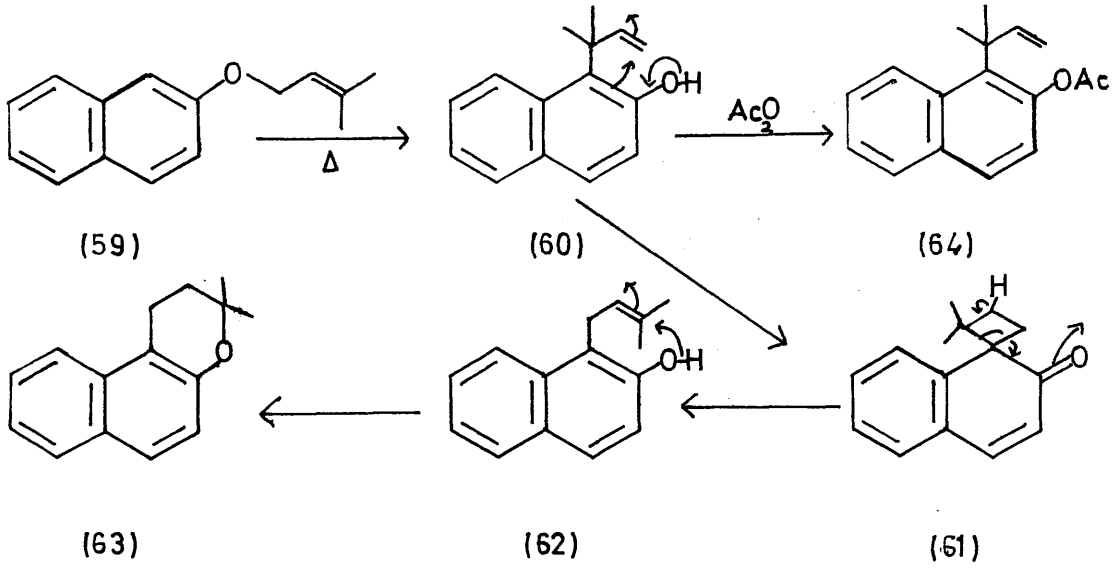
Further routes to 1-t-butyl-2-naphthol were envisaged. Many substituted naphthalene syntheses involving Diels-Alder addition to benzynes[47, 51] could be adapted to the synthesis of 1-t-butyl-2-naphthol, for example[47],



Synthesis of 1-t-pentyl-2-naphthol (58).

Owing to the difficulties encountered in the preparation of 1-t-butyl-2-naphthol, the synthesis of an alternative 1-t-alkyl-2-naphthol, viz. the title compound (58) was undertaken.

Buckle and Waight[55] reported the preparation of 1-(1,1-dimethyl-prop-2-enyl)-2-acetoxynaphthalene (64) by the Claisen rearrangement of 2-(3-methylbut-2-enyloxy) naphthalene (59) in a mixture of acetic anhydride and quinoline. It was suggested that, in the absence of acetic anhydride, the initially formed naphthol (60) undergoes a rearrangement via the spirocyclobutane intermediate (61) to give the naphthol (62), which could then cyclise to the naphthopyran (63). This naphthopyran was isolated in high yield when acetic anhydride was not used.



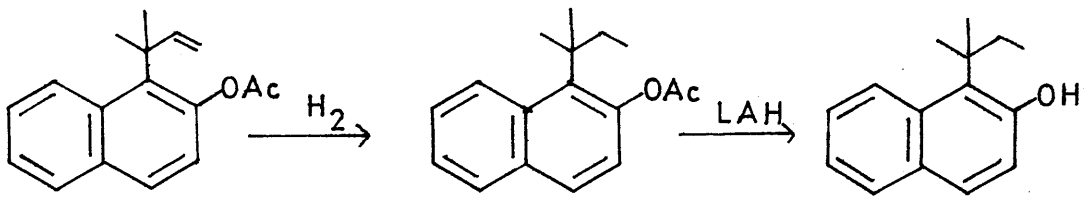
(59) (60) (64)

(63) (62) (61)

A simpler mechanism, involving a 1,3-sigmatropic shift in the ether (59), is thermally forbidden by the Woodward-Hoffman rules. The failure of the t-pentenylnaphthol (60) to cyclise to a naphthopyran was attributed to steric crowding as a result of peri-interactions.

The t-pentenyl acetate (64) was seen as a starting material for

the preparation of 1-t-pentyl-2-naphthol (58) by the following method.



(64) (65) (58)

Several attempts to prepare 1-t-butyl-2-acetoxynaphthalene from the acetate (64) by ozonolysis of the double bond, followed by thioketalisation and desulphurisation by Raney nickel have been unsuccessful[56].

The synthesis of 1-t-pentyl-2-naphthol (58) was undertaken by me. The preparation of the dimethylallyl ether (59) proceeded smoothly as described, the pure product being obtained without undue difficulty. The products of the Claisen rearrangement were subjected to column chromatography on silica, eluted successively with light petroleum, and then with light petroleum - ethyl acetate mixtures. In this manner, reasonably pure samples of the desired acetate (64) could be obtained in moderate yield, along with unchanged ether (59) and 2-acetoxynaphthalene. The major impurity in the samples of (64) obtained was 2-acetoxynaphthalene. Attempts to purify this compound by vacuum distillation resulted in partial decomposition. Preparative t.l.c. gave the pure acetate (64) as a colourless oil, which could be unambiguously characterised by spectroscopic methods. The appearance of the peri-proton signal in the n.m.r. spectrum at τ 1.80 can again be attributed to peri-strain.

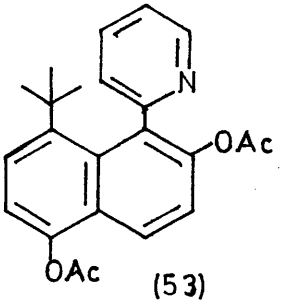
Pure samples of the t-pentenyl acetate (64) were hydrogenated rapidly in quantitative yields in ca. thirty five minutes in methanol, using a 10% palladium-charcoal catalyst. Samples of 1-t-pentyl-2-acetoxynaphthalene (65) were purified by vacuum distillation. Attempts

to hydrogenate impure samples of the t-pentenyl acetate (64) prior to purification by chromatography or distillation resulted in no reaction.

The u.v. spectrum of (65) ($\lambda_{max.}$(EtOH) 226(4.8), 270.5(3.78), 278(3.85), 287(sh), 318(sh) nm.) bears a striking resemblance to that of 1-t-butyl-2-acetoxynaphthalene ($\lambda_{max.}$(EtOH) 226(4.9), 268.5(3.68), 278(3.72), 288(sh), 320(sh) nm.).

The signal corresponding to H-8 in the n.m.r. of (65) (τ 1.73) is considerably deshielded relative to the other aromatic signals (cf. H-8 in 1-t-butyl-2-acetoxynaphthalene τ 1.54).

The base peak in the mass spectrum of (65) (m/e 256(M^+,30), 214(55), 185(100)) corresponds to the loss of the t-pentyl group, a process which is not normally favoured, (cf. 1-t-butyl-2-acetoxy-naphthalene, m/e 242(M^+,20), 200(60), 185(100)) and may be associated with peri-strain in these molecules. Fields and Regan[51] found that the loss of a t-butyl fragment in the mass spectrum of (53) is a highly favoured process, and attributed this to peri-strain.



(53)

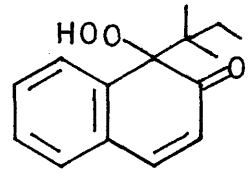
Preparation and autoxidation of 1-t-pentyl-2-naphthol (58).

The title compound could be obtained in quantitative yield from 1-t-pentyl-2-acetoxynaphthalene (65), by treatment with lithium aluminium hydride in refluxing ether, followed by a non-acidic work-up. (It was expected that dealkylation would occur readily in acidic media, cf. page 67). The product was found to react rapidly with atmospheric oxygen, and was never obtained in a crystalline state. However, by rigorous exclusion of oxygen, samples could be obtained which displayed

spectral characteristics totally compatible with the assigned structure (58). The expected deshielding of the peri-proton was observed (τ 1.63).

Oxygenation of pure samples of the strained naphthol (58) yielded in ca. thirty minutes, virtually quantitative yields of 1-t-pentyl-1-hydroperoxy-2(1H)-naphthalenone (66), m.p. 113-115° (decomposition), pale yellow needles from light petroleum-benzene, whose spectral characteristics were extremely similar to the analogous t-butyl hydroperoxide (41). On one occasion, uptake of oxygen did not commence until the solution had been stirred under oxygen for twelve minutes.

The hydroperoxide (66) was found to be even less stable to heat or light than the t-butyl analogue (41). A sample heated at 40° under reduced pressure decomposed explosively to a black tar containing many components. Samples stored in the dark in a freezer partially decomposed over several days. The only product of this decomposition which could be identified was 1,2-naphthaquinone, which could be compared with an authentic sample.



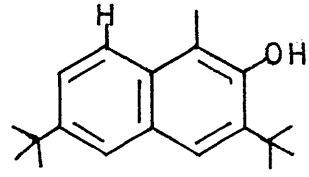
(66)

Attempted preparation of 1-methyl-3,6-di-t-butyl-2-naphthol (67).

One of the possible explanations for the instability of 1-t-butyl- and 1-t-pentyl-2-naphthol is that the increased electron density at C-1 in these compounds compared to 1-methyl-2-naphthol stabilises the naphthoxy radical intermediate in these cases, so that hydrogen abstraction by the chain-propagating peroxy radical is accelerated.

The title compound (67) should resemble 1-methyl-2-naphthol electronically at C-1. It was predicted, however that (67) would be subject to considerable strain by virtue of the buttressing effect of

the 3-t-butyl group, combined with the peri-interaction between H-8 and the 1-methyl group. This steric congestion may result in more facile autoxidation of this molecule relative to 1-methyl-2-naphthol.



(67)

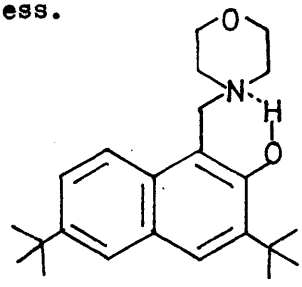
The buttressing effect suggested above may well be more severe than in the case of 1,3,8-tri-t-butylnaphthalene (49), where the 3-t-butyl group results in selective isomerisation of the right hand ring on photolysis (see pp. 66,67).

The naphthol (67) resembles strained, highly substituted phenols (see introduction page 24 et seq.) which readily undergo autoxidation.

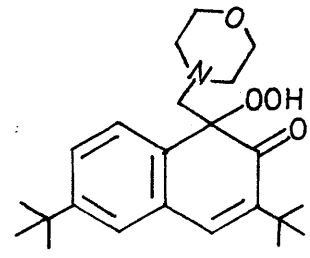
3,6-Di-t-butyl-2-naphthol (8, R = H) was chosen as a starting material for the synthesis of (67). Three general methods are available for the introduction of a methyl group into the 1-position of 2-naphthols, viz. Wolff-Kishner reduction[57] of the 1-formyl derivative[58], nickel-alloy hydrogenolysis[59] of the 1-morpholinomethyl derivative[60], and reduction of the 1-formyl derivative with sodium dihydro-bis (2-methoxyethoxy) aluminate.[91] Owing to difficulties encountered in the preparation and reduction of 1-formyl-2-naphthol[2], the second method was chosen for the preparation of the desired naphthol (67).

1-Morpholinomethyl-3,6-di-t-butyl-2-naphthol (68) was prepared in high yield by the literature method for the parent 1-morpholinomethyl-2-naphthol[60]. This compound was found to be inert to atmospheric oxygen over indefinite periods in the solid state. Oxygenation of ethyl acetate solution of (68) for one week produced a trace of 3,6-di-t-butyl-1,2-naphthaquinone (10). The stability of (68) to autoxidation could be due to inductive withdrawal of electrons by

nitrogen, or to the intramolecular chelation which is apparent from the extremely broad O-H stretching frequency in the i.r.. This may inhibit hydrogen atom abstraction in the radical chain autoxidation process.



(68)

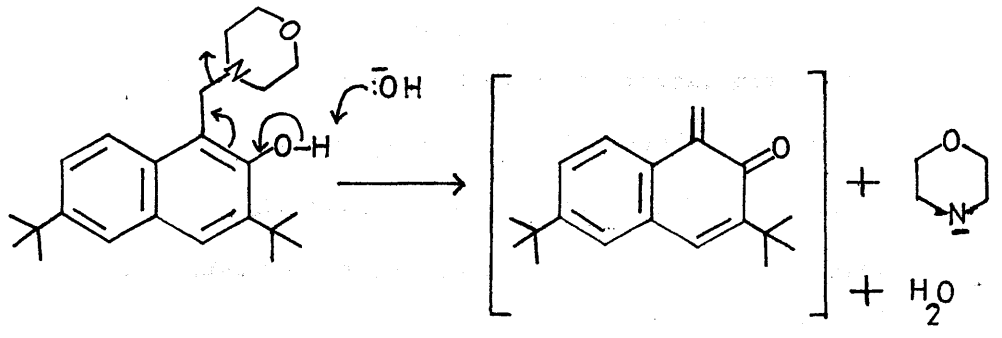


(69)

Alternatively, the intermediate hydroperoxide (69) may readily decompose to the quinone (10), so that initiation by hydroperoxide does not occur.

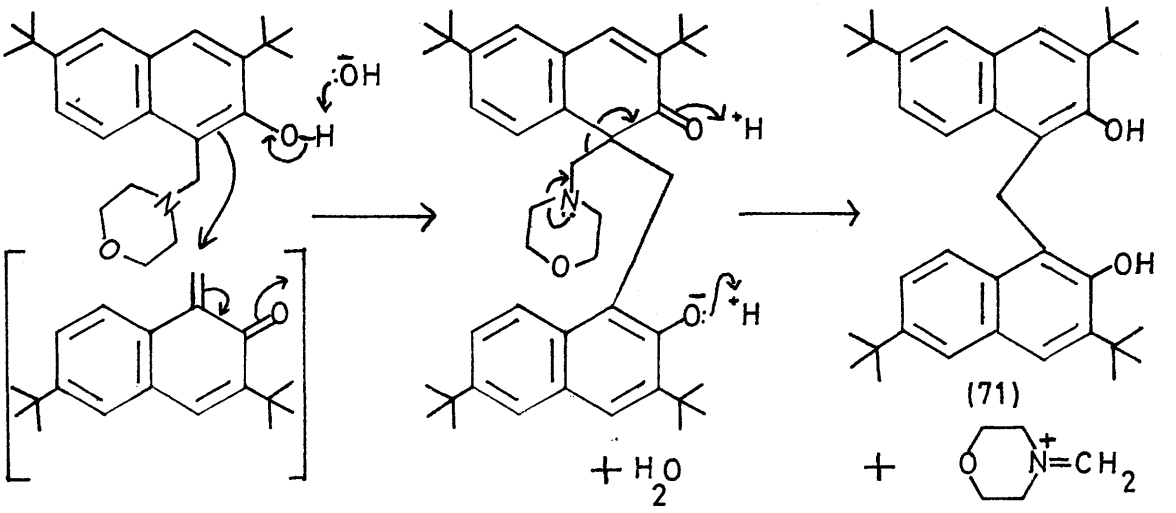
Reaction of the morpholinomethylnaphthol (68) with Raney-nickel alloy and alkali.

The reaction was executed according to the method of Gandhi and co-workers[59], and the work-up and isolation carried out with exclusion of oxygen to give colourless crystals, m.p. 215-220°(decomposition) from chloroform-light petroleum. The spectral characteristics of this product, which was extremely unstable to oxygen, were in accord with the structure (71). This compound could be formed via. the mechanism outlined below.



(68)

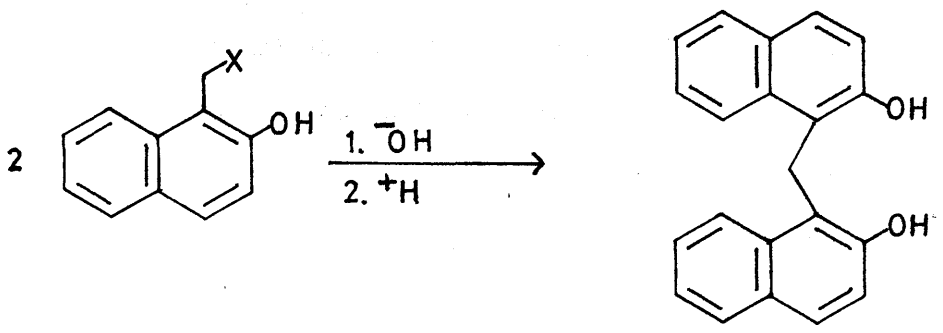
(70)



This mechanism involves only the action of alkali. Treatment of an ethanolic solution of the morpholinomethylnaphthol (68) with aqueous sodium hydroxide gave a quantitative yield of the same product. The bisnaphthylmethane (71) was also prepared directly from 3,6-di-t-butyl-2-naphthol by treatment with sodium acetate and formaldehyde in aqueous ethanol, by analogy with the literature preparation of the parent compound (72)[61].

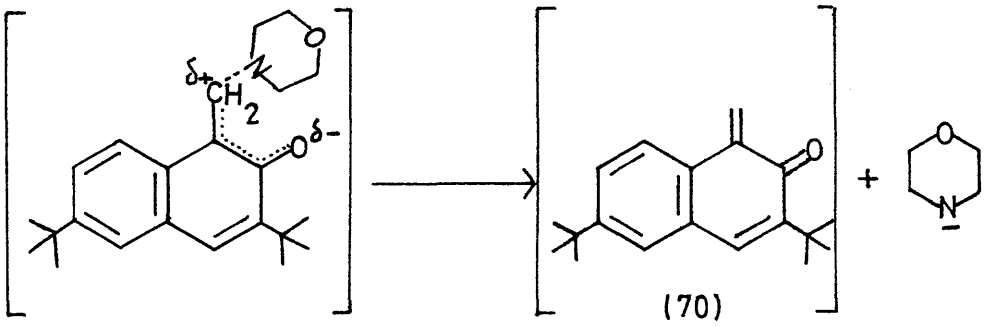
This reaction probably involves the intermediacy of 1-hydroxymethyl-2-naphthol, and indeed, when the reaction was monitored by t.l.c., a third component was present until the starting material was completely consumed, when only one component could be detected by t.l.c..

The formation of the bisnaphthylmethane (71) by reaction of the morpholinomethylnaphthol (68) with alkaline nickel alloy was unexpected, since 1-morpholinomethyl-2-naphthol itself gives high yields of 1-methyl-2-naphthol under identical conditions[59]. However, the self condensation of substituted phenols and naphthols of this type to give biarylmethanes is a well known reaction[62-64], (see over), although the aminomethyl derivatives normally require more forcing conditions, or else prior formation of the methiodide.



X = OH, OMe, Cl, NR_2. (72)

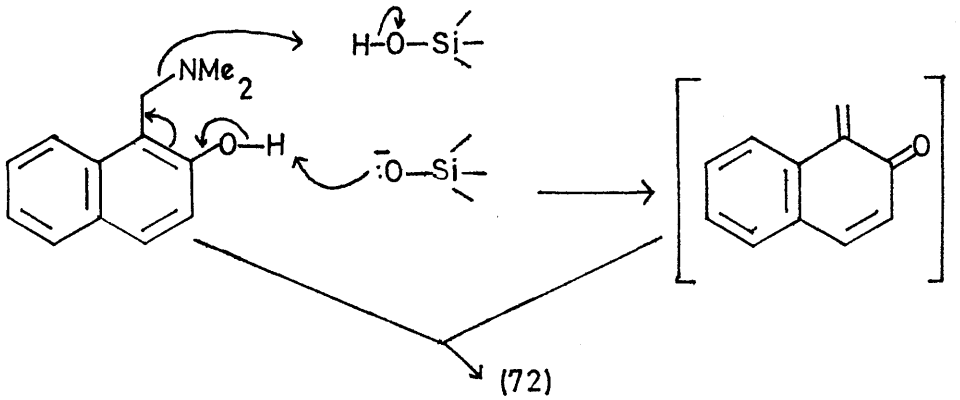
Gardner[63] suggests that this reaction is favoured when the deaminated moeity can more easily sustain positive charge. The electronic release by the t-butyl groups in (68) may therefore stabilise the transition state leading to the postulated quinone methide intermediate (70).



(70)

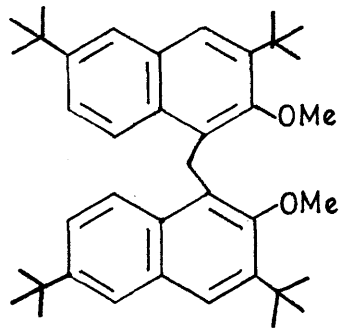
It is also conceivable that steric congestion weakens the C-N bond, so that heterolysis is facilitated.

It was also noted that the morpholine methylnaphthol (68) decomposed fairly rapidly on silica t.l.c. plates to give a mixture identical to that obtained from the autoxidation of (71) (see below). It is reported that 1-dimethylamine-2-naphthol is transformed into the bisnaphthylmethane (72) on silica columns, and this was attributed to the amphoteric nature of silica[64].



(72)

Owing to the instability of the dinaphthol (71), it was not possible to obtain samples suitable for analysis. Treatment of this compound with sodium hydride in dmso, followed by methyl iodide (2 moles), gave the dimethyl ether (73), m.p. 275-278°, which could be fully characterised.



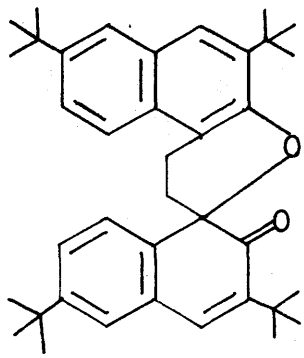
(73)

The appearance of the peri-protons at low field in the bisnaphthylmethanes (71) and (73) (τ 1.89 and 1.81 respectively) may be due to deshielding by the second naphthalene nucleus in these cases.

Autoxidation of the dinaphthol (71).

The instability of the title compound (71) to oxygen may be due to the steric congestion inherent in its structure. In contrast, the parent compound (72), is not reported to be unstable in air[62-64]. 1-Benzyl-2-naphthol is also stable to oxygen[2].

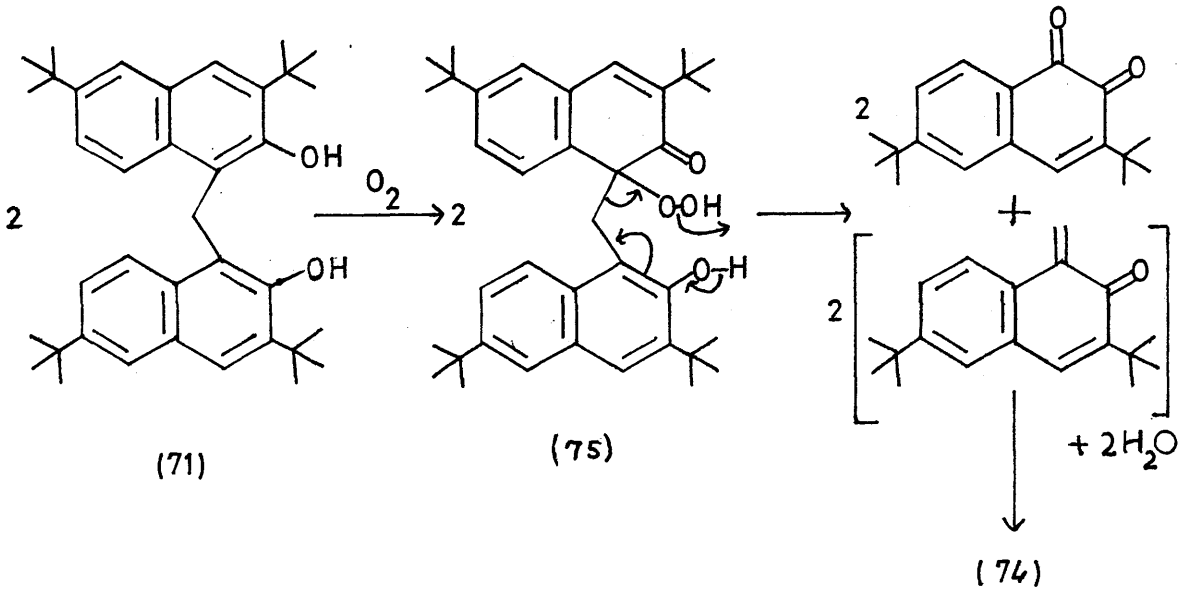
Oxygenation of pure samples of (71) was complete in 60 ± 5 minutes, ca. 1.5 moles of oxygen per mole of substrate having been taken up. The product was a red, semi-crystalline oil, containing two major components which could readily be separated by fractional crystallisation followed by chromatography of the residue. Exhaustive oxygenation of 1.31 g. (2.5 mmole) of (71) gave 0.90 g. (3.3 mmole) of 3,6-di-t-butyl-1,2-naphthaquinone (10), and 0.44 g. (0.8mmole) of pale yellow prisms, m.p. 154-157° (decomposition) from methanol, which were assigned the structure (74), on the basis of its spectral characteristics.



(74)

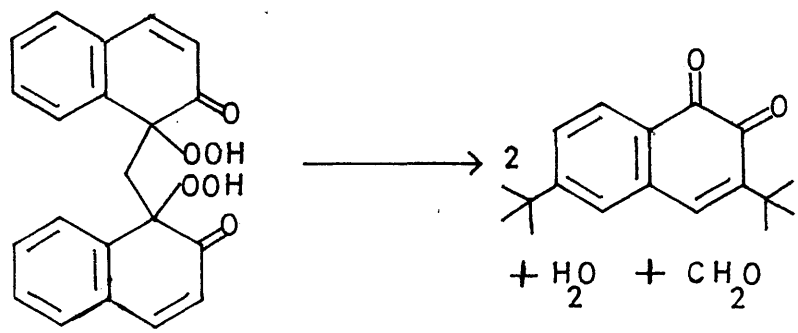
The u.v. spectrum ($\lambda_{max.}$(EtOH) 241(4.98), 268(3.89), 279(3.93), 291(sh), 316(4.02), 332(sh) nm.) can be explained in terms of a molecule constructed from the two systems 1,1-disubstituted-2-(1H)-naphthalenone, and a substituted naphthalene. The band at 1690 cm^{-1} in the i.r. is consistent with the presence of a naphthalenone system. Four non-equivalent t-butyl groups can be detected in the n.m.r., as well as four non-equivalent methylenic hydrogens, which are seen as a complex multiplet (τ 6.8-8.1). Attempts to elucidate the n.m.r. using europium shift reagents were unsuccessful. The highest ion measured in the mass spectrum is 536(40). This compound would not analyse correctly for $C_{38}H_{48}O_2$, possibly as a result of the inclusion of solvent molecules in its crystalline lattice, or because of the presence of traces of impurities. (see below). Many samples obtained could not be purified sufficiently to give a clean melting point, especially those samples which had been exposed to mild heat. The compound was found to decompose slowly in the solid state, or in solution to give traces of the naphthaquinone (10).

These products can be rationalised on the basis of the following scheme.



(71) (75) (74)

However, this scheme does not account for the product distribution (which should be (10) : (74) = 2 : 1 if this scheme operates exclusively), nor for the fact that ca. 1.5 moles of oxygen are absorbed in the oxygenation reaction. The formation of the dihydroperoxide (76) may be a competitive pathway in this autoxidation, the extent of its formation being dependent upon the relative rates of decomposition and further oxygenation of the mono-hydroperoxide (75) in the above scheme.

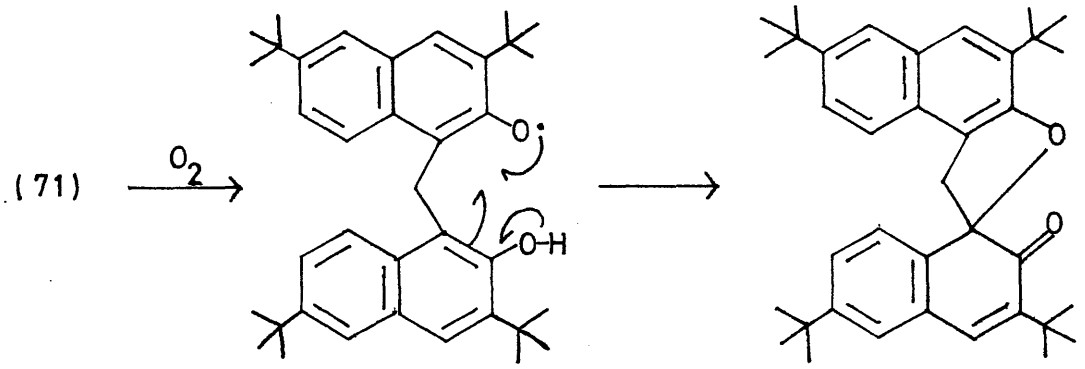


(76)

Attempts to detect the presence of hydroperoxides in this reaction by carrying out the oxygenation at low temperature (ice-salt bath) were unsuccessful.

The purification of the spirochroman derivative (74) was frustrated

by the presence of traces of impurities, which could not be removed by physical methods. These impurities could be detected in the expanded n.m.r. spectrum (shoulders on the t-butyl signals), and in the mass spectrum (the trace peak at 522, M^+-14, could not be accounted for on the basis of (74)). It was proposed that the spirocoumaran (77) could be produced by the intramolecular coupling process outlined below (cf. autoxidation of 1-ethyl- (p.41) and 1-t-butyl-2-naphthol (p.71)).

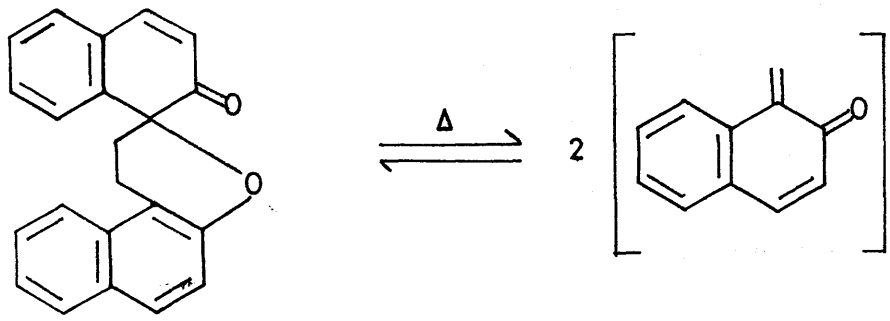


(77)

This is, in fact, a termination step in the autoxidation process.

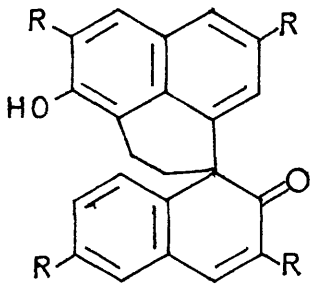
In order to test this hypothesis, the dinaphthol (71) was oxidised in the absence of oxygen with alkaline potassium ferricyanide, to give a high yield of pale yellow flakes, m.p. 245-255°, whose spectral characteristics were in accord with the structure (77). However, traces of the quinone methide dimer (74) were detected in the n.m.r. and mass spectrum, which could have arisen by the action of base upon (71) and dimerisation of the resulting quinone methide (see above).

The quinone methide dimer (78) is a well documented compound, and has been studied by many workers[64-66]. It is known to decompose thermally to two molecules of o-naphthaquinone methide, which can then undergo Diels-Alder addition with dienophiles to give substituted naphthochromans.

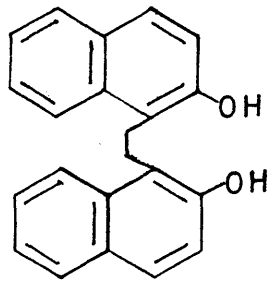


(78)

The dimer (78) is commonly prepared by thermal de-amination of Mannich base derivatives of 2-naphthol, by refluxing in high boiling solvents[64]. Catterall[66] has recently reported that, under these conditions, the spiro dimer (78) isomerised irreversibly to form the spirophenalene (79, R = H).



(79)



(80)

I find that the spiro dimer (74) is produced in low yield along with the bisnaphthylmethane (71) when a sample of 1-morpholinomethyl-3,6-di-t-butyl-2-naphthol (68) is refluxed for three hours in mesitylene. Samples of the dimer (74) obtained by this method were very impure. Attempts to isomerise (74) to (79, R = ^{t}Bu) by refluxing the former in glacial acetic acid[66] produced a small quantity of a compound containing a hydroxyl group, which was not present in sufficient quantity for characterisation. The reported[64] hydrogenolysis of the spiro dimer (78) to the ethylene-bis-2-naphthol (80) could not be reproduced in the case of the t-butyl analogue (74), possibly because of steric hindrance to access by the catalyst, or because of trace impurities in the sample employed.

Attempted preparation of 1-methyl-3,6-di-t-butyl-2-naphthol (67) by hydride reduction of the o-quinone methide (70).

The known[63, 67] susceptibility of quinone methides to attack by nucleophilic reagents, and the reported[63] preparation of 1-methyl-2-naphthol by hydride reduction of o-naphthaquinone methide prompted me to investigate the reactivity of 1-morpholinomethyl-3,6-di-t-butyl-2-naphthol (68) to hydride reagents.

Prolonged treatment of (68) with lithium aluminium hydride or sodium dihydro-bis(2-methoxyethoxy) aluminate[89] under reflux conditions resulted in the recovery of unchanged starting material, no other compound being detected.

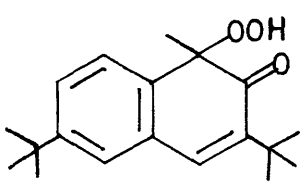
Preparation of 1-methyl-3,6-di-t-butyl-2-naphthol by hydrogenolysis of the morpholinomethylnaphthol (68).

Owing to the highly substituted nature of the naphthol (68), and its low solubility in common solvents, the catalytic hydrogenolysis was not expected to be a facile reaction. The reaction was attempted under many conditions using different metal catalysts, solvents, and added acid catalysts with no success. Attempts to prepare the methiodide to facilitate this, and some of the previously mentioned reactions of this compound were also unsuccessful.

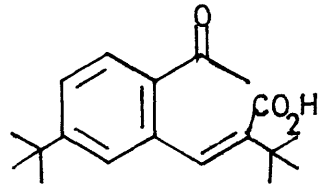
The hydrogenolysis proceeded slowly in methanol (0.0075 molar solution) employing a palladium-charcoal catalyst. Heat was required to aid dissolution. The reaction was worked up under nitrogen to give a high yield of 1-methyl-3,6-di-t-butyl-2-naphthol (67), m.p. 119-121°, the spectral characteristics of which were totally in accord with this structure. A sample suitable for analysis could not be obtained owing to the instability of this compound to oxygen. A sample was methylated (NaH, dmso, MeI) in moderate yield, to give 1-methyl-3,6-di-t-butyl-2-methoxynaphthalene, m.p. 70-71°, which could be characterised fully.

Oxygenation of pure samples of the naphthol (67) was complete in 36 ± 5 hours, and fractional crystallisation of the product mixture from benzene-light petroleum gave pale yellow prisms, m.p. 139-142° (decomposition) which was assigned the structure 1-hydroperoxy-1-methyl-3,6-di-t-butyl-2(1H)-naphthalenone (81) on the basis of analytical and spectral data.

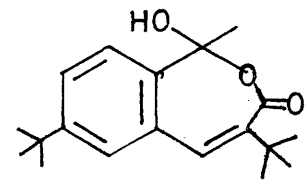
Preparative chromatography of the residue gave a further sample of the hydroperoxide (81), and two other compounds in small quantity. The less polar of these was identical in all respects to the spirochroman (74).



(81)



(82)



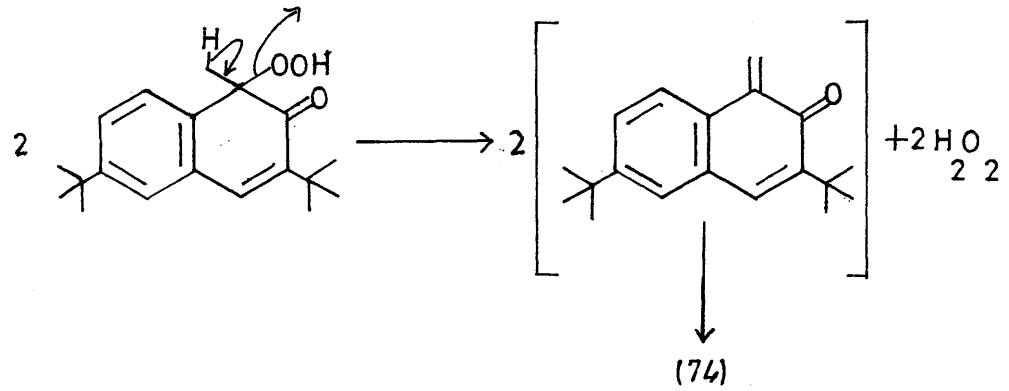
(83)

The second component, which was highly polar, and found to be soluble in aqueous sodium bicarbonate, was assigned the structure α-t-butyl-2-acetyl-5-t-butylcinnamic acid (82) (cis or trans). The spectral and analytical data were complately in accord with this assignment. The appearance of a carbonyl band at 1735 $cm.^{-1}$ in the solution i.r. spectrum suggested that this compound may exist in equilibrium with the cyclic hemiacetal form (83), but no evidence of this was seen in the n.m.r..

Benzene solutions of the hydroperoxide (81) were found to decompose slowly on standing in a nitrogen atmosphere in diffuse sunlight to a mixture of (74) and (82). This process was accelerated by heat, complete decomposition having occurred after refluxing a benzene solution of (81) for twenty four hours. Many other components were produced in trace quantities which could not be identified.

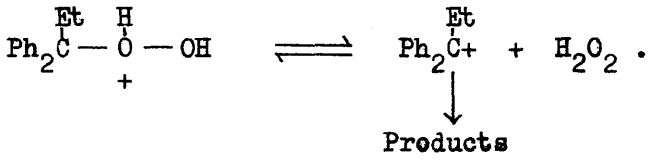
The formation of the spirochroman (74) may proceed <u>via</u> the

following mechanism.

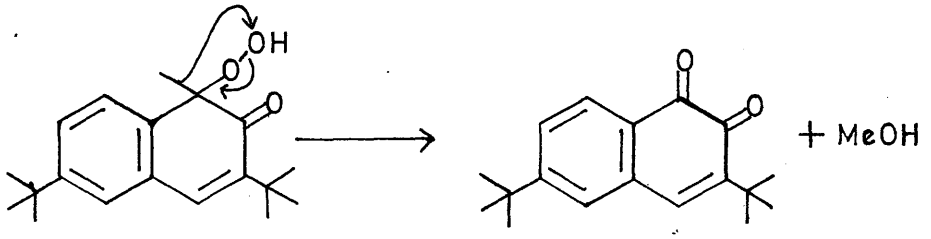


(74)

Hydroperoxide decompositions involving the production of hydrogen peroxide are normally acid catalysed[41], for example,

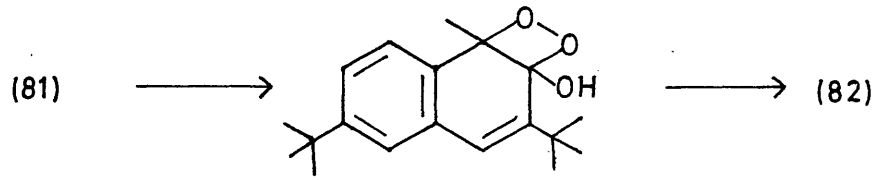


The absence of the o-quinone (10) in the mixture is probably a consequence of the poor migratory aptitude of the methyl group, so that the process



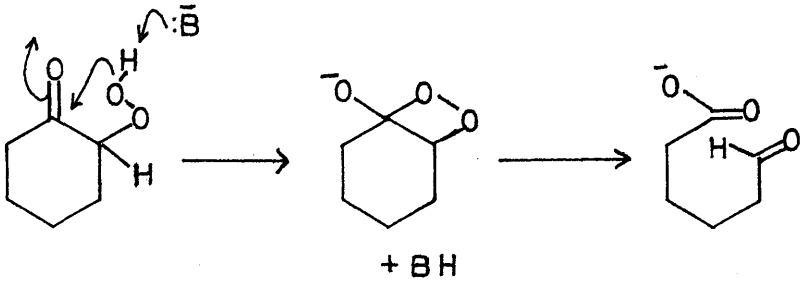
(10)

is not favoured. The keto acid (82) may arise by the following process.



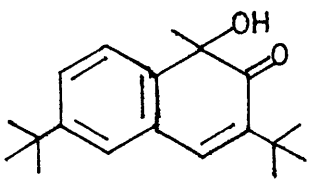
(84)

Dioxetane intermediates of the type (84) have been suggested for the base catalysed decomposition of other α-keto-hydroperoxides[41], for example,

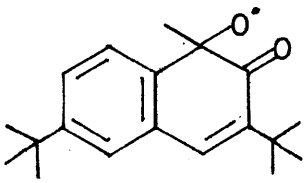


The decomposition of dioxetanes should involve the emmission of light, and in some cases, this has been detected[68]. When the hydroperoxide (81) was heated in dmso, decomposition proceeded, but no light emmission was detected.

When 1-methyl-3,6-di-t-butyl-2-naphthol (67) was oxygenated in the presence of triphenylphosphine, the reaction proceeded extremely slowly. After one week, only about one half of the naphthol had autoxidised. Preparative chromatography gave a low yield of 1-hydroxy-1-methyl-2(1H)-naphthalenone (85), which could be prepared in quantitative yield by the action of dimethyl sulphide upon the hydroperoxide (81).



(85)



(86)

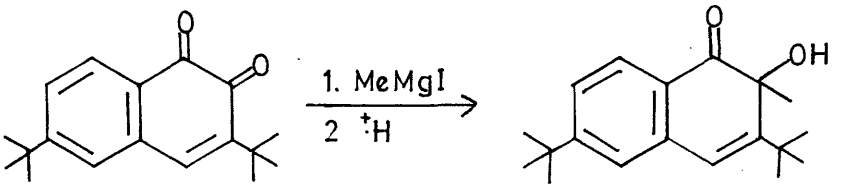
The extremely slow rate of the autoxidation reaction in the presence of triphenylphosphine can be interpreted in two ways.

(a) The chain carrying peroxy radical is reduced to the corresponding alkoxy radical (86) by triphenyl phosphine[41], and this radical is incapable of propagating the chain by abstracting a hydrogen atom from the naphthol (67).

(b) A more likely explanation is that initiation is inhibited by the reduction of the hydroperoxide (81) to the alcohol (85) as soon as it is produced. This implies that initiation due to the product hydroperoxide

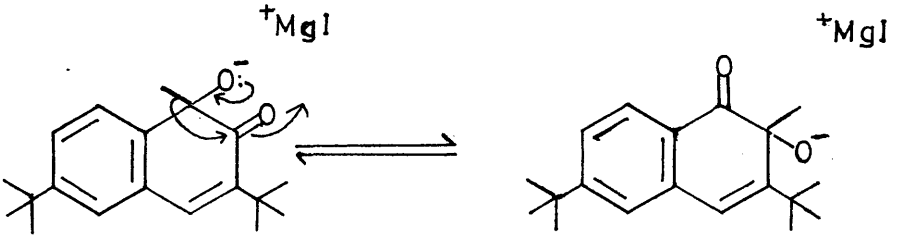
is important in determining the overall rate of autoxidation.

In an investigation into the possible uses of the naphthaquinone (10) as a starting material for the preparation of 1-alkyl-3,6-di-t-butyl-2-naphthols, it was found that treatment of this compound with methyl Grignard reagent gave exclusively 2-hydroxy-2-methyl-3,6-di-t-butyl-1(2H)-naphthalenone (87), which could readily be distinguished from the isomeric ketol (85), especially by the presence of the acetophenone chromaphore in the u.v. spectrum.



(10) (87)

This Grignard reaction must involve the magnesium alkoxide derived from the alcohol (87). This may arise partly <u>via</u> rearrangement of the isomeric alkoxide (88).



(88)

The analogous 1-hydroxy-1-isopropyl-2(1H)-naphthalenone (40) is known[2] to isomerise in strongly basic conditions to give the 1-keto isomer in high yield. The t-butyl analogue (42) isomerises in mildly basic conditions to give a 1:1 mixture of the isomeric ketols (42) and (43) (see page 60). It is surprising that the ketol (87) was the sole product of the reaction in this case. This may have arisen by the totally regioselective attack by Grignard reagent at the 2-position. The resulting alkoxide may be unable to isomerise due to the low migratory aptitude of the methyl group.

Preparation of 1-methyl-6-t-butyl-2-naphthol (89).

A possible explanation for the fast rate of autoxidation of 1-methyl-3,6-di-t-butyl-2-naphthol and 1-t-butyl-2-naphthol is that the additional electronic release by the t-butyl groups stabilises the intermediate phenoxy radical, and therefore accelerates the propagation step in the autoxidation process (see introduction).

In order to test this hypothesis, the preparation of the title compound (89) was undertaken. If electronic factors are of prime importance in determining the stability of the substituted naphthols, then the naphthol (89) should autoxidise at a rate which is intermediate between 1-methyl-2-naphthol and 3,6-di-t-butyl-1-methyl-2-naphthol.

The naphthol (89) was prepared in high yield by catalytic hydrogenolysis of 6-t-butyl-1-morpholinomethyl-2-naphthol[60] in a similar manner to the method used to prepare the di-t-butylnaphthol (67).

Prolonged oxygenation of (89) resulted in a slight discolouration of the solution, but no component other than starting material could be detected by t.l.c. or spectroscopic methods. This naphthol would not seem to be more reactive towards oxygen than 1-methyl-2-naphthol.

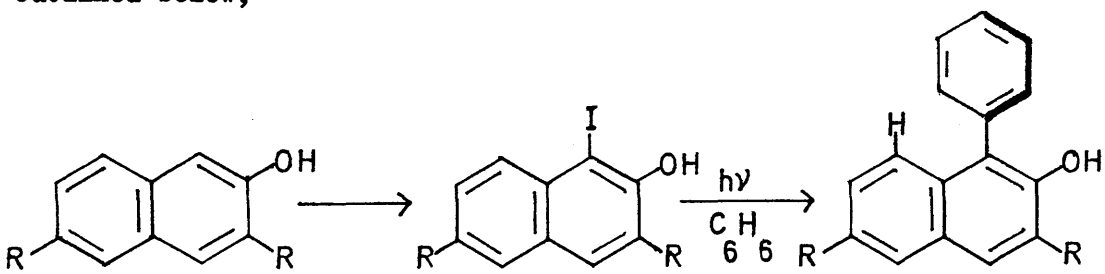
Preparation of 1-phenyl-2-naphthols.

1-Phenyl-2-naphthol (90, R = H), has been prepared by several groups, employing multistage routes[15]. No comment on the reactivity of this compound to oxygen was made. Inspection of models indicates that the peri-hydrogen in this compound prevents co-planarity between the naphthalene nucleus and the benzene ring. The degree of strain in (90, R = H) relative to 1-methyl-2-naphthol is difficult to predict. House and co-workers[69] have found that the distortions in 1,8-diphenylnaphthalene and related compounds, where the benzene rings lie virtually perpendicular to the naphthalene nucleus, are extensive, and are similar to the distortions found in 1,8-dimethylnaphthalene. However, 1-benzyl-2-naphthol is stable to oxygen, whereas 1-ethyl-2-naphthol

is not[2]. The reported stability of 1-triphenylmethyl-2-naphthol[13] would imply that this molecule is less strained than 1-t-butyl-2-naphthol. 1,3-Diphenyl-2-naphthol is a known compound[71] and no comment is made about its reactivity with oxygen. A complicating factor which arises in comparing 1-methyl-2-naphthol and 1-phenyl-2-naphthol is the electron withdrawing effect of the phenyl group, but this should be small.

It was decided to prepare 1-phenyl-2-naphthol and 1-phenyl-3,6-di-t-butyl-2-naphthol in order to compare their autoxidation rates with each other, and with the other substituted naphthols under investigation.

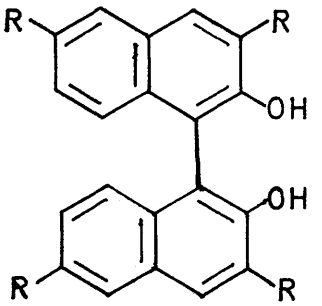
The route chosen for the preparation of these compounds is outlined below,



(90)

Several literature methods[72] for the preparation of 1-iodo-2-naphthol were attempted. Two of these methods[72(a),(b)] failed to give any of the required material. The third method[72(c)] gave a 70% yield of 1-iodo-2-naphthol. Photolysis[73] of a degassed benzene solution of 1-iodo-2-naphthol under nitrogen for 21 hours, and preparative chromatography of the product gave a small quantity of the known dinaphthol (91), m.p. 215-217° (lit.[16] 216-218°), starting material, and 1-phenyl-2-naphthol (42%), m.p. 77.5-78.5°. The reported m.p.'s of this compound (65-67° [15(a)], 81-83° [15(b)]) are considered to be erroneous. The melting point was not depressed on mixing this product with samples obtained from other sources[74] (and purified in this laboratory), and the spectral characteristics of all the samples in hand were found to be identical.

Prolonged oxygenation of a benzene solution of (90, R = H) produced no other species, even when the potential initiator, cobalt III acetylacetonate, was added.



(91) R = H

(11) R = ^{t}Bu

1-Phenyl-3,6-di-t-butyl-2-naphthol (90, R = ^{t}Bu) was prepared in a similar manner, along with the dinaphthol (11), which was identical to samples obtained by ferricyanide oxidation of 3,6-di-t-butyl-2-naphthol.[23] The unknown naphthol (90, R = ^{t}Bu) displayed spectral and analytical characteristics consistent with the assigned structure.

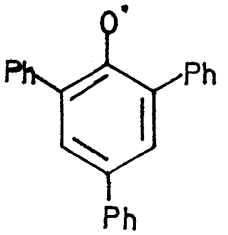
Prolonged oxygenation of (90, R = ^{t}Bu) produced a faint discolouration of the solution, but the only material detected after seven days was unchanged starting material.

The u.v. spectra of the naphthols (90) are virtually identical to the analogous naphthols containing no substituent in the 1-position. This indicates that the 1-phenyl substituent is not in conjugation with the naphthalene nucleus, as would be expected[69].

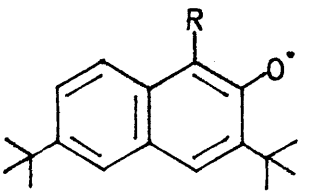
The stability of the naphthol (90, R = ^{t}Bu) to oxygen may be a result of steric inhibition, preventing the access of oxygen to C-1. This argument has been used to account for the stability of 2,4,6-triphenylphenoxy (92) towards oxygen[75], although extended electron delocalisation must also be a contributing factor in this case.

The dinaphthol (11) is known to give a stable naphthoxy radical[20]. By analogy with this report, and the known stability of the phenoxy radical (92), it can be predicted that the naphthoxy radicals

(93, R = Br, Ph) would be stable to dimerisation, and may be isolable in the solid state.



(92)



(93)

Attempts to prepare (93, R = Br) by the action of ferric chloride or lead dioxide on 1-bromo-3,6-di-t-butyl-2-naphthol resulted in the recovery of ca. 80% of unchanged starting material, and 3,6-di-t-butyl-1,2-naphthaquinone (10) (ca. 10%). Two highly coloured components decomposed rapidly to a mixture of starting material, and the quinone (10) on silica. No attempt has been made as yet to prepare (93, R = Ph).

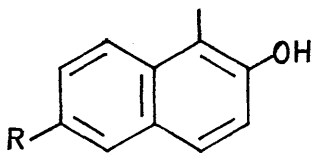
1-Iodo- and 1-bromo-3,6-di-t-butyl-2-naphthol failed to autoxidise to any measurable extent on prolonged oxygenation. In view of the bulk of the 1-substituents in these cases, these compounds might be expected to be subject to considerable strain. The inductive effect of an iodine atom should be similar to that of a methyl group. The failure of these compounds to autoxidise cannot readily be explained.

Attempted preparation of 1,8-dimethyl-2-naphthol.

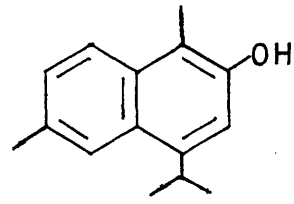
The naphthols investigated so far are sterically compressed mainly by virtue of the peri-interaction between H-8 and the substituent at C-1. The replacement of H-8 by a larger substituent such as methyl should increase the strain within the molecule dramatically. It has been reported[70] that 1,8-dimethylnaphthalene is considerably distorted as a result of the peri-interaction (see introduction p. 29). A crystal structure analysis, and strain energy minimisation calculations indicate that the interaction between the methyl groups is reduced mainly by bond-angle distortion at the junction between the naphthalene nucleus and the methyl groups, but the molecule is found to be

essentially planar. The naphthalene nucleus in 3-bromo-1,8-dimethylnaphthalene was found by X-ray analysis to be buckled[76]. The total molecular strain in 1,8-dimethylnaphthalene has been estimated at 8.4 kcal. mole^{-1} [70]. (An earlier estimate of 7.9 kcal. mole^{-1} is in fair agreement with this value[77]).

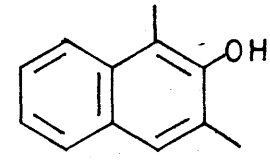
The introduction of an -OR group into the 2-position in 1,8-dimethylnaphthalene would be expected to increase the degree of steric congestion. Out of plane deformations may be less favoured in this case, since this could result in a substantial decrease in conjugation of the -OR group with the naphthalene nucleus. Several alkylated 1-methyl-2-naphthols have been reported, and in no case has any comment on their reactivity with oxygen been made.



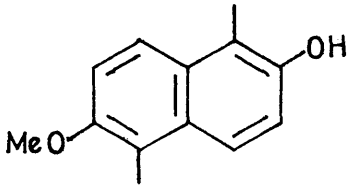
R = Me,Et,Pr,Bu,Amyl,Hexyl.
(Ref. 78)



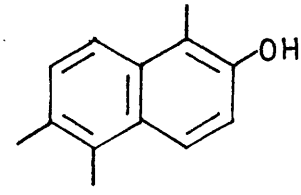
2-hydroxycadalene
(Ref, 79)



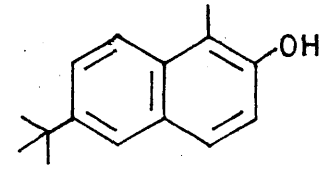
(Ref. 80)



(Ref. 81)



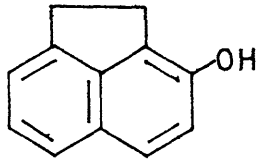
(Ref. 82)



(page 91)

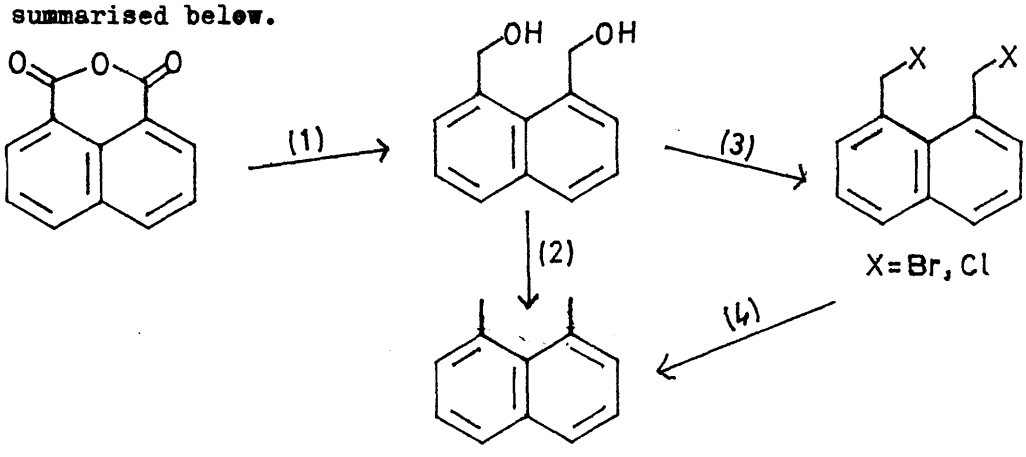
In all of these examples, the naphthalene nucleus should be electronically more activated than in 1,8-dimethyl-2-naphthol. The reactivity of this compound towards oxygen is therefore of interest in this study, since any tendency to autoxidise should be attributable mainly to peri-strain.

A reported preparation of 1,7,8-trimethyl-2-naphthol was later discounted by Ruzicka and co-workers[82], who proved that this compound was in fact 1,5,6-trimethyl-2-naphthol. They also synthesised 1,7,8-trimethyl-2-methoxynaphthalene by an elaborate route, but did not report the corresponding naphthol. 3-Hydroxyacenaphthene (94), the only other compound of this type to be reported[83], is not known to autoxidise, but this compound is very different from 1,8-dimethyl-2-naphthol in terms of strain.



(94)

1,8-Disubstituted naphthalenes are commonly prepared from 1,8-naphthalic anhydride, a readily available starting material. Van Bekkum et al.[31] prepared 1,8-diisopropylnaphthalene in low yield by an eight stage synthesis. Several groups have prepared 1,8-dimethylnaphthalene by multistage reduction of 1,8-naphthalic anhydride[84]. These syntheses are summarised below.



(1) Hydride reduction. (2) Catalytic hydrogenolysis.

(3) Phosphorus tribromide or concentrated hydrochloric acid.

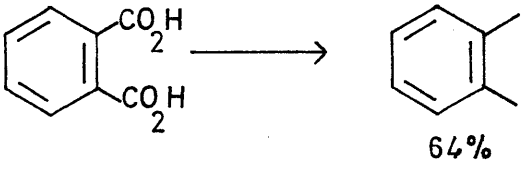
(4) Hydride reagents, zinc or aluminium amalgam.

I set out to prepare 1,8-dimethyl-2-methoxynaphthalene from 2-methoxy-1,8-naphthalic anhydride (95), which is readily obtained from 3-methoxyacenaphthenequinone[85] by treatment with alkaline hydrogen peroxide[86]. The anhydride (95) is sparingly soluble in the majority of organic solvents. Recrystallisation from glacial acetic acid gave deep yellow crystals, m.p. 255-6° (lit.[86(a)] 255°). Recrystallisation from large volumes of 95% ethanol gave colourless needles, m.p. 261-263° (lit.[86(b)] 261-2°). Owing to the low solubility of (95) in most organic solvents, it does not readily undergo reaction, especially in aprotic solvents. Similar problems were encountered in the reactions of 1,8-naphthalic anhydride[84].

Benkeser *et al.*[87] have reported the one-step reduction of aromatic carboxyl groups to methyl groups in high yield employing trichlorosilane, and have suggested that the reaction proceeds *via* the anhydride,

$$ArCO_2H \xrightarrow{SiHCl_3} \begin{matrix}(ArCO)_2O \\ \text{or} \\ (ArCO_2)_xSiHCl_y\end{matrix} \xrightarrow[R_3N,\Delta]{SiHCl_3} ArCH_2SiCl_3 \xrightarrow{KOH/MeOH} ArCH_3 .$$

for example,



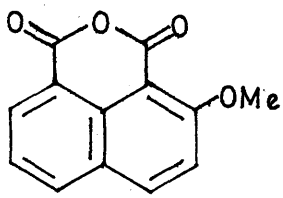
64%

Benzoic anhydride also undergoes reductive silylation to form benzyltrichlorosilane.

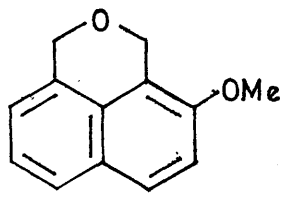
The reaction was carried out using the anhydride (95) in the manner reported[87]. The only identifiable product, formed in low yield, was 4-methoxy-1H,3H-naphtho(1,8-c,d) pyran (96), which was identical in all respects to an authentic sample from another source (see below).

The production of the cyclic ether (96) was not expected. The phenanthrene derivatives (97(a), (b)) are reported to give low yields of cyclic ether (97(c)) under these conditions, and no methyl derivatives

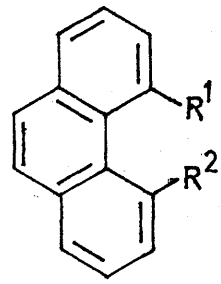
were isolated[88].



(95)



(96)



(97)

(a) R^1 = CHO, R^2 = CO_2H

(b) R^1 = R^2 = CO_2H

(c) R^1,R^2 = $-CH_2OCH_2-$

(d) R^1 = R^2 = $-CH_2SiCl_3$.

This was claimed to be the first reported case of nucleophilic attack of hydroxide on carbon displacing silicon, but the benzylic silane (97(d)) was not isolated. The mechanism of these reactions has not been fully investigated, and the cyclic ethers (96) and (97(c)) may be formed via a different mechanism.

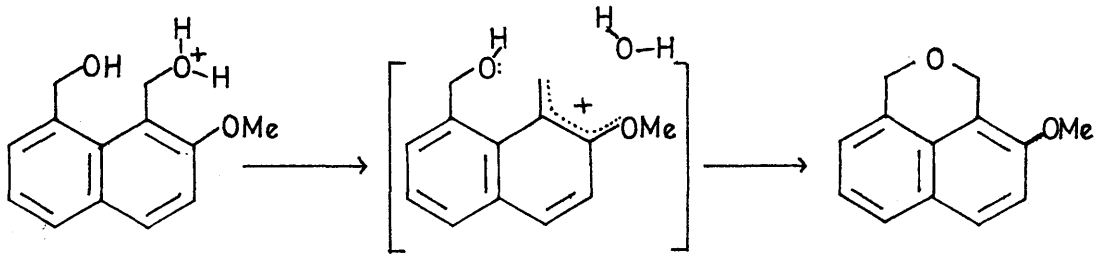
Attempted preparation of 1,8-di(hydroxymethyl)2-methoxynaphthalene (98).

The diol (98) was prepared in moderate yield by prolonged treatment of 2-methoxynaphthalic anhydride with a large excess of lithium aluminium hydride (LAH) in a benzene-ether solvent, using a non-acidic work-up to avoid dehydration of the product to the naphthopyran (96). The main drawbacks in this method are the extremely low solubility of the anhydride (95) in ether, and the low solubility of LAH in benzene, so that neither substrate nor reagent are present in reasonable concentration[84]. Isolation of the product is made difficult by the formation of aluminium hydroxide in the non-acidic work-up.

Sodium dihydro-bis(2-methoxyethoxy) aluminate (SDA)[89] is a stable hydride reagent which is completely soluble in the majority of organic solvents, and often gives higher yields than LAH. It was hoped that the high solubility of this reagent in benzene may facilitate the

reduction of the anhydride (95) to the diol (98) in that solvent. The reaction mixture can be worked-up using aqueous sodium hydroxide when the products are acid sensitive.

Addition of the anhydride (95) to a benzene solution of SDA resulted in vigorous effervescence to give a deep yellow, homogeneous solution. This mixture was refluxed for two hours, the reaction being monitored by t.l.c.. The product was isolated using a basic work-up, and was found to contain two major components, one of which was the diol (98). This compound could be isolated in up to 30% yield by fractional crystallisation, but on occasion, this yield was considerably lower. The diol (98) dehydrated readily in mildly acidic media to give the naphthopyran (96). This is in contrast with 1,8-di(hydroxymethyl)-naphthalene, which is reported to be stable to acids[84]. This difference in reactivity is probably due to stabilisation of positive charge at the benzylic position ortho to the methoxyl group.



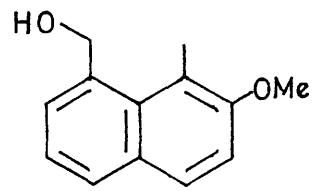
(96)

In view of the difficulties encountered in separating the highly polar diol (98) by chromatography or crystallisation, the product of the reaction was washed with dilute hydrochloric acid, and subsequent preparative chromatography gave ca. 40% yield of the naphthopyran (96). The u.v. spectrum ($\lambda_{max.}$(EtOH) 232(4.8), 278(sh), 286(3.75), 297(3.68), 326(3.27), 339(3.31) nm.) is similar to those of other 2-methoxy-naphthalenes. In the n.m.r. spectrum, the high field singlet (τ 5.04, 2H) is probably due to the benzylic hydrogens attached to the ortho-

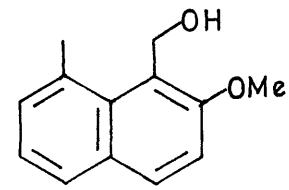
methoxylated ring, the low field singlet (τ 4.94, 2H) being due to the benzylic hydrogens attached to the 8-position. The pyran (96) was found to autoxidise slowly in air, but the products of this reaction could not be formed in sufficient quantity to be identified. The autoxidation of benzylic ethers is a well known process[90].

The other component from the reaction of SDA with 2-methoxy-1,8-naphthalic anhydride was a low melting solid containing mainly one compound, which is assigned the structure 8-hydroxymethyl-2-methoxy-1-methylnaphthalene (99) on the basis of the following data.

The u.v. ($\lambda_{max.}$(EtOH) 233, 276(sh), 286.5, 297, 326, 335(sh) nm.) was similar to other 2-methoxynaphthalenes. In the i.r., the band at 3,400 cm^{-1} supported this assignment.



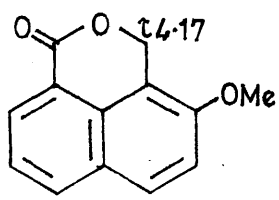
(99)



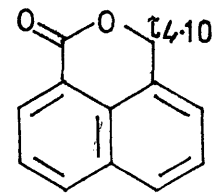
(100)

The n.m.r. did not distinguish between the isomeric structures (99) and (100), but the structure (99) is favoured, since the activated C-O bond (ortho to methoxyl) in the diol (98) would be expected to be cleaved more readily than the relatively unactivated C-O bond at the other benzylic position. This compound contained an impurity (ca.10% estimated by n.m.r.), which was assigned the structure (101) on the basis of a singlet in the n.m.r. at τ 4.17, and a band in the i.r. at 1720 cm^{-1}. These values are in broad agreement with the published data for 1,8-naphthalide (102), which was obtained by LAH reduction of the corresponding anhydride[91].

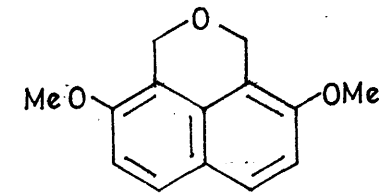
This mixture proved to be inseparable by chromatography, and was not investigated further.



(101)



(102)



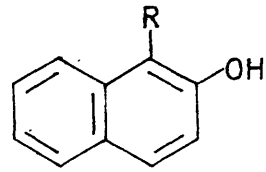
(103)

Cason and co-workers[91] report that, while 1,8-naphthalic anhydride reacts with LAH to give only 1,8-di(hydroxymethyl)naphthalene and 1,8-naphthalide (102), 2,7-dimethoxynaphthalic anhydride produces only the naphthopyran (103) via the corresponding naphthalide. They conclude that, while naphthalides are common intermediates in these reactions, the 4,9-dimethoxynaphthopyran (103) is formed directly, and not via the diol, despite the fact that they employed acidic work-up conditions. In the non-acidic work-up of either the LAH or SDA reduction of 2-methoxy-1,8-naphthalic anhydride (95), no naphthopyran was detected by me. It is probable that 1,8-di(hydroxymethyl)-2,7-dimethoxynaphthalene is the primary product of LAH reduction of the corresponding anhydride, and that dehydration of this compound to the naphthopyran (103) occurs very readily in acidic media.

The SDA reduction of 2-methoxynaphthalic anhydride was carried out at room temperature (30 hours), in an attempt to minimise the proportion of the over-reduced product (99), but t.l.c. indicated that only traces of the desired diol had been produced during this time. This route to the diol (98) was therefore abandoned, since treatment of the anhydride (95) with LAH gave up to 60% yield of this compound.

The production of 8-hydroxymethyl-2-methoxy-1-methylnaphthalene (99) is of interest, since it might undergo catalytic hydrogenolysis to give the desired 1,8-dimethyl-2-methoxynaphthalene, and since its formation under mild SDA reduction conditions is unprecedented.

Cerny and Malek[92] report that hydroxy-substituted aromatic aldehydes, ketones, carboxylic acids, and carbinols undergo reduction and hydrogenolysis to give the corresponding alkyl compounds in high yield on treatment with SDA under forcing conditions. This occurs only where the position of the phenoxide allows resonance stabilisation of the intermediate benzylic carbonium ion. For example, the 1-substituted 2-naphthols (104), on treatment with SDA in refluxing xylene for ca. 2 hours, give > 90% yields of 1-methyl-2-naphthol.



R = CHO, CO_2H, CH_2OH

(104)

In my hands, SDA reduction of 1-formyl-2-naphthol in refluxing xylene gave a 95% yield of 1-methyl-2-naphthol.

Brewster et al.[93] have reduced benzylic alcohols to alkyl benzenes employing aluminium chloride-LAH mixtures in high boiling solvents. Benkeser[87] has reduced aromatic carboxylic acids to the methyl compounds by reductive silylation followed by alkaline hydrolysis (see above). Doyle et al.[94] recently reported the reduction of activated aromatic aldehydes and aralkyl ketones to the methylene compounds in high yield employing trialkylsilanes in trifluoroacetic acid. Apart from the classical Clemmensen and Wolff-Kishner reduction methods, these are the only reported methods of one-step reduction of oxygenated functional groups to the corresponding hydrocarbon.

The production of the methylnaphthalene (99) by the action of SDA seems to be unprecedented. The activating effect of the methoxyl group would hardly seem to account for this facile hydrogenolysis under such mild conditions. In an attempt to obtain the methylnaphthalene (99) in reasonable yield, a sample of 2-methoxy-1,8-naphthalic anhydride

was treated with SDA in refluxing benzene for 22 hours. Acidic work-up followed by preparative chromatography gave a 45% yield of the naphthopyran (96), but pure samples of the methylnaphthalene (99), which was present in small quantity, could not be obtained. Many other unidentified products of high polarity were produced in this reaction, along with a large quantity of polymeric materials.

By carrying out this reaction under more forcing conditions, it was hoped to accelerate the production of the desired 8-hydroxymethyl-2-methoxy-1-methylnaphthalene (99) and minimise polymerisation. Treatment of 2-methoxy-1,8-naphthalic anhydride with SDA in refluxing xylene for six hours followed by chromatography gave impure samples of 1,8-dimethyl-2-methoxynaphthalene (105) (properties to be discussed below) and 1,8-dimethylnaphthalene. A small component on t.l.c. corresponding to the monomethyl compound (99) could not be obtained in a pure state. A considerable degree of polymerisation occurred during this reaction. 1,8-Dimethyl-2-methoxynaphthalene was obtained in a pure state by fractional distillation in ca. 50% yield. 1,8-Dimethylnaphthalene could readily be purified by crystallisation, and could be unambiguously characterised by spectroscopic methods, and by comparison with literature reports of this compound[84]. The unexpected production of dimethylnaphthalene will be discussed below. Several attempts were made to minimise the production of 1,8-dimethylnaphthalene in this reaction. The use of shorter reaction times, lower temperatures (toluene reflux), different substrates (naphthopyran (96), and 1,8-di(hydroxymethyl)-2-methoxynaphthalene (98)), and a lower proportion of SDA did not decrease the relative proportion of 1,8-dimethylnaphthalene produced. In the majority of cases, considerably lower yields of the desired 1,8-dimethyl-2-methoxynaphthalene were obtained.

It has already been shown that 8-hydroxymethyl-1-methyl-2-methoxynaphthalene (99) is an intermediate in these reactions, and can be

isolated under less vigorous conditions. The hydrogenolysis of this compound by SDA was not expected, since the 8-position in 2-methoxynaphthalenes is only mildly activated[92]. 8-Hydroxymethyl-2-naphthol was found to be reduced very much more slowly than the 1,8-disubstituted compounds under similar conditions (see below). The facile reduction of 1,8-di(hydromethyl)-2-methoxynaphthalene, presumed to be a common intermediate in these reactions, may be a consequence of the degree of strain in this molecule, but a detailed explanation for this behaviour cannot readily be found.

Treatment of 2-methoxynaphthalenes with SDA.

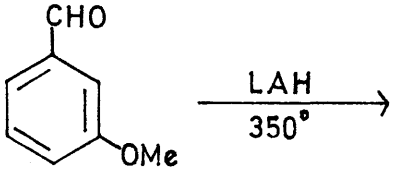
The unexpected production of 1,8-dimethylnaphthalene in the above reactions seemed to merit further investigation. Treatment of a pure sample of 1,8-dimethyl-2-methoxynaphthalene (105) with SDA in refluxing xylene for four hours produced a mixture containing 1,8-dimethylnaphthalene (ca. 30% by g.l.c. and n.m.r.) and unchanged starting material. This indicates that the Ar-O bond may be cleaved at any time during the SDA reduction of 2-methoxy-1,8-naphthalic anhydride.

It was found that 2-methoxynaphthalene did not react under these conditions over several days. Similar treatment of methyl 2-methoxy-1-naphthoate did not produce a detectable quantity of 1-methylnaphthalene, and treatment of 1-methyl-2-methoxynaphthalene gave only unchanged starting material[95]. Prolonged (18 hours) treatment of 1-t-butyl-2-methoxynaphthalene with SDA under these conditions produced some 1-t-butyl-2-naphthol, polymers, and unchanged starting material. Similar treatment (10 hours) of 1-methyl-3,6-di-t-butyl-2-methoxynaphthalene produced an intractible oil containing ca. 10% unchanged starting material, and many other components which were not identified.

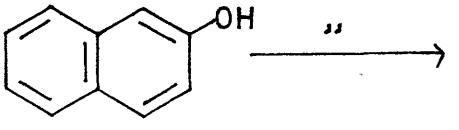
The anomalous formation of 1,8-dimethylnaphthalene in the preparation of 1,8-dimethyl-2-methoxynaphthalene remains unexplained. This may be a consequence of peri-strain, but other strained 2-methoxy-

naphthalenes do not behave in an analogous manner.

The methyl ethers of phenols are cleaved by a wide range of reagents, but the O-CH_3 bond is normally broken in preference to the O-Ar bond. However, it has recently been reported[40] that many phenols and methyl ethers of phenols can be cleaved in low yield at the O-Ar bond by employing excess LAH at 350°, for example,



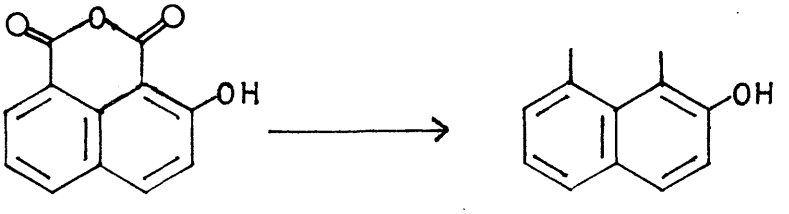
19%



43%

Substituted anisoles (ArOMe) are reported[96] to undergo aryl-oxygen cleavage on photolysis in the presence of trimethylaluminium to give a mixture of the methylated (Ar-Me) and protonated (Ar-H) derivatives. It would seem that aluminium compounds are unique in this respect.

Preparation of 1,8-dimethyl-2-naphthol (107) by SDA reduction of 2-hydroxy-1,8-naphthalic anhydride (106).



(106) (107)

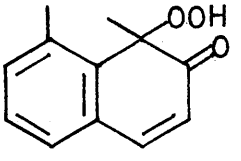
In order to avoid the ether cleavage described above, the direct preparation of the desired dimethylnaphthol (107) by SDA reduction of (106) was attempted. It was thought that the greater activation of the naphthalene nucleus by the oxide group (relative to methoxyl) may also facilitate this reaction[92].

Demethylation of 2-methoxy-1,8-naphthalic anhydride employing hydrogen bromide in aqueous acetic acid gave a mixture of the required 2-hydroxy-1,8-naphthalic anhydride (106), and 7-hydroxy-1-naphthoic acid (108) which could be separated by fractional crystallisation.

The anhydride (106) has been reported to undergo decarboxylation to give the naphthoic acid (108) when heated with concentrated sodium hydroxide solution, or when fused with potassium hydroxide[97]. Attempts to achieve demethylation by hydrogen bromide in non-aqueous conditions, or by using pyridine hydrochloride were unsuccessful.

The anhydride (106) when treated with SDA in refluxing xylene, gave ca. 60% yield of 1,8-dimethyl-2-naphthol. However, pure samples of this compound could not be isolated from the reaction mixture due to its extreme instability to oxygen (see below), so that partial autoxidation could not be avoided in the course of isolating this product from the by-products. This problem could have been overcome by treating the reaction mixture with methyl iodide or acetic anhydride in dmso, and isolating the resulting methoxy or acetoxy compound. This approach has not been attempted. 1,8-Dimethylnaphthalene was not detected in the product mixture.

Oxygenation of impure samples of the dimethylnaphthol (107) obtained from this reaction gave a high yield of 1-hydroperoxy-1,8-dimethyl-2(1H)-naphthalenone (109), which was identical in all respects to samples obtained from another source which is described below.



(109)

Preparation of 8-methyl-2-naphthol (110) by reduction of 7-hydroxy-1-naphthoic acid (108).

The production of 7-hydroxy-1-naphthoic acid as a by-product from the reaction of 2-methoxy-1,8-naphthalic anhydride with hydrogen bromide, prompted us to investigate the reaction of this compound with SDA. A quantitative yield of the naphthoic acid (108) could be obtained by extending the time of the demethylation reaction. This might provide a simple preparation of 8-methyl-2-naphthol which may then be alkylated further to provide a series of 1-alkyl-8-methyl-2-naphthols. 8-Methyl-2-naphthol (110) has been prepared previously by multistage syntheses[98].

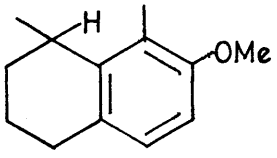
Treatment of 7-hydroxy-1-naphthoic acid with SDA in refluxing xylene for six hours gave a mixture of two compounds. Fractional crystallisation gave a pure sample of 8-hydroxymethyl-2-naphthol (111) (75%). Crystallisation of the mother liquors gave 8-methyl-2-naphthol (110) (16%). The low yield of 8-methyl-2-naphthol indicates that the facile reduction by SDA of 2-hydroxy-1,8-naphthalic anhydride to 1,8-dimethyl-2-naphthol is unique to this molecule, and that in general, the 8-position in 2-naphthol is not sufficiently activated to facilitate cleavage of the benzylic C-O bond. A quantitative yield of 8-methyl-2-naphthol was obtained from 8-hydroxymethyl-2-naphthol by catalytic hydrogenolysis.

Alternative routes to 1,8-dimethyl-2-naphthol (107).

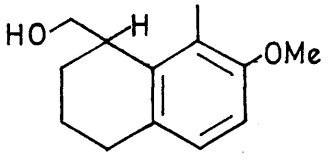
Owing to the difficulties encountered in preparing the title compound in a pure state by one-step reduction of 1,8-naphthalic anhydrides, alternative routes to this compound were investigated.

The naphthopyran (96) could be obtained in moderate yield by reduction (SDA or LAH) of 2-methoxy-1,8-naphthalic anhydride (95) followed by an acidic work-up. Several attempts to reduce this pyran to 2-methoxy-1,8-dimethylnaphthalene by catalytic hydrogenolysis[99], or by using LAH-aluminium chloride mixtures[99, 100] were unsuccessful.

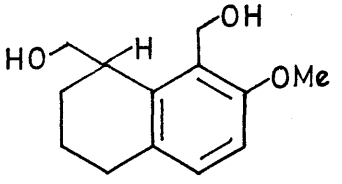
1,8-Di(hydroxymethyl)-2-methoxynaphthalene (98), obtained by LAH reduction of 2-methoxy-1,8-naphthalic anhydride, could be catalytically hydrogenated over a palladium-charcoal catalyst in methanol. When the reaction was terminated after two moles of hydrogen per mole of substrate had been taken up, a mixture containing four identifiable components was obtained. These were isolated by preparative chromatography, and identified as 1,8-dimethyl-2-methoxynaphthalene (105) (maximum yield 50%) and the tetrahydronaphthalene derivatives (112), (113), and (114).



(112)



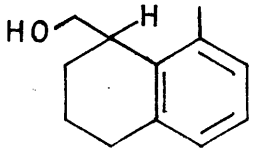
(113)



(114)

Many attempts to augment the yield of the desired dimethyl compound (105) failed.

The hydrogenation of the naphthalene nucleus is competing successfully with the hydrogenolysis reaction. This would not normally be expected. The facile hydrogenation of these 1,8-disubstituted compounds may be a result of peri-strain. It has been reported that 1,4-di-t-butylnaphthalene, which is subject to considerable peri-strain, is hydrogenated ca. 13 times more quickly than naphthalene itself (see Intro. p. 32). Two groups have reported independently that , in the catalytic hydrogenolysis of 1,8-di(hydroxymethyl)naphthalene, more than two moles of hydrogen are taken up[84(b), (e)]. One of these groups[84(e)] identified a by-product of this reaction, viz. 1-hydroxymethyl-8-methyl-1,2,3,4-tetrahydronaphthalene (115).



(115)

Purification of 1,8-dimethyl-2-methoxynaphthalene from the hydrogenation reaction proved to be difficult, since the dimethyl-tetrahydronaphthalene (112) could not be completely separated by preparative chromatography. Attempts to re-aromatise the tetrahydro derivative (112) employing 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ)[101], or by heating with a palladium-charcoal catalyst in high boiling solvents[102] were only partially successful. These reactions converted the tetrahydronaphthalene derivative (112) to a mixture of 1,8-dimethyl-2-methoxynaphthalene, and a second component, which was probably a dihydronaphthalene derivative, but which was not characterised. (Mixtures were analysed by g.l.c..) Samples of 1,8-dimethyl-2-methoxynaphthalene suitable for analysis (and giving one peak on g.l.c.) could be obtained by low temperature (DriKold-acetone bath) crystallisation from pentane. The pure compound is an oil at room temperature.

The spectral characteristics of this compound were totally in accord with the assigned structufe. Some ambiguity arises in assigning the methyl signals in the n.m.r.. However by comparison with the n.m.r. of other compounds, the singlet at τ ($CDCl_3$) 7.23 can be assigned to the 1-methyl group (cf. 1-methyl-2-methoxynaphthalene, τ ($CDCl_3$) 7.25(Ar-CH_3)), and the singlet at τ 7.10 can be assigned to the 8-methyl group (cf. 1,8-dimethylnaphthalene, τ ($CDCl_3$) 7.07(Ar-CH_3)). The u.v. spectrum of (105) ($\lambda_{max.}$(EtOH) 232(4.8), 278(sh), 286(3.75), 297(3.68), 326(3.27), 339(3.31) nm.) suffers considerable bathochromic and hyperchromic shifts relative to 2-methoxynaphthalene ($\lambda_{max.}$(EtOH) 227(4.9), 262(3.64), 272(3.68), 282.5(3.50), 314(3.20), 328.5(3.30) nm.), which may be associated with the strain in the dimethyl compound (105)[47,51]. The combined effect of the two methyl groups in (105) upon the u.v. should be a ca. 5-6 nm. red shift relative to 2-methoxynaphthalene, by analogy with published data.

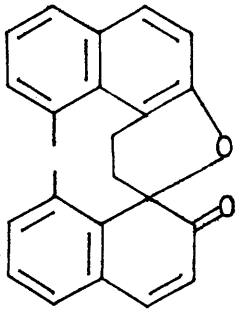
Preparation and autoxidation of 1,8-dimethyl-2-naphthol (107).

1,8-Dimethyl-2-methoxynaphthalene (105) was quantitatively demethylated using hydrogen bromide in aqueous acetic acid. The product was isolated and recrystallised with the exclusion of oxygen to give pure samples of 1,8-dimethyl-2-naphthol as colourless needles, m.p. 92-95°, whose spectral characteristics were completely in accord with the assigned structure. A quantitative yield of 1,8-dimethyl-2-acetoxynaphthalene, m.p. 60-61.5° could be obtained by treatment of the naphthol with acetic anhydride in anhydrous pyridine. (A crystalline derivative was required for X-ray analysis.)

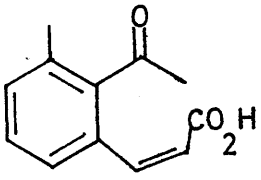
Oxygenation of benzene solutions of the pure dimethylnaphthol (107) was complete in 12 ± 2 hours, giving a high yield of 1-hydroperoxy-1,8-dimethyl-2(1H)-naphthalenone (109), as colourless prisms, m.p. 144-6°, whose spectral and analytical characteristics were totally in accord with this structure. Preparative chromatography of the mother liquors gave, as well as the hydroperoxide (109), small quantities of two further components. Traces of these components were also produced when pure samples of the hydroperoxide were dissolved in benzene, and stored in diffuse sunlight under nitrogen at room temperature for several days. This decomposition was not accelerated by prolonged refluxing in benzene, but refluxing in toluene resulted in complete decomposition of the hydroperoxide to a tar containing small quantities of both components obtained from the autoxidation reaction. Treatment of a methanolic solution of (109) with aqueous sodium carbonate at room temperature for twenty four hours resulted in no reaction. Similar treatment with 1M aqueous sodium hydroxide for four hours at room temperature gave a mixture containing many components including spots on t.l.c. which corresponded with the two components obtained from the autoxidation reaction above.

The spectral characteristics of these components were in accord

with the structures (116), and (117), but complete characterisation was not achieved, since neither could be obtained in a pure state in sufficient quantity. These tentative structural assignments are made by analogy with the known decomposition products of 1-hydroperoxy-3,6-di-t-butyl-1-methyl-2(1H)-naphthalenone (81) (see page 87), and by comparison of the spectral characteristics of these decomposition products with (116) and (117). These data are fully reported in the experimental section.

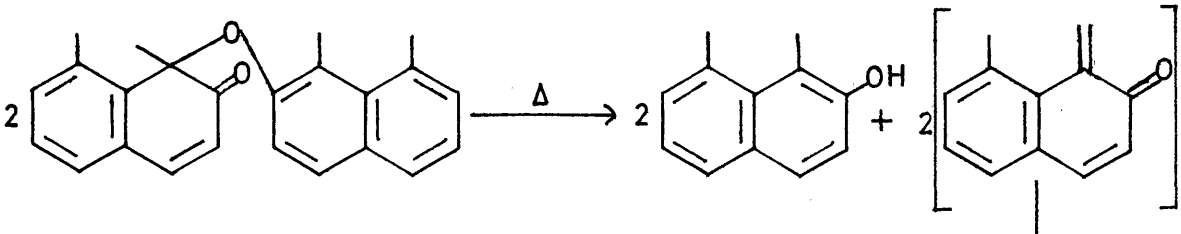


(116)



(117)

The production of the quinone methide dimer (116) may be preceded by the formation of the O-C dimer (118), which may decompose thermally to give the dimethyl naphthol (107), and quinone methide monomer. The C-O dimer formed by oxidation of 1-methyl-2-naphthol is reported to behave in this manner[103].



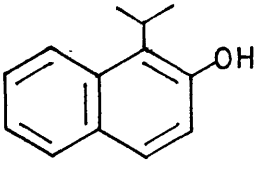
(118) (116)

Preparation and autoxidation of 1-isopropyl-2-naphthol (119).

The autoxidation of the title compound (119) has been studied previously and the resulting hydroperoxide (120) has been fully characterised[2, 6]. However, in order to compare the behaviour of the series of substituted naphthols under investigation, it was necessary to study the autoxidation of this naphthol under identical conditions.

1-Isopropyl-2-naphthol was prepared in moderate yield by isopropylation of sodium 2-naphthoxide in refluxing toluene, and was separated from the by-products (2-isopropoxynaphthalene and 2-naphthol) by fractional distillation followed by several recrystallisations[2].

Oxygenation of benzene solutions of this naphthol gave virtually quantitative yields of the extremely stable hydroperoxide (120) after 16 ± 2 hours.



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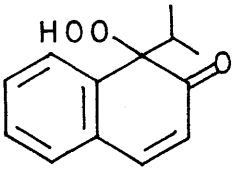


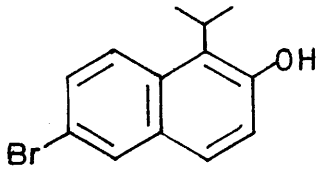
(120)

Oxygenation of a solution of the naphthol in diffuse sunlight was found to proceed much more quickly in the early stages (see Appendix, fig.A), but the time taken for completion of oxygen uptake (14 ± 2 hours) was not altered substantially. Oxygenation of a benzene solution of the pure naphthol in the presence of triphenylphosphine proceded extremely slowly, unreacted starting material being present after one week. The product, which was isolated by preparative chromatography, was the known[2] 1-hydroxy-1-isopropyl-2(1H)-naphthalenone (40), which could be prepared in quantitative yield by treatment of the hydroperoxide (120) with dimethyl sulphide.

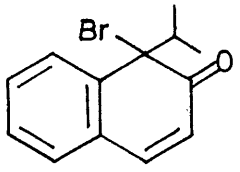
Preparation and autoxidation of 6-bromo-1-isopropyl-2-naphthol (121).

Fries[104] has reported that 6-bromo-1-methyl-2-naphthol is much more stable to oxygen than 1-methyl-2-naphthol. It is also reported that while 1-ethyl-2-naphthol autoxidises fairly rapidly[2, 3(b)], 6-bromo-1-ethyl-2-naphthol is stable to oxygen[3(b)]. In order to ascertain the effect of an electron withdrawing substituent such as bromine upon the autoxidation reaction of unstable naphthols, an investigation into the effect of a 6-bromo substituent upon the rate of autoxidation of the highly reactive 1-isopropyl-2-naphthol was undertaken.

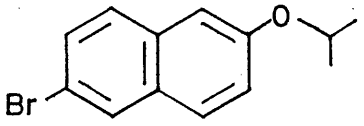
The attempted preparation of 6-bromo-1-isopropyl-2-naphthol by direct bromination of 1-isopropyl-2-naphthol was only partially successful, the major product being 1-bromo-1-isopropyl-2(1H)-naphthalenone (122). This compound was found to equilibrate slowly to the desired 6-bromo compound when heated in a saturated solution of hydrogen bromide in glacial acetic acid[104], but complete conversion could not be achieved in this manner.



(121)



(122)



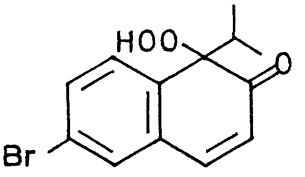
(123)

Pure samples of the 6-bromonaphthol (121) could not be obtained directly from this reaction. By acetylating impure samples of the naphthol, and subsequent crystallisation, pure 2-acetoxy-6-bromo-1-isopropylnaphthalene could be obtained in low yield, which was identical with an authentic sample from another source (see below).

6-Bromo-1-isopropyl-2-naphthol could be obtained in low yield, and in a pure state, by isopropylation of 6-bromo-2-naphthol[105] in a manner analogous to that used to prepare 1-isopropyl-2-naphthol[2]. Distillation of the product mixture gave impure samples containing traces of 6-bromo-2-isopropoxy-2-naphthol (123). Extraction with Claisen's alkali, followed by acidification and re-extraction gave the required bromonaphthol (121), m.p. 74-77° (light petroleum). Unchanged 6-bromo-2-naphthol could be recovered in high yield, and re-cycled. The spectral characteristics of the bromonaphthol (121) bore a close resemblance to those of 1-isopropyl-2-naphthol.

Oxygenation of benzene solutions of pure samples of 6-bromo-1-isopropyl-2-naphthol (obtained directly from the above reaction, or by LAH reduction of analytically pure samples of the corresponding acetate),

was complete after 80 ± 5 hours, one mole of oxygen having been taken up. Removal of solvent gave a virtually quantitative yield of 6-bromo-1-hydroperoxy-1-isopropyl-2(1H)-naphthalenone (124), m.p. 137-140° (benzene-petrol), whose spectral and analytical characteristics were completely in accord with this structure. This hydroperoxide was found to be extremely stable to heat and light, and no other species could be detected in the solution from the autoxidation reaction (cf. the hydroperoxide (120), which is also extremely stable).



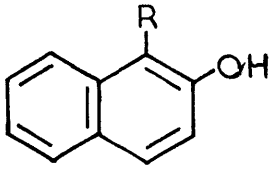
(124)

The slow rate of autoxidation of the bromonaphthol (121) relative to 1-isopropyl-2-naphthol (119) can be interpreted mechanistically in many ways (discussed fully below), but does indicate that electron withdrawing substituents stabilise 2-naphthols towards oxygen.

Autoxidation of strained 1-alkyl-2-naphthols. Steric acceleration in a radical chain reaction.

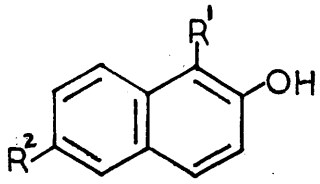
The results of autoxidation studies carried out in the course of this work are summarised in Table I of the Appendix. Included in this table, where appropriate, are the chemical shifts (measured in $CDCl_3$) of the peri-proton, and the yield of 1-alkyl-1-hydroperoxy-2(1H)-naphthalenone, averaged over three experiments. The time taken for uptake of 0.5 moles of oxygen per mole of substrate (averaged over at least three experiments), under the standard conditions described in the experimental section, is quoted in each case, since this value was found to be reproducible, and could be measured relatively accurately. The total time taken for completion of the autoxidation is also given, with an indication of the reproducibility of this value. In some cases, inhibition periods of up to one hour were recorded, where no uptake of oxygen occurred. These are probably the result of trace impurities present in the samples employed, and are not included in the values reported since they varied from one experiment to another. It is possible, and even probable, that all samples contained traces of both initiators and inhibitors, but the reproducibility of the results obtained indicate that these do not have a profound effect upon the overall rate.

A list of the compounds of interest to this discussion is outlined below, those which have been found to autoxidise at an appreciable rate being marked.



Unstable:- R = Et[2], ^{i}Pr[6], c-hexyl[2], sec-butyl[2], ^{t}Bu, t-pentyl.

Stable :- R = Me[2], CH_2Ph[2], Ph, 2-hydroxy-1-naphthyl, isopropenyl, $C(Me_2)OH$, iodo, acetyl, ~~carboxymethyl~~ methoxycarbonyl.

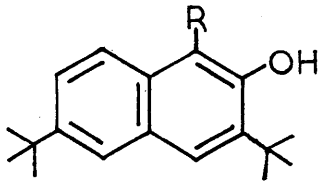


Unstable:- $R^1 = {}^iPr$ $R^2 = Br$

Stable :- $R^1 = H$ $R^2 = {}^tBu$

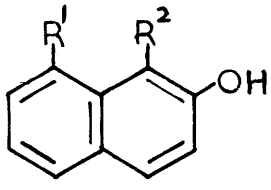
$R^1 = Me$ $R^2 = {}^tBu$

R^1 = morpholinomethyl, $R^2 = {}^tBu$



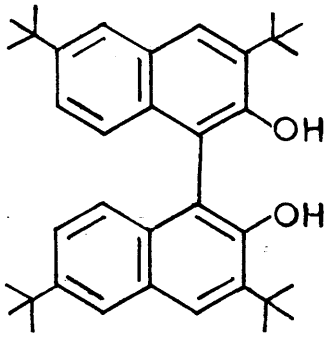
Unstable:- R = Me

Stable :- R = H, morpholinomethyl, Ph, iodo, bromo.

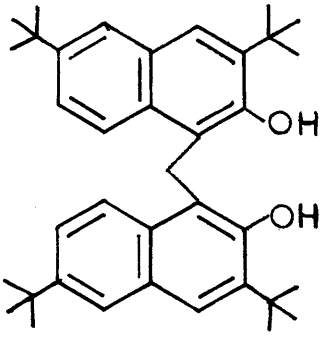


Unstable:- $R^1 = R^2 = Me$

Stable :- $R^1 = R^2 = H$; $R^1 = CO_2H$, $R^2 = H$; $R^1 = -CH_2OH$, $R^2 = H$.



(11) Stable



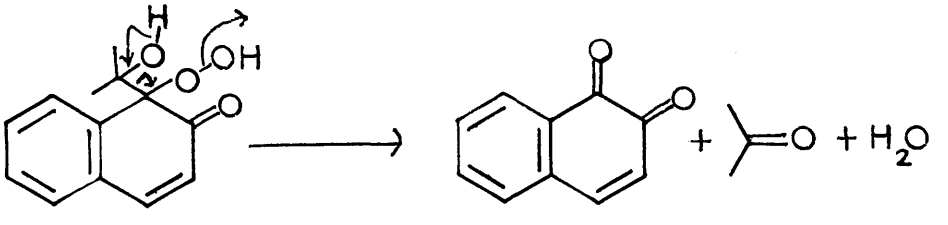
(71) Unstable

Stable 2-naphthols.

An examination of the comprehensive list of 2-naphthols which have been studied in the course of this work shows that, with one exception (the bisnaphthylmethane (71)), only those compounds having an unfunctionalised alkyl group at C-1 show an appreciable tendency to autoxidise, despite the fact that some of these stable naphthols must be considerably strained. In the cases of 1-benzyl-, 1-phenyl-, 1-isopropenyl-, and 1-acetyl-2-naphthol, the 1-substituents can adopt

a conformation such that peri-interactions are small. In the cases of 1-phenyl- and 1-isopropenyl-2-naphthols and the dinaphthol (11), the u.v. spectra indicate that the 1-substituent is not in conjugation with the aromatic system (see page 91), viz. these substituents do not lie in the plane of the naphthalene nucleus. The stability of 1-acetyl and 1-~~carboxymethyl~~ methoxycarbonyl-2-naphthol may be similarly explained, but electron withdrawing effects, and intramolecular hydrogen bonding with the 2-hydroxyl group may be more important.

1-Phenyl-3,6-di-t-butyl-2-naphthol and the dinaphthol (11) seem to be even more stable towards oxygen than 3,6-di-t-butyl-2-naphthol itself[2]. This may be a consequence of the electron withdrawing effect of the 1-aryl group, or of steric inhibition to abstraction of a hydrogen atom by the intermediate peroxy radical (see page 93.). The possible explanation for the stability of 1-morpholinomethyl-3,6-di-t-butyl-2-naphthol has been discussed earlier (page 78). Similar arguments can be proposed to account for the stability of 2-(2-hydroxy-1-naphthyl)propan-2-ol (38), which would be expected to be extremely strained (cf. 1-isopropyl-2-naphthol). Intramolecular hydrogen bonding may inhibit hydrogen abstraction, or the hydroperoxide may decompose spontaneously by an ionic pathway, thus preventing autocatalysis.



The i.r. spectrum of (38) ($\nu_{max.}$ 3,380-2,400 cm^{-1}) indicates that strong intramolecular H-bonding does exist, but no evidence of the formation or decomposition of the hydroperoxide which has been proposed was obtained.

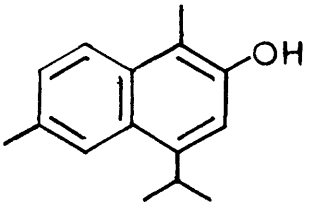
The stability of 1-iodo-3,6-di-t-butyl-2-naphthol is difficult

to account for, in view of the instability of the 1-methyl analogue (67). The readily polarisable iodine atom may introduce less strain into the system than a methyl group, or the derived hydroperoxide may decompose, so that initiation by hydroperoxide does not occur.

A consideration of the factors influencing the rate of autoxidation of 2-naphthols.

Those 2-naphthols which are known to autoxidise readily have two features in common, viz. they have an alkyl substituent at C-1, and they are subject to strain as a result of steric congestion. The electronic characteristics of substituents on the naphthalene nucleus at positions other than C-1 have been shown to be of secondary importance, as in the case of 6-bromo-1-isopropyl-2-naphthol. Strained 2-naphthols containing no substituent at C-1 may also autoxidise readily, but no such naphthols have, as yet, been prepared. An investigation of a molecule such as 8-t-butyl-2-naphthol would be of interest for this reason. Snyckers and Zollinger[28] have prepared 8-isopropyl-2-naphthol, and made no comment on its stability in air. 3,6-Di-t-butyl-2-naphthol, which is known to autoxidise slowly[2], may be strained by virtue of the buttressing effect of the 3-t-butyl group.

The exact steric requirements for instability of 2-naphthols to oxygen are not yet clear. 2-Hydroxycadalene (129)[79] is not reported to be unstable to oxygen, although this compound must be subject to considerable peri-strain between the 4-isopropyl group and H-5. However, hydroperoxide formation at C-1 would not remove this interaction. This would indicate that strain-relief is the essential feature facilitating these reactions.



(129)

The mechanism of autoxidation of 2-naphthols (RH) is assumed to involve a radical chain process of the type proposed for the large majority of autoxidation processes (see Introduction, p. 3), viz.,

Initiation :
$$\left.\begin{array}{l} RH \longrightarrow R^{\bullet} \\ ROOH \longrightarrow RO^{\bullet} + {}^{\bullet}OH \\ 2\ ROOH \longrightarrow RO^{\bullet} + H_2O + ROO^{\bullet} \end{array}\right\} \quad (a)$$

Propagation :
$$R^{\bullet} + O_2 \longrightarrow ROO^{\bullet} \quad (b)$$
$$ROO^{\bullet} + RH \longrightarrow ROOH + R^{\bullet} \quad (c)$$

Termination :
$$\left.\begin{array}{l} R^{\bullet} \\ ROO^{\bullet} \end{array}\right\} \longrightarrow \text{molecules} \quad (d)$$

The autoxidation of 1-isopropyl-2-naphthol has been shown to be accelerated by the addition of radical initiators (cobalt III acetylacetonate, α,α'-azobisisobutyronitrile), and inhibited by radical scavengers (2,6-di-t-butyl-p-cresol)[2]. The factors which may influence each of the steps (a-d) in the radical chain process will be discussed in turn.

Initiation (step (a)) (see Introduction p. 3) :

In the early stages of autoxidation (<1% conversion), where the hydroperoxide concentration is zero or very low, initiation can be induced thermally, photochemically, by trace metal impurities, by wall-effects etc.. These processes are thought to involve bimolecular and/or termolecular processes between substrate and oxygen, in which the weakest bond in the substrate (in this case the O-H bond) is homolysed to give radicals. These processes could therefore be accelerated by a weakening of the O-H bond in the 2-naphthols. The O-H bond in sterically congested phenols has been shown to be considerably weakened relative to unhindered phenols (Introduction, p. 23). The O-H bond in strained 2-naphthols may also be weakened, possibly for different reasons. Factors which stabilise the naphthoxy radical may also facilitate initiation processes, but such stabilisation cannot

readily be rationalised as being a result of steric strain, since the formation of a planar naphthoxy radical does not remove any of the unfavourable interactions in these molecules.

However, it is known that initiation processes are normally controlled by hydroperoxide concentration, and can be directly related to this value in some cases (see Introduction, p. 4). This involves the steps,

$$ROOH \longrightarrow RO^{\bullet} + {}^{\bullet}OH ,$$

at low concentrations of hydroperoxide, and

$$2\ ROOH \longrightarrow RO^{\bullet} + H_2O + ROO^{\bullet} ,$$

at high concentrations of hydroperoxide. The overall rate of autoxidation becomes insensitive to hydroperoxide concentration when this becomes very high. This dependency upon hydroperoxide concentration results in the typical autocatalytic curve for oxygen uptake in the early stages of autoxidation reactions. A plot of oxygen uptake versus time for the autoxidation of 1-isopropyl-2-naphthol displays this shape (see Fig. A, Appendix), i.e. the rate is extremely fast in the earlier stages (up to ca. 0.5 mole uptake of oxygen per mole of substrate), and decreases substantially in the later stages. Homolysis of the peroxide bond in hydroperoxides can be accelerated by u.v. light. I find that, when 1-isopropyl-2-naphthol is autoxidised in diffuse sunlight, the initial gradient of the absorption curve for the reaction is greater than for autoxidations carried out in the absence of light, although the overall time for complete conversion to hydroperoxide is not substantially different (see Fig. A, Appendix). The autoxidation rate of 1-isopropyl-2-naphthol was not noticeably affected by the addition of 0.1 mole per mole of substrate of 1-hydroperoxy-1-isopropyl-2(1H)-naphthalenone (120), although, in this case, no inhibition period was recorded.

When the autoxidation of 1-isopropyl-2-naphthol or 1-methyl-

3,6-di-t-butyl-2-naphthol was carried out in the presence of triphenylphosphine, the rate was drastically reduced. Two reasons can be proposed for this phenomenon. The alkoxy radical (RO$^{\bullet}$) produced by the reaction (Introduction ref. 1(a)),

$$ROO^{\bullet} + Ph_3P \longrightarrow Ph_3P{=}O + RO^{\bullet} ,$$

may be incapable of propagating the chain. A more likely explanation is that the removal of the hydroperoxide (ROOH) as it is produced could reduce the initiation rate effectively to zero.

$$ROOH + Ph_3P \longrightarrow Ph_3P{=}O + ROH .$$

The results discussed above indicate that initiation is a major factor in determining the overall rate of autoxidation, and that the stability of the O-O bond in the product hydroperoxides to homolysis will affect this rate. It was found that the hydroperoxides produced in the autoxidation of the 2-naphthols under investigation displayed a wide range of stabilities to light and heat, although the mechanism of decomposition is probably ionic in nature in the majority of cases. The stability of these hydroperoxides does not correlate with the rates of autoxidation of the parent naphthols. For example, the isopropyl hydroperoxides (120) and (124), and the dimethyl hydroperoxide (109) were found to be extremely stable to both heat and light over prolonged periods, although the parent naphthols were found to autoxidise rapidly. The dissociation energy of the O-O bond in alkyl hydroperoxides has been found to be a function of the degree of branching at the α-carbon atom (Introduction ref. 1(a)). The series of hydroperoxides prepared in the course of this work are structurally very similar, all of them bearing a tertiary carbon $\underline{\alpha}$ to the hydroperoxy group. The reactivity of the series of 2-naphthols to oxygen cannot therefore be related to the rate of initiation by the derived hydroperoxides.

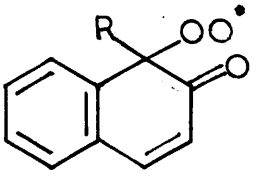
Although initiation is undoubtedly a contributing factor in

determining the overall rate of autoxidation of 2-naphthols, it cannot be invoked to rationalise their relative reactivities. 1-Methyl-2-naphthol and 1-phenyl-3,6-di-t-butyl-2-naphthol do not autoxidise at an appreciable rate even in the presence of potential initiators such as cobalt III acetylacetonate, alkaline potassium ferricyanide, or the isopropyl hydroperoxide (120). A comparison of the relative rates of autoxidation of the substituted 2-naphthols in the presence of the same radical initiator (see Introduction p. 5) would help to elucidate the role of initiation in these processes.

Propagation (step (c)) : $ROO^{\bullet} + RH \longrightarrow ROOH + R^{\bullet}$.

The abstraction of a hydrogen atom from the substrate (RH) by the intermediate peroxy radical ($ROO^{\bullet}$) is normally found to be the rate determining propagation step in the autoxidation reactions (see Introduction p. 5). The rate of this step can be influenced by several factors, which have been discussed fully in the introduction.

The reactivity of the intermediate peroxy radical can have a substantial effect upon the rate of this propagating step. It has been shown that the reactivity of alkyl peroxy radicals to hydrogen abstraction is a function of the degree of branching on the α-carbon, and that peroxy radicals of similar structure have similar reactivities (Introduction, p. 9). The peroxy radicals (125) involved in the autoxidation of substituted 2-naphthols are all tertiary at the α-carbon, and so should have similar reactivities towards hydrogen abstraction.



(125)

This hypothesis could be readily tested by studying these autoxidations in the presence of the same hydroperoxide, such as t-butyl hydroperoxide so that the propagation step (c) involves the same peroxy radical (e.g. $^{t}BuOO^{\cdot}$) in each case (Introduction, p. 8, ref. 11).

The dissociation energy of the R-H bond is also important in determining the rate of step (c). In the case of hydrocarbons, where a C-H bond must be cleaved (dissociation energy ca. 84-104 kcal. $mole^{-1}$), this step can be endothermic, since the ROO-H bond (dissociation energy ca. 88 kcal. $mole^{-1}$) can be considerably weaker. The normal strength of the O-H bond in phenols (ca. 85 kcal. $mole^{-1}$) has been found to be considerably reduced (ca. 76 kcal. $mole^{-1}$) in the case of sterically congested phenols (Introduction, p. 23), so that, in these cases, step (c) would be expected to be fairly exothermic. The O-H bond strength in strained 2-naphthols may be considerably weaker than in unstrained cases as a result of distortions of bond lengths and bond angles, so that the propagating step (c) would be accelerated.

The ease of hydrogen abstraction from the substrate (RH) is also affected by the stability of the radical ($R^{\cdot}$) being produced. Free radical stability can be influenced by delocalisation, polar and steric factors (Introduction, p. 12).

The major stabilising influence upon naphthoxy radicals, and phenoxy radicals in general, is delocalisation of the unpaired electron through the aromatic nucleus, and any distortions as a result of strain would be expected to destabilise the naphthoxy radical in this sense, thus retarding the hydrogen abstraction step.

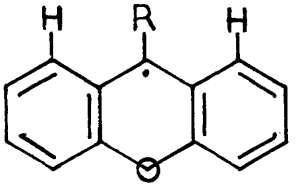
Electron releasing groups would be expected to stabilise the naphthoxy radicals, electron withdrawing groups having the opposite effect. Thus, 1-t-butyl-2-naphthoxy and 1-methyl-3,6-di-t-butyl-2-naphthoxy would be expected to be more stable than 1-methyl-2-naphthoxy, and 6-bromo-1-isopropyl-2-naphthoxy would be expected to be less stable

than 1-isopropyl-2-naphthoxy. However, 1-methyl-2-naphthoxy should be stabilised by hyperconjugation, whereas 1-t-butyl-2-naphthoxy should not. 1,8-Dimethyl-2-naphthoxy should be less stable than 1-methyl-6-t-butyl-2-naphthoxy if inductive release by alkyl groups is important, but the former autoxidises rapidly, and the latter was found to be virtually inert towards oxygen. While electronic factors probably play some rôle in determining the rate of autoxidation of these naphthols, it seems improbable that they could adequately account for the observed differences in these rates. However, the rate of autoxidation of 6-bromo-1-isopropyl-2-naphthol relative to 1-isopropyl-2-naphthol (ca. 1 : 4 respectively) could be rationalised by electronic differences.

Steric effects may influence the rate of step (c) in several ways. Steric crowding in the region of the O-H bond may retard the hydrogen abstraction by the attacking peroxy radical. The stability of some stable phenoxy radicals to oxygen has been rationalised in this manner, and 1-phenyl-3,6-di-t-butyl-2-naphthol may be stable for this reason. However, the order of reactivity of the naphthols cannot be explained on this basis, e.g. 1-t-butyl-2-naphthol is extremely unstable, whereas 1-methyl-2-naphthol is not.

The formation of a naphthoxy radical from a sterically strained 2-naphthol is unlikely to decrease the strain in the system, unless the radical can adopt a non-planar configuration at C-1. Any departure from planarity in the naphthoxy radical should be energetically expensive, since this would decrease the degree of resonance delocalisation of the unpaired electron. There is no evidence that in-plane deformations should be more facile in the naphthoxy radical relative to the parent naphthol. Sevilla et al.[106] have shown by e.s.r. and theoretical calculations that the 9-alkyl-xanthyl free radicals (126, R = H, Me, Et, ^{i}Pr, Ph) are planar, despite the severe peri-strain in

some of these cases. The barrier to rotation of the 9-substituent was found to increase with the degree of α-branching, which indicates that the steric congestion increases proportionately. All of these radicals were found to react rapidly with oxygen.



(126)

It therefore seems reasonable to assume that the intermediate 2-naphthoxy radicals under discussion are planar, and that no relief of peri-strain is achieved in the hydrogen abstraction step.

It has been found that the propagation rates of many autoxidation reactions are dependent upon the concentration of substrate, and this has been interpreted as evidence for a rate-controlling hydrogen-abstraction step. An investigation of the influence of naphthol concentration upon the rate of these autoxidations may therefore be of value in determining the factors controlling the relative autoxidation rates.

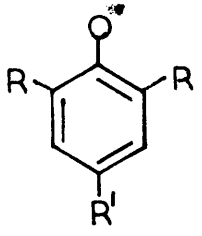
Large deuterium isotope effects have been measured for some radical-chain processes. 2,6-Di-t-butyl-4-methylphenol-OD was found a much poorer antioxidant than the undeuteriated phenol (ArOH) (Introduction, p. 22), which indicates that the chain transfer process,

$$ArOH + ROO^{\cdot} \longrightarrow ArO^{\cdot} + ROOH$$

is a slow step in the radical chain process. The rates of autoxidation of deuteriated 2-naphthols should be slower than those of the undeuteriated compounds if step (c) is rate determining. However, it is conceivable that the kinetics may be drastically altered by the replacement of the phenolic H by deuterium.

Propagation (step (b)) : $R^{\bullet} + O_2 \longrightarrow ROO^{\bullet}$

This step is normally considered to be fast and non rate-determining in autoxidation reactions, and assumed to be diffusion controlled (Introduction, p. 5). However, for particularly stable radicals, the reaction with oxygen can be slow. The triphenylmethyl radical reacts slowly, and reversibly with oxygen to form the triphenylmethylperoxy radical. The rate of reaction of hindered phenoxy radicals with oxygen is dependent upon structure.



Time taken for complete autoxidation: R = R' = ^{t}Bu , 0.5 hours

R = ^{t}Bu, R' = Ph , 8 hours

R = R' = Ph , v. slow reaction.

Electron withdrawing substituents, or those extending the delocalisation of the unpaired electron, decrease the reactivity of phenoxy radicals towards oxygen[54]. It is generally assumed that steric hindrance to attack by molecular oxygen is not important, oxygen having a low steric requirement.

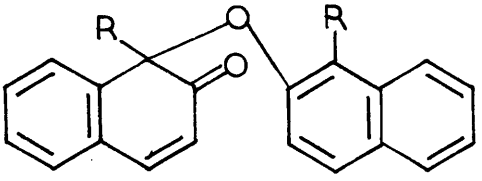
2-Naphthoxy radicals should be stabilised relative to phenoxy radicals, by virtue of the more extensive delocalisation of the unpaired electron. It therefore seems reasonable to postulate that the slow step in the autoxidation of 2-naphthols may be step (b). The reaction of the 2-naphthoxy radical with oxygen would be accelerated by factors which destabilise the naphthoxy radical relative to the peroxy radical being produced. This could occur in the case of the strained 2-naphthols under investigation, since the unfavourable peri-interaction is not present in the product peroxy radicals. The slow rate of

autoxidation of 6-bromo-1-isopropyl-2-naphthol relative to 1-isopropyl-2-naphthol is compatible with this proposal, since electron withdrawing substituents are known to stabilise phenoxy radicals with respect to their rate of reaction with oxygen. I have found that the naphthols react much more slowly in air than in pure oxygen (especially 1-t-butyl-2-naphthol - see p. 71) which suggests that the rate depends on the oxygen concentration. In the autoxidation of 1-ethyl-2-naphthol[2], it was found that dimerisation of 1-ethyl-2-naphthoxy radicals competed successfully with the reaction of these radicals with oxygen (see p. 41), indicating that these processes occur at similar rates. It could be argued that for the more sterically hindered 2-naphthoxy radicals, e.g. 1-t-butyl-2-naphthoxy, steric hindrance to dimerisation is prohibitive, but I found that this process did occur when the oxygen concentration was low (see p. 72). In the autoxidation of 1,8-dimethyl-2-naphthol, no naphthoxy radical dimer was detected, although no hindrance to dimerisation can be invoked in this case. Oxygenation of 1-methyl-2-naphthol or 1-phenyl-2-naphthol in the presence of potential radical initiators did not give any hydroperoxides. This indicates that the 2-naphthoxy radicals, which must be produced under these conditions, react more slowly with oxygen than with each other in these cases. A quantitative study of the effect of oxygen concentration upon the rate of autoxidation of 2-naphthols would help to determine the role of step (b) in these reactions.

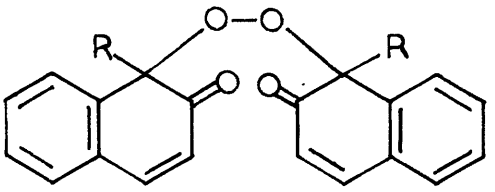
Termination (step (d)) : $\left.\begin{matrix} R^{\cdot} \\ ROO^{\cdot} \end{matrix}\right\} \longrightarrow$ molecular products.

The rate of termination has been found to affect the overall rate of autoxidation reactions (Introduction, p. 9). A consideration of the factors influencing the termination step does not help to rationalise the relative rates of autoxidation of 2-naphthols. The structurally similar peroxy radicals involved should dimerise at similar rates.

Dimerisation of 2-naphthoxy radicals to form O-C dimers (3), or reaction of a naphthoxy radical with a peroxy radical to form peroxides (128), should be particularly favoured when the group R is small, or when the naphthoxy radical reacts slowly with oxygen.



(3)



(128)

The dimer (3, R = Et) was isolated in considerable yield from the autoxidation of 1-ethyl-2-naphthol[2], but was not detected in the products from the autoxidation of 1,8-dimethyl-2-naphthol. The peroxides (128) have not been detected in this work. Peri-strain may be expected to accelerate rather than retard the termination steps involving the production of (3) or (128) since, in both cases, the formation of a tetrahedral C-1 should remove this interaction.

Summary :

Two plausible rationalisations of the observed rate of autoxidation of substituted 2-naphthols emerge from a consideration of the mechanism.

(a) The distortions caused by peri-interactions and other buttressing effects may result in a weakening of the O-H bond, thus facilitating the hydrogen abstraction step (c).

(b) The reaction of the intermediate phenoxy radical with oxygen (step (b)) maybe accelerated by increased peri-strain, this strain being alleviated when C-1 becomes tetrahedral.

Much more quantitative kinetic investigations are necessary before any definitive theories can be proposed to explain the observed autoxidation rates. It is conceivable that the kinetics, or even the detailed mechanism, may vary from one case to another. However, there can be little doubt that unfavourable steric interactions accelerate

the overall rate of autoxidation of 2-naphthols. This observation could be employed to predict the stability of unknown 2-naphthols, and also to rationalise the known reactivity of other enols, phenols, and enamines towards oxygen (Introduction, pp. 19-28).

Evidence of peri-strain within 2-naphthols.

Many of the compounds studied in the course of this work display anomalous chemical and spectroscopic (n.m.r., u.v., m.s.) characteristics. These have been discussed fully at appropriate points in the text.

In an attempt to obtain a more quantitative estimate of steric strain within these molecules, an X-ray structural determination of a series of 2-acetoxynaphthalenes has been undertaken.

A series of ^{13}C n.m.r. spectra were obtained, in the hope that some estimate of peri-strain may emerge from a comparison of chemical shifts. Analysis of the spectra of 2-methoxynaphthalene, 1-methyl-2-methoxynaphthalene, and 1,8-dimethyl-2-methoxynaphthalene, and comparison with literature spectra of methylnaphthalenes[109], does not lead to any simple additivity rules for this series of molecules. Doddrell[109] found that, while the majority of dimethylnaphthalenes obey simple additivity rules, none of the carbon resonances in the spectrum of 1,8-dimethylnaphthalene correlated with these rules. The ^{13}C n.m.r. spectrum of 1,8-dimethyl-2-methoxynaphthalene with tentative assignments made by comparison with published data and other spectra in hand, is laid out below. These resonances do not correlate with any additivity relationships which can be set up for substituted naphthalenes or benzenes.

$\delta(CDCl_3)$ 155.5, singlet, (C-2), 134.6 and 134.3, singlets, (C-8, C-9), 130.8, singlet, (C-10), 130.0, 128.3, and 127.6, doublets, (C-4, C-5, C-7), 123.0, doublet, (C-3), 121.3, singlet, (C-1), 113.4, doublet, (C-6), 56.8, quartet, (OCH_3), 26.2, quartet, ($8\text{-}CH_3$), 15.0, quartet, ($1\text{-}CH_3$).

EXPERIMENTAL.

General :

Melting points (m.p.) were recorded on a Kofler microscope hot-stage, and are uncorrected.

Routine infra-red (i.r.) spectra (Nujol mulls, liquid films) were recorded on Pye Unicam S.P. 200 or Perkin Elmer 257 spectrophotometers; solution, and potassium bromide disc (KBr) i.r. spectra were recorded on Perkin Elmer 257 or 225 spectrophotometers.

Ultra-violet (u.v.) spectra were measured on a Pye Unicam S.P. 800 spectrophotometer as solutions in 95% ethanol. Extinction coefficients are quoted as log values, and are placed in brackets.

Nuclear magnetic resonance (n.m.r.) spectra were recorded on Varian T-60 and H.A. 100 spectrometers, using approximately 0.3M solutions in deuteriochloroform, unless otherwise stated, employing tetramethylsilane as an internal standard. Double irradiation experiments were carried out on the Varian H.A. 100 instrument. Carbon-13 n.m.r. spectra were recorded by the University of Edinburgh Fourier Transform Service.

Mass spectra (m.s.) were recorded on a G.E.C.-A.E.I. M.S. 12 spectrometer. The molecular ion (M^+) is quoted first in all cases. All peaks are quoted as a fraction of the base peak (100). High resolution mass measurements were made on a A.E.I. M.S. 90 2S machine.

Microanalyses were carried out by Miss F. Cowan and Mrs. W. Harkness.

Analytical gas-liquid chromatography (g.l.c.) was carried out on a Perkin Elmer F11 instrument using a flame ionisation detector, and a 2½% S.E. 30 column. Thin layer chromatography (t.l.c.) was carried out using Merck Kieselgel H.F. 254 and developed in 20% ethyl acetate-light petroleum (b.p. 60-80°) unless otherwise stated. Preparative chromatoplates (1 mm. thick) (p.l.c.) were prepared and developed using

the same materials and conditions unless otherwise stated.

Solutions were dried over anhydrous magnesium sulphate, and solvents removed on a rotary evaporator. All experiments involving reactants or products which are unstable to oxygen were carried out in an atmosphere of dry nitrogen, and worked up under nitrogen using de-oxygenated solvents. In oxygenation experiments, the term 'quantitatively oxygenated' indicates that the uptake was measured at regular intervals. The 'standard conditions' used for these experiments are defined in the experimental section.

EXPERIMENTAL

Friedel-Crafts t-butylation of 2-methoxynaphthalene.

Finely ground aluminium chloride (0.5 g.) was mixed thoroughly with 2-methoxynaphthalene (6.3 g., 0.04 mole) and the mixture suspended in anhydrous light petroleum (b.p. 60-80°) (25 ml) in a round-bottomed flask fitted with a reflux condenser and a drying tube. t-Butyl chloride (8.3 g., 0.1 mole) was added and the system was then refluxed for six hours, after which time t.l.c. (5% EtOAc-petrol) indicated the complete disappearance of starting material, and the formation of two less polar products, as well as some polymeric material.

Dilute hydrochloric acid was carefully added to the cooled reaction mixture, and the organic layer separated off. The aqueous layer was extracted with ether (3 x 25 ml), and the combined organic extracts washed to neutrality with water, dried, and solvent removed to give a pale yellow, low melting solid.

Fractional crystallisation of the mixture from methanol-water gave colourless plates of the less soluble 6-t-butyl-2-methoxy-naphthalene (6, R = Me), (3.8 g., 44%), m.p. 75.5-76.5°, (lit. 95° [19], 35° [22]),

$\lambda_{max.}$(EtOH) 229(5.0), 250(sh.), 259.5(3.63), 269(3.61), 303(sh.), 316(3.13), 330(3.31) nm.

$\nu_{max.}$(KBr) 1395 and 1365 (^{t}Bu deformation), 820 and 810 (2 sets of 2 adjacent aromatic H) cm^{-1}.

τ($CDCl_3$) 2.17-2.97, multiplet, 6H, (Aromatics), 6.10, singlet, 3H, ($-OC\underline{H}_3$), 8.60, singlet, 9H, ($-C(C\underline{H}_3)_3$).

m/e 214(M^+, 30), 199(100).

Required for $C_{15}H_{18}O$: C 84.07% , H 8.46%

Found : C 84.16% , H 8.31% .

Repeated crystallisation from methanol-water gave a pure sample of 3,6-di-t-butyl-2-methoxynaphthalene (8, R = Me) as colourless plates (2.1 g., 19%), m.p. 81-82°.

$\lambda_{max.}$(EtOH) 233(4.7), 253(3.70), 262(3.76), 272(3.72), 300(sh.), 314(3.30), 328.5(3.41) nm.

$\nu_{max.}$(KBr) 1390, 1385, 1360, 1355 (^{t}Bu deformations), 850 (2 adj. aromatic H), cm^{-1}.

$\tau(CDCl_3)$ 2.20-2.70, multiplet, 4H, (4 aromatic H), 2.90, broad singlet, 1H (aromatic $\underline{H}_1$), 6.12, singlet, 3H ($-OC\underline{H}_3$), 8.62 and 8.54, singlets, 18H ($-C(C\underline{H}_3)_3$).

m/e 270(M^+, 25), 255(100).

Required for $C_{19}H_{26}O$: C 84.41% , H 9.65%

Found : C 84.67% , H 9.40% .

The mother liquors contained only these two compounds (comparative g.l.c. and t.l.c.), no trace of starting material being detected. G.l.c. analysis indicated that the original product mixture consisted of ca. 60% of the mono-t-butyl derivative, and 40% of the di-t-butyl derivative.

Attempts to produce a tri-t-butyl derivative using prolonged reaction times resulted in extensive polymerisation, and increasing proportions of the di-t-butyl derivative.

Treatment of the mono-t-butyl derivative with aluminium chloride and t-butyl chloride under identical conditions gave a similar mixture of the mono- and di-t-butyl compounds.

Methylation of the t-butyl-2-naphthols (6, R = H) and (8,R = H).

6-t-Butyl-2-naphthol (2.0 g., 0.01 mole) (prepared by Friedel-Crafts t-butylation of 2-naphthol[2]) was dissolved in anhydrous dmso (5 ml), and added dropwise, under dry nitrogen, to a stirred suspension of petrol-washed sodium hydride (0.014 mole) in anhydrous dimethyl sulphoxide (10 ml). Methyl iodide (2.1 g., 0.15 mole) was then added

to the solution in three portions, which was then stirred for fifteen minutes.

The reaction mixture was carefully diluted with crushed ice (ca. 30 g.), and extracted with ether (3 x 25 ml). The combined extracts were washed thoroughly with water, dried, and solvent removed to give 6-t-butyl-2-methoxynaphthalene (6, R = Me) which on crystallisation from methanol-water or ethanol-water gave colourless plates, (2.0 g., 93%), m.p. and mixed m.p. 75.5-76.5°, identical in all respects to samples obtained by t-butylation of 2-methoxynaphthalene. The same product could be prepared in quantitative yield by methylation using aqueous sodium hydroxide and dimethyl sulphate.

Methylation of 3,6-di-t-butyl-2-naphthol (prepared by Friedel-Crafts t-butylation of 2-naphthol[2]) using sodium hydride in dmso, followed by methyl iodide, gave a 94% yield of 3,6-di-t-butyl-2-methoxynaphthalene (8, R = Me), recrystallised from methanol-water as colourless plates m.p. and mixed m.p. 81-82°, identical in all respects to the product of di-t-butylation of 2-methoxynaphthalene.

Oxidation of 3,6-di-t-butyl-2-naphthol with lead tetraacetate.

3,6-Di-t-butyl-2-naphthol (1.28 g., 0.05 mole) was dissolved in glacial acetic acid (15 ml), and acetic anhydride (1 ml). The solution was cooled to 0°, and freshly crystallised lead tetraacetate (3.0 g.) added. The mixture was left at room temperature for one hour, moisture being excluded, and the acetic anhydride distilled off, leaving ca. 5 ml in the reaction flask. The residue was diluted with water, and extracted with ether (3 x 20 ml). The combined extracts were washed with water, saturated aqueous sodium bicarbonate, and finally with brine. The solution was dried, and solvent removed to give a red, low melting solid. T.l.c. indicated that no starting naphthol remained, and that two products had been produced.

Fractional crystallisation from ethanol-water gave the less

soluble 3,6-di-t-butyl-1,2-naphthaquinone (10) as bright red needles, m.p. 134-5°.

$\lambda_{max.}$(EtOH) 225(3.41), 260(4.44), 348(3.69), 414(3.26), nm.

$\nu_{max.}$(Nujol) 1690, 1660 (conjugated C=O), 860 (isolated aromatic H), 810 (2 adj. aromatic H) cm^{-1}.

τ ($CDCl_3$) 1.90-2.85, multiplet, 4H, (Aromatics and C<u>H</u>=C-C=O), 8.60 and 8.65, singlets, 18H, ($(C\underline{H}_3)_3C$-).

m/e 270(M^+) .

Required for $C_{18}H_{22}O_2$: C 79.97% , H 8.17%

Found : C 79.75% , H 8.05% .

The less polar species, 1,1-diacetoxy-3,6-di-t-butyl-2(1H)-naphthalenone (9), crystallised as colourless needles from ethanol-water, m.p. 146-148°.

$\lambda_{max.}$(EtOH) 245, 329 nm.

$\nu_{max.}$(Nujol) 1750 (CH_3COO-), 1680 (conj. C=O) cm^{-1} .

τ ($CDCl_3$) 2.3-2.9, multiplet, 4H (aromatics and C<u>H</u>=CH-C=O), 8.05, singlet, 6H ($C\underline{H}_3COO$-), 8.76, singlet, 18H ($-C(C\underline{H}_3)_3$, accidentally coincident).

Treatment of the diacetate (9) with aqueous ethanolic potassium carbonate on a steam bath for two hours, and crystallisation of the product from ethanol-water gave a quantitative yield of the quinone (10) (overall yield from 3,6-di-t-butyl-2-naphthol 98%).

1-t-Butyl-2-naphthol (37).

Attempted preparation of 1-t-butyl-2-methoxynaphthalene (48) from 1-bromo-2-methoxynaphthalene.

Treatment of 1-bromo-2-methoxynaphthalene with t-butylmagnesium bromide in refluxing ether for one hour gave a quantitative yield of 2-methoxynaphthalene, identical in all respects to an authentic sample. The addition of anhydrous copper iodide to an ethereal solution of

t-butylmagnesium bromide at -70° [24], followed by slow addition of an ethereal solution of 1-bromo-2-methoxynaphthalene, and subsequent stirring at room temperature for six hours gave only 2-methoxynaphthalene and unchanged starting material.

Attempted preparation of 1-t-butyl-3,4-dihydronaphthalene (14).

t-Butyl magnesium chloride (0.15 mole) was prepared as an ether solution (25 ml) and excess magnesium filtered off. To the stirred solution, under nitrogen, was added dropwise redistilled, anhydrous α-tetralone (14.6 g., 0.1 mole) over one hour. The mixture was stirred for a further two hours, and left overnight at room temperature under dry nitrogen.

A saturated solution of ammonium chloride was carefully added with stirring, and the ether layer separated off. The aqueous layer was extracted with ether (2 x 25 ml), and the combined ether extracts washed to neutrality, dried, and solvent removed to give a pale yellow oil (17.3 g.). T.l.c. indicated the presence of four components, including starting material, the other three being more polar.

Comparative t.l.c. and n.m.r. indicated that a major product was α-tetralol, (prepared independently by the treatment of α-tetralone with LAH in anhydrous ether), as well as the derived dehydration product, 1,2-dihydro-naphthalene. N.m.r. of the mixture indicated the presence of at least two t-butylated products.

Attempts to remove the starting ketone using Girard 'T' reagent were unsuccessful.

The oil was treated with thionyl chloride in anhydrous pyridine to dehydrate all alcohols present. The i.r. spectrum of the recovered material indicated that this had been achieved (disappearance of OH bands).

The mixture was subjected to chromatography, and pure samples of α-tetralone and 1,2-dihydronaphthalene were obtained. A pure sample of 1-t-butyl-3,4-dihydronaphthalene (14) was not obtained. All fractions

containing t-butylated material were intractable mixtures of unidentified, and presumably rearranged, compounds.

Preparative t.l.c. gave samples of the desired material as an inseparable mixture with 1,2-dihydronaphthalene. (g.l.c. analysis). The use of silica plates incorporating silver nitrate did not improve the separation. Vacuum distillation led to extensive polymerisation.

The n.m.r. ($CDCl_3$) of the impure 1-t-butyl-3,4-dihydronaphthalene (14) showed a multiplet between τ 2.2-3.0, a triplet at τ 3.96, J = 5 Hz, 1H, (C=C<u>H</u>-CH_2-), a multiplet between τ 6.4-8.2, (-C<u>H</u>$_2$-), and a singlet at τ 8.67 (-C(C<u>H</u>$_3$)$_3$). By comparison of integrals, and employing g.l.c. analysis, this material was estimated to contain <u>ca</u>. 30% of 1,2-dihydronaphthalene.

$\nu_{max.}$ (liquid film) 1392 and 1363 cm^{-1} (^{t}Bu deformations).

The reaction was repeated several times, using large excesses of Grignard reagent, and heat (refluxed for up to 72 hours in ether and tetrahydrofuran), but no improvement on the overall yield of the desired material was achieved. (Maximum yield of 1-t-butyl-3,4-dihydronaphthalene estimated by g.l.c. and n.m.r. <u>ca</u>. 20%).

<u>Attempted preparation of t-butyl-benzene via cumyl bromide.</u>

A solution of hydrogen bromide in glacial acetic acid (0.025 mole) was dissolved in ether (20 ml), and added dropwise to a stirred solution of α-methylstyrene (2.36 g., 0.02 M) in ether (40 ml) at 0°. The mixture was left standing for three hours.

The solution was diluted with iced water (30 ml), and the ether layer separated off. The aqueous layer was extracted with ether (2 x 25 ml), and the combined ether extracts washed with iced water, saturated aqueous sodium bicarbonate, and finally with brine. The solution was then evaporated to 20 ml under reduced pressure without heating, and dried three times over anhydrous magnesium sulphate

before being placed in a dropping funnel at 0°.

A small sample was taken up in $CDCl_3$ and ether was removed under reduced pressure. Cumyl bromide has the following spectral characteristics $\nu_{max.}$(liquid film) 1380, 1390 ($-C(CH_3)_2-$ deformation), 770 (5 adj. aromatic H), (cf. α-methylstyrene $\nu_{max.}$(liquid film) 1625 (C=C stretch), 890 ($C=CH_2$ deformation), 780 (5 adj. aromatic H).
τ ($CDCl_3$) 2.26-2.90, multiplet, 5H (aromatics), 7.80, singlet, 6H, ($-(CH_3)_2C-$).
Traces of α-methylstyrene were detected in all spectra.

The solution of cumyl bromide in anhydrous ether (20 ml) was added dropwise with stirring to a solution of methyl magnesium bromide (0.025 mole) in ether (15 ml), and the mixture was stirred at room temperature for four hours before being refluxed for eight hours. To the cooled reaction mixture was added a saturated aqueous solution of ammonium chloride. The organic layer was separated off, and the aqueous layer extracted with ether (2 x 25 ml). The combined ether extracts were washed with water, dried, and the ether solvent carefully removed without heating, to give a low melting, colourless solid.

N.m.r. of the product indicated the presence of the starting α-methylstyrene (ca. 25%), but no trace of t-butylbenzene could be detected (by comparison with authentic spectra). Recrystallisation from pentane gave colourless rhombs (1.77 g., 75%), m.p. 115-118°, (lit.[32] 118-118.5°), of 1,2-diphenyl-1,2-dimethylbutane (19).
$\lambda_{max.}$(c-hexane) 217, 258(2.62), 242(sh.), 248(sh.), 252(2.53), 265(2.53) nm.
$\nu_{max.}$ 1602, 1500 (Aromatic C=C), 1380, symmetrical doublet ($-C(CH_3)_2$ deformation), 765 (5 adj. aromatic H) cm^{-1}.
τ ($CDCl_3$) 2.94, singlet, 10H, (Aromatics), 8.70, singlet, 12H, ($-CH_3$).
m/e 238(M^+).

The reaction was repeated in the presence of anhydrous cuprous iodide (1 mole per 2 moles of Grignard reagent) at room temperature

for twelve hours. The only isolated product apart from starting material, was the cumyl dimer (19) in 80% yield.

Attempted preparation of 1-t-butyl-2-methoxynaphthalene (48) from 1-isopropenyl-2-methoxynaphthalene (26).

Dry hydrogen chloride gas was bubbled through a stirred solution of 1-isopropenyl-2-methoxynaphthalene (300 mgs., 1,5 mmole) (for preparation see below) in anhydrous ether (50 ml) at 0° for four hours. The solution was then poured onto crushed ice (100 g.), and the ether layer separated off. The aqueous layer was extracted with ether (2 x 25 ml), and the combined ether extracts were washed to neutrality with iced water, and dried three times over anhydrous magnesium sulphate before being reduced to 40 ml without heating, and dried yet again.

This solution was then added dropwise, under dry nitrogen, to a stirred solution of methyl magnesium bromide (10.0 mmole) in anhydrous ether (10 ml) over one hour at room temperature. After standing at room temperature for 20 hours, t.l.c. indicated that a trace of the desired 1-t-butyl-2-methoxynaphthalene had been produced.

The solution was refluxed for four hours. The cooled reaction mixture was then diluted with saturated aqueous ammonium chloride solution, and the organic layer separated off. The aqueous layer was extracted with ether (2 x 25 ml), and the combined ether extracts washed to neutrality, dried, and solvent removed to give a pale yellow oil (300 mgs.). T.l.c. (30% benzene-petrol) indicated the presence of 1-isopropenyl-2-methoxynaphthalene (26) and 1-t-butyl-2-methoxy-naphthalene (48). Comparative g.l.c. and n.m.r. indicated that the product contained ca. 6% of the desired product, (for spectral data see below), the only other identified material being starting material.

The action of Grignard reagents upon 1-methoxycarbonyl- and 1-acetyl-2-naphthol.

1-Acetyl-2-naphthol.

This was prepared by the Fries rearrangement[34] of 2-acetoxy-naphthalene (prepared from sodium 2-naphthoxide and acetic anhydride). Equimolar amounts of 2-acetoxynaphthalene and aluminium chloride were mixed thoroughly in a mortar before being heated at 60°, the temperature being raised slowly to 110° over one hour, and held at that temperature for a further hour.

The reaction mixture was finely ground, and slowly added, with stirring to a large volume of crushed ice. The solution was acidified, and the resulting precipitate filtered off and washed with water. Several recrystallisations from light petroleum gave pale yellow rhombs, m.p. 63-64° (lit.[34] 64°) in 82% yield. Small quantities of 2-naphthol (12%) and 6-acetyl-2-naphthol (4%) were also isolated.

1-Acetyl-2-naphthol had the following spectral characteristics.

$\nu_{max.}$ ($CHCl_3$) ca. 2500-3500 (chelated OH), 1625 (C=O) cm^{-1}.

(KBr) 1620 (C=O), 825 (2 adj. aromatic H), 757 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) -4.6, singlet, 1H, (OH, D_2O exchange), 1.8-3.0, multiplet, 6H (Aromatics), 7.20, singlet, 3H (CH_3-C=O).

Many attempts to prepare this compound using the reported conditions[34] gave very low yields, the major product being 2-naphthol.

1-Acetyl-2-methoxynaphthalene (24) was prepared by methylation (NaH, dmso, MeI) of 1-acetyl-2-naphthol (86% yield). Crystallisation from light petroleum gave pale yellow prisms, m.p. 57-59° (lit.[34] 57-9°),

$\lambda_{max.}$ (EtOH) 225(4.80), 280.5(3.58), 290(3.59), 320(sh.), 333.5(3.49) nm.

$\nu_{max.}$ (KBr) 1688 (conj. C=O), 815 (2 adj. arom.H), 755 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.1-2.9, multiplet, 6H (aromatics) 6.12, singlet, 3H (CH_3O-), 7.40, singlet, 3H (CH_3-C=O). m/e 200(M^+).

2-(2-Hydroxy-1-naphthyl)propan-2-ol(38) and 1-isopropenyl-2-naphthol (39).

A solution of methyl magnesium iodide (3 mmole) was prepared in anhydrous ether (20 ml) under dry nitrogen, and a solution of 1-acetyl-2-naphthol (190 mg., 1 mmole) in ether (10 ml) was added dropwise with stirring. A white precipitate formed immediately. The mixture was refluxed for two hours, when t.l.c. indicated that very little product had been formed. When the mixture had been refluxed for twelve hours, the reaction was worked up using saturated aqueous ammonium chloride. Recrystallisation of the product from pentane gave colourless needles, m.p. 107-111° (decomposition) (154 mg., 75%) of 2-(2-hydroxy-1-naphthyl) propan-2-ol (38).

$\nu_{max.}$(Nujol) 3,300-2,400 (chelated OH), 1380, 1355 ($(CH_3)_2C$- deformation), 828 (2 adj. arom.H), 765 (4 adj. arom.H), cm^{-1}.

τ ($CDCl_3$) -1.20, broad singlet, 1H (chelated O<u>H</u>, D_2O exchange), 6.70, broad singlet, 1H (-O<u>H</u>, D_2O exchange), 2.1-3.0, multiplet, 6H, (aromatics), 8.03, singlet, 6H, ($(C\underline{H}_3)_2C$-).

This compound was completely stable to atmospheric oxygen over prolonged periods, but dehydrated on standing to 1-isopropenyl-2-naphthol (39). Treatment with dilute hydrochloric acid at room temperature gave a quantitative conversion to (39), b.p. 72°/0.015 mm.

$\lambda_{max.}$(EtOH) 229(4.8), 267(3.61), 277(3.71), 287(3.62), 333(3.42) nm.

$\nu_{max.}$(liquid film) 3,500 (OH), 1620 (conj. C=C), 910 ($C=CH_2$), 820 (2 adj. arom.H), 750 (4 adj. arom.H) cm^{-1}.

τ($CDCl_3$) 1.9-3.0, multiplet, 6H (aromatics), 4.23, broad singlet, 1H, (O<u>H</u>, D_2O exchange), 4.37 and 4.85, multiplets, 2H (CH_3-C=C<u>H</u>$_2$), 7.88, doublet, J = 1 Hz., 3H, ($C\underline{H}_3$-C=CH_2).

All attempts to obtain a sample suitable for analysis (preparative chromatography or vacuum distillation) were unsuccessful, owing to polymerisation (especially rapid on silica).

Treatment of a fairly pure sample of the naphthol (39) with acetic

anhydride in anhydrous pyridine for twelve hours at room temperature followed by an aqueous work-up and ether extraction gave a pure sample of 2-acetoxy-1-isopropenylnaphthalene, as colourless needles from pentane, m.p. 31-35°,

$\lambda_{max.}$(EtOH) 230(4.8), 271(3.78), 281(3.85), 289(3.71), 320(2.69) nm.

$\nu_{max.}$(Nujol) 1770 (acetate C=O), 1630 (C=C), 915 (C=CH_2), 810 (2 adj. arom.H), 750 (4 adj. arom.H), cm^{-1}.

τ($CDCl_3$) 2.0-3.1, multiplet, 6H (aromatics), 5.00 and 4.53, multiplet, 2H (C=C$\underline{H}_2$), 7.70, singlet, 3H, ($C\underline{H}_3$-COO), 7.93, doublet, J = 1.5 Hz., 3H ($C\underline{H}_3$-C=CH_2).

m/e 226(M^+, 25), 184(100).

<u>2-(2-Methoxy-1-naphthyl)propan-2-ol (25) and 1-isopropenyl-2-methoxy-naphthalene (26)</u>.

1-Acetyl-2-methoxynaphthalene (2.0 g., 0.01 mole) was taken up in anhydrous ether (20 ml) and added dropwise over one hour to a stirred solution of methyl magnesium iodide (0.015 mole) in ether (50 ml), which was then refluxed under dry nitrogen for three hours.

Saturated aqueous ammonium chloride was carefully added to the cooled reaction mixture, and the ethereal layer separated off. The aqueous layer was extracted with ether, and the combined ethereal extracts washed with water, dried, and solvent removed. Crystallisation from light petroleum gave colourless plates (1.95 g., 91%), m.p. 95-6° (decomposition), of the alcohol (25).

$\nu_{max.}$(Nujol) 3,300 (OH), 1380, 1370 (-C(CH_3)$_2$-), 812 (2 adj. arom.H), 750 (4 adj. arom.H), cm^{-1}.

τ($CDCl_3$) 1.43, broad doublet, J = 9 Hz., 1H (<u>peri-H</u>), 2.2-2.9, multiplet, 5H (Aromatics), 5.49, broad singlet, 1H (-O<u>H</u>, D_2O exchange), 6.08, singlet, 3H (-O$C\underline{H}_3$), 8.09, singlet, 6H (-C($C\underline{H}_3$)$_2$-).

This compound was found to dehydrate on mild heating, and treatment with dilute hydrochloric acid gave quantitative conversion to

1-isopropenyl-2-methoxynaphthalene (26) as a colourless oil,

$\lambda_{max.}$(hexane) 232(4.9), 282(3.74), 294(3.68), 337(3.44) nm.

$\nu_{max.}$(liquid film) 1635 (C=C), 900 ($C=CH_2$), 820 (2 adj. arom.H), 750 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.9-2.8, multiplet, 6H, (Aromatics), 4.45 and 5.00, multiplets, 2H (CH_3-C=C$\underline{H}_2$), 6.05, singlet, 3H, ($C\underline{H}_3O$-), 7.85, doublet, J = 1 Hz., 3H ($C\underline{H}_3$-C=CH_2).

Treatment of methyl 2-hydroxy-1-naphthoate (34) with Grignard reagents.

Treatment of methyl 2-hydroxy-1-naphthoate[39] with excess methyl magnesium iodide in refluxing ether for twelve hours followed by a non-acidic work-up (saturated aqueous ammonium chloride) gave a ca. 75% yield of the tertiary alcohol (38), and 1-acetyl-2-naphthol in ca. 25% yield (see above).

The reaction of (34) with methyl Grignard reagents at elevated temperatures was attempted under a variety of conditions of temperature and reaction time. A general description of the procedure follows.

Methyl 2-hydroxy-1-naphthoate was taken up in anhydrous ether (ca. 1 Molar solution) and added dropwise to a stirred ethereal solution of methyl Grignard reagent (ca. 2 Molar solution, 5-11 Molar excess) which was magnesium-free. The solution was then refluxed under dry nitrogen for 12-24 hours, before distilling off the solvent with exclusion of moisture.

The residue was heated at 110-115° for 18-20 hours. When the reaction was worked up at this stage employing deoxygenated aqueous ammonium chloride, and with rigorous exclusion of oxygen, a mixture containing 1-acetyl-2-naphthol,2-(2-hydroxy-1-naphthyl)propan-2-ol (38), 1-isopropenyl-2-naphthol (39), and 1-t-butyl-2-naphthol (37) was obtained. (Analysed by n.m.r. and comparison with spectra of authentic samples). Details of the proportions of products formed under different conditions are laid out in Table 2 of the Appendix.

The spectral characteristics of 1-t-butyl-2-naphthol (37) will be reported below. This compound could not be isolated from the mixture of products.

Exposure of a chloroform solution of this mixture to atmospheric oxygen for ca. 15 minutes effected the complete disappearance of the signals attributable to (37) in the n.m.r. of the mixture.

Fractional crystallisation from benzene-petrol gave pale yellow prisms, m.p. 134-137° (decomposition) of 1-hydroperoxy-1-t-butyl-2(1H)-naphthalenone (41). (Maximum isolated yield 15%). (Spectral characteristics reported below). On occasions, the m.p. of this compound was considerably lower.

1-t-Butyl-2-methoxynaphthalene (48).

Methyl 2-hydroxy-1-naphthoate (34) was treated with methyl Grignard reagent as described above.

The cooled reaction mixture was taken up in anhydrous dmso (5 ml per gram of (34)), and the solution stirred under dry nitrogen. Methyl iodide was added dropwise to the cooled solution until the bright colour of naphthoxide ions had been discharged. The solution was stirred at room temperature for a further 30 minutes. Water was added, and the solution was extracted thoroughly with light petroleum. The combined extracts were washed several times with water, dried, and solvent removed. Comparative t.l.c. (30% benzene-petrol) and n.m.r. showed that the product mixture contained 1-acetyl-2-methoxynaphthalene (24), 2-(2-methoxy-1-naphthyl)propan-2-ol (25), 1-isopropenyl-2-methoxy-naphthalene (26), and 1-t-butyl-2-methoxynaphthalene (48). The relative proportions of products obtained by this method are laid out in Table 2 of the Appendix.

Isolation of the desired 1-t-butyl-2-methoxynaphthalene (48) from the reaction mixture was complicated by poor separation on t.l.c. from the isopropenyl compound (26). Preparative t.l.c. using silica plates

coated with 10% by weight of silver nitrate, and using 20% benzene-petrol mixtures as solvent, gave a pale yellow oil which contained traces of the isopropenyl compound (26) (<1% by g.l.c.).

For large scale preparations the product was chromatographed on a column of silica coated with 10% by weight of silver nitrate, eluting firstly with petrol, and then with 10% benzene-petrol mixtures, giving an oil containing ca. 15% of the isopropenyl compound (g.l.c.). This was further purified by preparative t.l.c. to give an oil of similar purity to that obtained by preparative t.l.c. of the crude reaction mixture (above).

Vacuum distillation (b.p. $80^{\circ}/0.03$ mm.) gave a colourless oil, which solidified at temperatures below ca. 5°. Yields of 25% of pure 1-t-butyl-2-methoxynaphthalene (48) could consistently be achieved by this method.

$\lambda_{max.}$(EtOH) 232(4.8), 274(sh.), 282(3.74), 291(sh.), 323(3.24), 335(sh.) nm.

$\nu_{max.}$(liquid film) 1392, 1362 ($-C(CH_3)_3$ deformation), 805 (2 adj. arom.H), 745 (adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.54, doublet of doublets, J_{ortho} = 8 Hz., J_{meta} = 3 Hz., 1H, (peri-H), 2.20-2.92, multiplet, 5H, (aromatics), 6.20, singlet, 3H ($-OC\underline{H}_3$), 8.27, singlet, 9H ($-C(C\underline{H}_3)_3$).

There was no observable change in the n.m.r. spectrum on cooling to -150° [48].

Double irradiation of the t-butyl signal resulted in a Nuclear Overhauser Effect on the peri-signal, the enhancement being measured as 20 ± 5% (compared with the other aromatic signals).

M^+ required for $C_{15}H_{18}O$: 214.135757

Found : 214.135803 .

m/e 214(M^+ 41%), 199(100%), 141(22%)

Required for $C_{15}H_{18}O$: C 84.07% , H 8.47%

Found : C 84.24% , H 8.44% .

(G.l.c. was carried out employing a 2½% S.E. 30 column at 180°).

Pure samples of 1-acetyl-2-methoxynaphthalene (24) (maximum isolated yield 10%), and 1-isopropenyl-2-methoxynaphthalene (26) (maximum isolated yield 55%) were also obtained from this reaction by preparative chromatography, and were identical in all respects to samples prepared independently (see above).

Treatment of 1-t-butyl-2-methoxynaphthalene (48) with mineral acids.

1-t-Butyl-2-methoxynaphthalene (44 mg.) was dissolved in methanol (5 ml), and a few drops of 5M hydrochloric acid were added. The solution was stirred at room temperature, the reaction being monitored by t.l.c.. After 18 hours, no starting material remained and one more polar product had been produced.

Water was added, and the solution was extracted with ether (2 x 10 ml). The combined ether extracts were washed to neutrality, dried, and solvent removed to give a colourless solid. Recrystallisation from light petroleum gave colourless lustrous plates (32 mg., 100%) of 2-methoxynaphthalene which were identical in all respects to an authentic sample.

Similar treatment of 3,6-di-t-butyl-2-methoxynaphthalene and 6-t-butyl-2-methoxynaphthalene over prolonged periods (up to 7 days) gave a quantitative recovery of starting material.

When hydrogen bromide in acetic acid was used, conversion of (48) to 2-methoxynaphthalene was complete in four hours.

Photolysis of 1-t-butyl-2-methoxynaphthalene (48).

The methoxynaphthalene (48) (50 mg.) was dissolved in anhydrous hexane (100 ml), and placed in a photolysis apparatus under dry nitrogen. The sample was irradiated for 20 hours, using a medium pressure mercury lamp. The solvent was removed under reduced pressure to give a yellow

oil (50 mg.). T.l.c. (30% benzene-petrol) indicated that some polymerisation had occurred, and traces of a less polar product had been formed. Spectral data indicated that the product was mainly starting material, the other species being present in insufficient quantity to be characterised.

O-acetylation of products from Grignard reaction in situ.

The Grignard reaction was carried out on the methyl naphthoate (34) at 110° for 18 hours as previously described.

The cooled reaction mixture was dissolved in dry dmso, and acetic anhydride slowly added until the bright colour of naphthoxide ions had been discharged. The mixture was then diluted with water, and extracted thoroughly with ether. The combined ether extracts were washed thoroughly with water, dried, and solvent removed to give a pale brown oil. Preparative chromatography (20% EtOAc-petrol) gave a mixture of 1-isopropenyl-2-acetoxynaphthalene and 1-t-butyl-2-acetoxynaphthalene (ca. 3 : 1 estimated by n.m.r. and by comparison with spectra of the pure compounds (see above, and below)) which could not be separated by chromatography, crystallisation or distillation.

The mixture was treated with LAH in anhydrous ether (30 minutes reflux), and subsequently exposed to atmospheric oxygen. Crystallisation from benzene-petrol gave an overall yield of 15% of the t-butyl hydroperoxide (41), m.p. 134-137° (decomposition).

Demethylation of 1-t-butyl-2-methoxynaphthalene (48).

(a) Using methyl magnesium iodide.

Many modifications of the literature methods[53] were attempted with only partial success.

In general, 1-t-butyl-2-methoxynaphthalene (48) was added to an ethereal solution of methyl magnesium iodide (3 molar excess) under nitrogen. The solvent was distilled off, moisture being excluded, and the residue heated in an oil bath under dry nitrogen. Ether was then

added to the cooled reaction flask, and a deoxygenated solution of ammonium chloride added slowly. The organic layer was separated off and the aqueous layer thoroughly extracted with ether. The combined extracts were washed with water, dried, and solvent removed. (Work-up was carried out in a nitrogen atmosphere).

The reaction was attempted at 120° for 18 hours which resulted in conversion of all the starting material to the desired naphthol, but t.l.c. and n.m.r. indicated the formation of substantial quantities of polymer.

Treatment at 110° for 18 hours resulted in the recovery of a mixture containing a small amount of starting material, the desired naphthol, and polymer.

Treatment at 175° for thirty minutes gave a large proportion of unreacted starting material, and a substantial proportion of 2-methoxy-naphthalene, as well as the desired naphthol, and traces of 2-naphthol.

Treatment at 185-190° for two hours resulted in partial conversion to the t-butylnaphthol, but substantial amounts of starting material, 2-methoxynaphthalene, and 2-naphthol were also detected.

Pure samples of 1-t-butyl-2-naphthol (37) could not be obtained from any of these mixtures. Stirring of the mixtures in air for thirty minutes resulted in conversion of the naphthol to 1-hydroperoxy-1-t-butyl-2(1H)-naphthalenone (41). Crystallisation from benzene-light petroleum gave the hydroperoxide as pale yellow plates, m.p. 124-137°, (decomposition), the yields varying between 0-20% (based upon (48)). All attempts to obtain sharply melting samples of (41) from these reactions were unsuccessful.

(b) Using sodium thioethoxide.

1-t-Butyl-2-methoxynaphthalene (642 mg., 3 mmole) was dissolved in anhydrous dimethylformamide (DMF) (20 ml.), and added to a stirred solution of sodium thioethoxide (15 mmole - prepared from petrol washed

sodium hydride and ethanethiol) in anhydrous DMF. The solution was refluxed under dry nitrogen for three hours.

A saturated solution of ammonium chloride (50 ml) was added to the cooled reaction mixture with stirring, and the solution was then extracted with ether (3 x 25 ml). The combined ether extracts were washed thoroughly with deoxygenated water, dried, and the solvent distilled off under nitrogen. The by-products (e.g. ethyl methyl sulphide) were blown off in a nitrogen stream. The resulting yellow oil was taken up in pentane, and activated charcoal (ca. 20 mg.) added to the solution. This was then filtered and solvent removed to give 1-t-butyl-2-naphthol (37) as a colourless oil (595 mg., 85%).

$\lambda_{max.}$(EtOH) 233,273(sh.), 282, 294, 326, 339(sh.) nm.

$\nu_{max.}$(liquid film) 3,400 (OH), 1390 and 1362 ($-C(CH_3)_3$ deformation), 805 (2 adj. arom.H), 745 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.59, doublet of doublets, J_{ortho} = 8 Hz., J_{meta} = 2 Hz., 1H (peri H), 2.20-2.80, multiplet, 4H (Aromatic H 4-7), 3.13, doublet, J = 9 Hz., 1H, (Aromatic H 3), 4.70, broad singlet, 1H (-OH, D_2O exchange), 8.22, singlet, 9H, ($-C(CH_3)_3$).

In a later experiment, the cooled reaction mixture was quenched with excess acetic anhydride, and worked up as before to give a colourless oil, whose spectral characteristics were consistent with 1-t-butyl-2-acetoxynaphthalene, the yield being quantitative.

$\lambda_{max.}$(EtOH) 226(4.9), 259(sh.), 268.5(3.68), 278(3.72), 288(sh.), 320(sh.) nm.

$\nu_{max.}$(liquid film) 1775 (C=O), 820 (2 adj. arom.H), 770 (4 adj. arom.H) cm^{-1}.

(CCl_4) 1768 (C=O), 1395, 1368 ($-C(CH_3)_3$ deformation) cm^{-1}.

τ ($CDCl_3$) 1.54, doublet of doublets, J_{ortho} = 9.5 Hz., J_{meta} = 2 Hz., 1H (peri H), 2.20-2.70, multiplet, 4H (Aromatic H 4-7), 3.10, doublet, J = 9 Hz., 1H (Aromatic H 3), 7.70, singlet, 3H (CH_3-C=O), 8.28, singlet, 9H ($(CH_3)_3$-C-). m/e 242(M^+, 20), 200(60), 185(100).

1-Hydroxy-1-t-butyl-2(1H)-naphthalenone (42) and 2-hydroxy-2-t-butyl-1(2H)-naphthalenone (43).

The t-butyl hydroperoxide (41) (116 mg., 0.5 mmole) was dissolved in anhydrous ether (20 ml), and the solution was cooled to 0°. Dimethyl sulphide was added dropwise to the stirred solution until t.l.c. indicated that no starting material remained. The solvent was removed under reduced pressure to give a pale yellow oil (105 mg.) which could not be induced to crystallise.

$\lambda_{max.}$ (EtOH) 236, 318 nm.

$\nu_{max.}$ (liquid film) 3,400 (H-bonded OH), 1660, broad, (conj. C=O), 1390, 1365 (^{t}Bu deformation) cm^{-1}.

τ ($CDCl_3$) 2.1-2.8, multiplet, 5H, (CH=CH-C=O and aromatics), 3.93, doublet, J = 9.5 Hz., 1H (CH=CH-C=O), 6.0, broad singlet, 1H, (-OH, D_2O exchange), 9.10, singlet, 9H, ($-C(CH_3)_3$).

m/e 216(M^+, 5), 160(100).

This was assigned the structure 1-hydroxy-1-t-butyl-2(1H)-naphthalenone (42), but all spectra contained trace peaks attributable to the isomeric 2-hydroxy-2-t-butyl-1(2H)-naphthalenone (43). Addition of a trace of acid or base to a solution of (42) gave spectra corresponding to a 1 : 1 mixture of these two isomers.

$\lambda_{max.}$ (EtOH) 235, 268, 278, 288, 320 nm.

In the i.r. spectrum, a slight broadening of the carbonyl and hydroxy bands was detected.

The peaks in the n.m.r. attributable to the isomer (43) are as follows, τ ($CDCl_3$) 3.50 and 3.90, doublet of doublets, J_{AB} = 10 Hz., 2H, ($-CH_A=CH_B-$), 6.43, broad singlet, 1H, (-OH, D_2O exchange).

The t-butyl signals in the n.m.r. of the isomeric mixture are accidentally coincident (τ 9.10).

All attempts to isolate (42) or (43) in a pure state were unsuccessful.

Standard conditions for autoxidation of 2-naphthols.

All oxygenation reactions have been carried out under identical conditions unless otherwise stated.

A pure sample of the naphthol (normally 3 mmole) was dissolved in anhydrous benzene (0.2 molar solution), and stirred magnetically at a defined rate and at room temperature under a slight positive pressure of pure oxygen in the absence of light. The rate of uptake of oxygen was monitored on a burette. All oxygenations were continued until no further uptake of oxygen was detected.

Oxygenation of 1-t-butyl-2-naphthol (37).

Freshly prepared 1-t-butyl-2-naphthol (500 mg., 2.5 mmole) was dissolved in dry benzene (12.5 ml), and stirred in the dark under standard conditions in an atmosphere of oxygen, the uptake being recorded at regular intervals. (Theoretical uptake = 56 ml).

For periods varying between 15 minutes and one hour, (in several independent experiments), no uptake was detected. When uptake commenced, the autoxidation proceeded extremely rapidly, 28 ml being taken up in $\leqslant$ 10 minutes, and after 30 $\pm$ 3 minutes, 52-56 ml had been taken up, no further uptake being detected. In all experiments, the uptake ceased 30 $\pm$ 3 minutes after it had commenced.

The solvent was removed under reduced pressure, no heat being used, to give a pale yellow solid which was recrystallised from benzene-petrol to give pale yellow plates (510 mg., 88%), m.p. 134-7° (decomposition) (the average yield over three experiments was 85%) of 1-hydroperoxy-1-t-butyl-2(1H)-naphthalenone (41).

$\lambda_{max.}$(EtOH) 235(4.20), 242(4.21), 318(3.91), nm.

$\nu_{max.}$(KBr) 3,400 (OH), 1678 (conj. C=O), 1390 and 1362 ($C(CH_3)_3$) cm^{-1}.

$\nu_{max.}$(CCl_4) 3,415 (OH) cm^{-1}.

τ ($CDCl_3$) 1.17, broad singlet, H (OO<u>H</u>, D_2O exchange), 2.20-2.80, multiplet, 5H (Aromatics and -C<u>H</u>-CH-C=O), 3.91, doublet, J = 9 Hz.,

1H, (CH=C<u>H</u>-C=O), 9.05, singlet, 9H (-C(C<u>H</u>$_3$)$_3$).

m/e 232(M^+, 2), 160(100), 159(95).

T.l.c. of the mother liquors indicated the presence of more hydroperoxide, and many other components. Preparative chromatography gave only a small quantity (15 mg.) of 1,2-naphthaquinone, identical in all respects to an authentic sample.

The hydroperoxide was found to be extremely unstable to light and heat. A sample was dissolved in dry benzene, and stored under nitrogen in diffuse light for three days. T.l.c. indicated that only traces of the hydroperoxide remained, and at least ten other species including 1,2-naphthaquinone had been produced. A pure sample of the hydroperoxide stored in a freezer under nitrogen in the absence of light had also partially decomposed in three days. All attempts to isolate pure samples of these decomposition products from (41) by preparative chromatography were unsuccessful, and these remain unidentified, excepting 1,2-naphthaquinone. One of the components isolated by chromatography displayed similar t.l.c. and spectral characteristics to the equilibrium mixture of the isomers (42) and (43) reported above, but also contained one further unidentified component in trace quantity.

The products obtained by oxygenation of 1-t-butyl-2-naphthol in atmospheric oxygen are reported fully in the discussion section (p. 71).

<u>1-t-Pentyl-2-naphthol (58).</u>

<u>2-(3-Methylbut-2-enyloxy)naphthalene (59).</u>

2-Naphthol (28.8 g., 0.2 mole) was dissolved in anhydrous dmso (20 ml), and added dropwise to a stirred solution of petrol-washed sodium hydride (4.8 g., 0.2 mole) in anhydrous dmso (100 ml) under dry nitrogen. The mixture became viscous after stirring at room temperature for ten minutes. When a further 100 ml of dmso had been added, the mixture became mobile.

1-Bromo-3-methylbut-2-ene (prepared by hydrobromination of isoprene[107]), (30 g., 0.2 mole) was dissolved in dmso (50 ml), and added dropwise to the stirring reaction mixture over 30 minutes, ensuring that the temperature remained below 10°, and the mixture was stirred at room temperature for a further hour.

Water (200 ml) was added to the reaction mixture, which was then extracted with light petroleum (3 x 100 ml). The combined organic extracts were washed several times with water, dried, and solvent removed to give a red oil. This was crystallised from light petroleum to give colourless plates (28.4 g., 67%), m.p. 48-49°, of 2-(3-methylbut-2-enyloxy)naphthalene (59),

$\lambda_{max.}$(EtOH) 229(5.0), 252(sh.), 261.5(3.62), 272(3.65), 282(sh.), 314(3.15), 328(3.27) nm.

$\nu_{max.}$(KBr) 1625 (C=C), 835 (2 adj. arom.H), 810 ($R_2C{=}\overset{R}{C}{-}H$ deformation), 747 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.17-2.93, multiplet, 7H (aromatics), 4.40, broad triplet, J = 7 Hz., 1H ($-CH_2-C\underline{H}=C(CH_3)_2$, with small allylic coupling), 5.37, doublet, J = 7 Hz., 2H ($-C\underline{H}_2-CH=C$), 8.20, broad singlet, 6H, ($(C\underline{H}_3)_2C=CH-$, accidentally equivalent).

2-Acetoxy-1-(1,1-dimethylprop-2-enyl)naphthalene (64).

The allyl ether (59) (9.4 g., 0.045 mole) was dissolved in dry redistilled quinoline (56 ml), and acetic anhydride (40 ml) added. The mixture was refluxed under dry nitrogen for 12 hours (internal temperature 165°), cooled and poured onto crushed ice (200 ml) before being extracted with light petroleum (3 x 100 ml). The combined extracts were washed with dilute hydrochloric acid, water, dilute sodium hydroxide, and finally with water to neutrality before being dried. Removal of solvent gave a brown oil (11.2 g.). T.l.c. (20% EtOAc-petrol) indicated the presence of traces of starting material, 2-acetoxynaphthalene, and one major component of intermediate polarity.

The oil was subjected to column chromatography on silica, eluting with petrol, and then with 5% EtOAc-petrol mixtures. In this way, 2-acetoxynaphthalene (2.2 g.), and the unreacted ether (0.9 g.) were isolated, along with a colourless oil (7.6 g.) which contained traces of 2-acetoxynaphthalene.

This material could be purified by preparative t.l.c. (5% EtOAc-petrol) (1.4g. of oil gave 0.9 g. of pure product; isolable yield of pure material was 4.9 g., 43%), and identified as 2-acetoxy-1-(1,1-dimethylprop-2-enyl)naphthalene (64),

$\lambda_{max.}$ (EtOH) 226(5.2), 270(3.70), 278(3.75), 287(sh.), 320(sh.) nm.

$\nu_{max.}$ (liquid film) 1780 (C=O), 1650 (C=C), 1385 ($(CH_3)_2C$-), 820 (2 adj. arom.H), 770 and 750 (mono-substituted double bond, and 4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.80, doublet of doublets, J_{ortho} = 7 Hz., J_{meta} = 3 Hz. (peri H), 2.10-2.80, multiplet, 4H (Aromatic H_{4-7}), 3.03, doublet, J = 8.5 Hz., 1H (Aromatic H_3), 3.63, quartet, J_{AX} = 18 Hz., J_{BX} = 9 Hz., 1H ($-CH_X=CH_AH_B$), 5.07 and 5.01, AB system, J_{AX} = 18 Hz., J_{BX} = 9 Hz., J_{AB} = 1.5 Hz., 2H, ($H_XC=CH_AH_B$), 7.70, singlet, 3H (CH_3-C=O), 8.30, singlet, 6H ($(CH_3)_2C$-).

m/e 254(M^+).

2-Acetoxy-1-t-pentylnaphthalene (65).

The pure acetate (64) (1.27g., 0.005 mole) was dissolved in anhydrous methanol (50 ml), and a 10% palladium-charcoal catalyst (100 mg.) added.

The mixture was quantitatively hydrogenated, 110 ml of hydrogen being taken up in 35 minutes. (Theoretical uptake = 112 ml). The solution was filtered, and solvent removed to give a colourless oil (1.28 g., 100%) of 2-acetoxy-1-t-pentyl-naphthalene (65), purified by vacuum distillation (b.p. 92°/0.02 mm.).

$\lambda_{max.}$ (EtOH) 226(4.8), 270.5(3.78), 278(3.85), 287(sh.), 318(sh.) nm.

$\nu_{max.}$ (liquid film) 1780 (C=O), 1385 ($(CH_3)_2C$-), 820 (2 adj. arom.H),

770 and 750 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.73, broad doublet, J = 7 Hz., 1H (peri H), 2.1-2.8, multiplet, 4H, (Aromatic H_{4-7}), 3.06, doublet, J = 7.5 Hz., 1H, (Aromatic H_3), 7.68, singlet, 3H, ($C\underline{H}_3$-C=O), 7.85, quartet, J = 7 Hz., 2H, (-$C\underline{H}_2$-CH_3), 9.27, triplet, J = 7 Hz., 3H (-CH_2-$C\underline{H}_3$).

M^+ required for $C_{17}H_{20}O_2$: 256.1463

Found : 256.1460 .

m/e 256(M^+, 30), 214(55), 185(100) .

1-t-Pentyl-2-naphthol (58).

The t-pentyl acetate (65) (768 mg., 3 mmole) was taken up in anhydrous ether (10 ml), and added dropwise under dry nitrogen to a stirred suspension of lithium aluminium hydride (130 mg., 3.5 mmole) in anhydrous ether (20 ml). The solution was refluxed for thirty minutes, cooled, and a saturated aqueous solution of sodium sulphate (degassed) added dropwise with stirring. The organic layer was separated off, and the aqueous layer extracted with ether (2 x 20 ml). The combined ether extracts were washed to neutrality, dried, and solvent distilled off under nitrogen to give a pale yellow oil (640 mg., 100%),

$\lambda_{max.}$ (EtOH) 231, 271(sh.), 280, 291, 322.5, 334(sh.) nm.

$\nu_{max.}$ (liquid film) 3,400 (broad OH), 1380, doublet ($(CH_3)_2C$-), 805, (2 adj. arom.H), 742 (4 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.63, broad doublet, J = 7 Hz., 1H (peri H_8), 2.2-2.8, multiplet, 4H (aromatic H_{4-7}), 3.17, doublet, J = 7 Hz., 1H (aromatic H_3), 4.88, broad singlet, 1H (O$\underline{H}$, D_2O exchange), 7.85, quartet, J = 7 Hz., 2H (-$C\underline{H}_2$-CH_3), 8.23, singlet, 6H ($(C\underline{H}_3)_2C$-), 9.18, triplet, J = 7 Hz., 3H (-CH_2-$C\underline{H}_3$).

Oxygenation of 1-t-pentyl-2-naphthol (58).

The naphthol (58) (640 mg., 3 mmole) was dissolved in anhydrous benzene, and quantitatively oxygenated under standard conditions in the dark.

In two separate experiments, 33 ml had been taken up after 10 ± 2 minutes. After 30 ± 5 minutes, uptake of oxygen ceased, 62 and 64 ml having been taken up in the two runs. (Theoretical uptake = 67 ml). On one occasion, an inhibition period of 12 minutes was detected when no oxygen uptake occurred. The oxygenation then proceeded at a similar rate to those measured previously.

Addition of light petroleum to the mixture resulted in the precipitation of pale yellow needles, which were filtered off and dried under vacuum to give 1-hydroperoxy-1-t-pentyl-2(1H)-naphthalenone (66) (708 mg., 95%), m.p. 113-115° (decomposition).

$\lambda_{max.}$ (EtOH) 235(4.16), 241(4.19), 317(3.89) nm.

$\nu_{max.}$ (CCl_4) 3490 (OH), 1672 (conj. C=O) cm^{-1}.

(KBr) 3400 (OH), 1655 (conj. C=O), 1395 and 1365 ($(CH_3)_2C$-), 768 (4 adj. arom.H), 725 (cis-disubstituted C=C) cm^{-1}.

τ ($CDCl_3$) 1.20, singlet, 1H, (OOH, D_2O exchange), 2.2-2.8, multiplet, 5H (Aromatics and CH=CH-C=O), 3.87, doublet, J = 9.5 Hz., 1H (CH=CH-C=O), 8.60, broad quartet, J = 7 Hz., 2H ($-CH_2-CH_3$), 9.03, broad singlet, 6H (non-equivalent $(CH_3)_2C$-), 9.20, triplet, J = 7Hz., 3H (CH_3-CH_2-).

The hydroperoxide (66) was found to be extremely unstable to heat. A sample warmed to 40° in a water bath under reduced pressure violently decomposed to a black tar containing many components. A solution in benzene stored under under nitrogen at room temperature in diffuse sunlight decomposed in 12 hours to many components. T.l.c. of the mother liquors from the oxygenation of the naphthol (58) indicated that this had a similar composition. The only identified component was 1,2-naphthaquinone which was identical to an authentic reference sample.

1-Methyl-3,6-di-t-butyl-2-naphthol (67).

Preparation of 1-morpholinomethyl-3,6-di-t-butyl-2-naphthol (68).

A solution of 3,6-di-t-butyl-2-naphthol (12.8 g., 0.05 mole) (prepared by Friedel-Crafts t-butylation of 2-naphthol[2]) in 95% ethanol (50 ml) was cooled to 0°. This solution was slowly added, to a stirred solution of morpholine (4.4 g., 0.05 mole) and formaldehyde (40% w/v solution, 4 ml) over twenty minutes, and the mixture stirred at 0° for a further 30 minutes.

The product precipitated out when water was slowly added to the stirred solution. This was filtered off, washed with water, and recrystallised from ethanol to give colourless prisms, (16.9 g., 95%), m.p. 141-143°.

$\lambda_{max.}$(EtOH) 236(4.7), 259(sh.), 269(3.71), 279(3.73), 289(sh.), 324(3.37), 336(3.46) nm.

$\nu_{max.}$(CCl_4) 3,400-2,200 (chelated OH) cm^{-1}

(KBr) 1390, 1360 ($-C(CH_3)_3$), 860 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) -0.9, broad singlet, 1H (OH disappears with D_2O), 2.2-2.7, multiplet, 4H (Aromatics), 5.88, singlet, 2H ($-CH_2-N$), 6.23, broad triplet, J = 5 Hz., 4H (CH_2-O-CH_2-), 7.36, broad triplet, J = 5 Hz., 4H ($-CH_2-N-CH_2-$), 8.50 and 8.63, singlets, 18H ($(CH_3)_3C-$).

m/e 355(M^+).

Required for $C_{23}H_{33}NO_2$: C 77.70% , H 9.36% , N 3.94%

Found : C 77.92% , H 9.39% , N 3.88% .

Reduction of the morpholinomethylnaphthol (68) with Raney-alloy and alkali.

The morpholinomethylnaphthol (68) (3.55 g., 0.01 mole), was added to 2M sodium hydroxide solution (60 ml) and the solution refluxed under nitrogen. Ethanol was added until the mixture became homogeneous. (60 ml required). Nickel-aluminium alloy (3 g.)was slowly added to the heated solution, maintaining a gentle evolution of hydrogen. When

addition was complete, the solution was heated for a further fifteen minutes under nitrogen when t.l.c. indicated that no starting material remained, one less polar product having been produced.

The cooled solution was filtered, and the nickel produced immersed in dilute nitric acid before disposal. The filtrate was added slowly with stirring to dilute hydrochloric acid (100 ml) (to prevent precipitation of aluminium salts). This solution was then extracted with ether (3 x 50 ml). The combined ether extracts were washed to neutrality, dried, and solvent distilled off under nitrogen to give a pale yellow solid. Recrystallisation from chloroform-light petroleum gave colourless microcrystals (2.4 g., 91%), m.p. 215-220° (decomposition), of 1,1'-methylene-bis-(3,6-di-t-butyl-2-naphthol) (71).

$\lambda_{max.}$ (EtOH) 229(5.0), 270(sh.), 280(3.93), 291(sh.), 325(3.56), 335.5 (3.58) nm.

$\nu_{max.}$ (KBr) 3,540 (OH), 1388 and 1362 ($-C(CH_3)_3$ deformation), 820 (2 adj. arom.H) cm^{-1}.

(Nujol) 3,550 (OH) cm^{-1}.

τ ($CDCl_3$) 1.89, broad doublet, J = 8Hz., 2H (peri H_8), 2.1-2.7, multiplet, 6H (aromatics), 4.18, singlet, 2H (-OH D_2O exchange), 5.17, singlet, 2H (Ar-CH_2-Ar), 8.60, singlet, 36H ($-C(CH_3)_3$, accidental coincidence).

Base treatment of 1-morpholinomethyl-3,6-di-t-butylnaphthalene (68).

The morpholinomethylnaphthol (68) (355 mg., 1 mmole), was dissolved in 2M sodium hydroxide (6 ml) and ethanol (6 ml) with heating, and the solution was refluxed under nitrogen for four hours, when t.l.c. indicated that no starting naphthol remained.

The cooled reaction mixture was treated as above, and recrystallisation of the product from chloroform-light petroleum gave colourless needles (200 mg., 76%), m.p. and mixed m.p. 215-220°, identical in all respects to the methylene-bisnaphthol (71) obtained above.

Direct preparation of the methylene bisnaphthol (71).

3,6-Di-t-butyl-2-naphthol (1.28 g., 0.005 mole) was added to a solution of sodium acetate (0.4 g., 0.005 mole) and formaldehyde (40% w/v, 0.006 mole), in aqueous ethanol (20 ml). The mixture was refluxed under nitrogen for two hours, and then allowed to cool. A white precipitate formed, and this was filtered off, washed with water, and recrystallised from chloroform-petrol to give colourless needles (1.3 g., 100%), m.p. and mixed m.p. 215-220°, identical in all respects to samples of the methylene bisnaphthol (71) obtained previously.

O-methylation of the methylene bisnaphthol (71).

A freshly crystallised sample of the methylene bisnaphthol (71) (1.57 g., 3 mmole) in dry dmso (2 ml), was added dropwise under dry nitrogen to a stirred suspension of petrol-washed sodium hydride (84 mg., 3.5 mmole), in dmso (5 ml), which had previously been stirred at room temperature for 30 minutes. Methyl iodide was slowly added to the stirring solution until the bright green colour of the bisnaphthoxide ion had been discharged.

The reaction mixture was diluted with water (20 ml), and extracted with ether (3 x 20 ml). The combined ether extracts were washed thoroughly with water, dried, and solvent removed. Recrystallisation from acetone-water (or ethanol-water) gave colourless plates (1.5 g., 90%), m.p. 275-278°, of the dimethyl ether (73).

$\lambda_{max.}$(EtOH) 227(5.0), 233(sh.), 284(3.89), 294(sh.), 329(3.17) nm.

$\nu_{max.}$(Nujol) 1390, 1365 ($-C(CH_3)_3$), 840 (2 adj. arom.H) cm^{-1}

(KBr) 1385, 1360 (^tBu), 830 and 822 (2 sets of 2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.81, doublet, J = 8 Hz., 2H (peri $H_{8,8'}$), 2.50-2.90, multiplet, 6H (Aromatics), 5.10, singlet, 2H (Ar-CH_2-Ar), 6.00, singlet, 6H, ($-OCH_3$), 8.45 and 8.73, singlets, 36H, (2 sets of 2-$C(CH_3)_3$).

m/e 552(M^+, 100).

Required for $C_{39}H_{52}O_2$: C 84.73% , H 9.48%

Found : C 84.99% , H 9.66% .

Oxygenation of the methylene bisnaphthol (71).

Solutions of the bisnaphthol (71) were found to turn red spontaneously in air, although crystalline samples were reasonably stable.

A freshly crystallised sample (1.31 g., 2.5 mmole) was dissolved in dry benzene (10 ml) and ethyl acetate (20 ml), (the naphthol is sparingly soluble in benzene), and quantitatively oxygenated under standard conditions in the dark. (Theoretical uptake of oxygen = 56 ml, assuming 1 mole of oxygen reacts with 1 mole of substrate).
After 10 ± 2 minutes, 28 ml of oxygen had been taken up.
After 60 ± 5 minutes, 79 ml of oxygen had been taken up, and no further uptake was detected.

The solvent was removed to give an orange, semicrystalline oil, (1.35 g.), containing two major components, and no starting material. Fractional crystallisation from benzene-petrol gave orange needles, m.p. and mixed m.p. 134-5°, which were identical in all respects to 3,6-di-t-butyl-1,2-naphthaquinone (10), obtained from the oxidation of 3,6-di-t-butyl-2-naphthol (above).

Preparative t.l.c. of the mother liquors (30% benzene-petrol), gave more of the quinone (overall yield 0.90 g., 66%), and a much less polar component which gave yellow prisms from methanol (0.44 g., 32%), m.p. 154-157° (decomposition). Spectral characteristics indicated that this is the tetra-t-butyl-1,2-dihydrobenzo(f)chroman-2'-spiro-1-naphthalen-2-one (74).

$\lambda_{max.}$(EtOH) 241(4.98), 268(3.89), 279(3.93), 291(sh.), 316(4.02), 332(sh.) nm.

$\nu_{max.}$(CCl_4) 1688 (conj. C=O), 1390 and 1365 ($-C(CH_3)_3$), 1210 and 1080 (ether C-O stretch) cm^{-1}.

(KBr) 1690, 1390, 1362, 1215, 1090; 830, 815 (2 sets of 2 adj. arom.H), cm^{-1}.

τ ($CDCl_3$) 2.3-2.9, multiplet, 8H (Aromatics and -CH=C-C=O), 6.8-8.1,

multiplet, 4H ($-C\underline{H}_2-C\underline{H}_2-$, all non-equivalent), 8.42, 8.58, 8.64, 8.68, all singlets, 36H, ($-C(C\underline{H}_3)_3$, all non-equivalent).

τ (C_6D_6), 8.24, 8.58, 8.72, 8.80, all singlets, 36H, ($-C(C\underline{H}_3)_3$).

The use of Europium shift reagents did not elucidate the spectrum.

m/e 536(M^+, 40, quinone methide dimer), 522 (~0, spirocoumaran (77)), 268 (40, quinone methide monomer), 253 (100, quinone methide monomer - CH_3), 211 (50, quinone methide monomer - ^tBu).

It was found that the spiro dimer (74), when kept in solution for ca. 12 hours, or in the crystalline state at room temperature for several days, decomposed partly, giving traces of highly polar materials, along with a trace of the quinone (10).

The intensity of the 522 peak in the m.s. varies for different samples. In the purest sample obtained (m.p. 154-157°) this peak was barely detectable.

Expansion of the t-butyl region in the n.m.r. spectra of impure samples showed shoulders which corresponded exactly with the n.m.r. of methylene spiro compound (77). One of the shoulders could not be accounted for, however. In the expanded n.m.r. of the purest samples of (74) obtained, these shoulders were barely detectable. These were obtained by isolating and recrystallising (74) without the use of heat several times.

Preparation of the tetra-t-butyl-1,2-dihydrobenzo(f)coumaran-2'-spiro-1-naphthalen-2-one (77).

Freshly prepared methylene bisnaphthol (71) (524mg., 1 mmole) was dissolved in ether (15 ml) and a solution of potassium ferricyanide (1.4 g.) and sodium hydroxide (0.4 g.) in deoxygenated water (15 ml) added. The two phase mixture was stirred vigorously under nitrogen for two hours. The organic layer was separated off, and the aqueous layer extracted with ether (2 x 10 ml). The combined ether extracts were washed to neutrality, dried, and solvent removed to give a pale

green solid. Recrystallisation from 95% ethanol gave pale yellow flakes, (510 mg., 98%), m.p. 245-255°, of the spirocoumaran (77). Repeated crystallisations did not sharpen the melting point.

$\lambda_{max.}$(EtOH) 241(5.0), 268(3.91), 280(3.94), 294(sh.), 317(4.11), 337 (sh.) nm.

$\gamma_{max.}$(CCl_4) 1695 (conj. C=O), 1390 and 1365 ($-C(CH_3)_3$), 1228 and 1090, (ether C-O), 830 (2 adj. arom.H) cm^{-1}.

(KBr) 1688, 1386, 1360; 828 and 812 (2 sets of 2 arom.H) cm^{-1}.

τ($CDCl_3$) 2.2-2.8, multiplet, 8H, (aromatics and C<u>H</u>=C-C=O), 6.10 and 6.63, doublet of doublets, J_{AB} = 16 Hz., ($-C\underline{H}_2-$), 8.40, singlet, 9H, 6.62, singlet, 9H, 6.68, broad singlet, 18H (four $-C(C\underline{H}_3)_3$). Examination of amplified spectra showed small shoulders on the t-butyl signals corresponding to the spirochroman (74).

m/e 522 (M^+, 50), 505 (100), 536 (trace).

Comparative t.l.c. of the spiro-compounds showed that they have very similar r.f.'s, and staining properties.

<u>Preparation of the spirochroman (74) by pyrolysis of the morpholinomethylnaphthol (68).</u>

The morpholinomethylnaphthol (68) (180 mg., 0.5 mmole) was refluxed in mesitylene (5 ml) under nitrogen for three hours. The solvent was distilled off, and preparative chromatography (30% benzene-petrol) gave a yellow solid, recrystallised from methanol as prisms, m.p. 130-155° (95 mg., 71%) which was similar (mixed m.p., i.r., n.m.r., u.v.) to the samples of (74) obtained previously, but attempts to obtain a cleanly melting sample failed. A spot on t.l.c., identical to the bisnaphthol (71) disappeared on exposure to air, and the naphthaquinone (10) was detected but not isolated.

<u>Preparation of 1-methyl-3,6-di-t-butyl-2-naphthol (67).</u>

For an account of the reaction of the morpholinomethylnaphthol (68) with hydride reagents, see dicussion section.

Hydrogenolysis of the morpholinomethylnaphthol (68).

The morpholinomethylnaphthol (68) (1.07 g., 3 mmole) was dissolved in the minimum quantity of anhydrous methanol, (400 ml), and a 10% palladium-charcoal catalyst (50 mg.) added.

The solution was quantitatively hydrogenolysed. After 18 hours, uptake of hydrogen ceased, 67 ml having been absorbed. (Theoretical uptake = 67 ml). The catalyst was filtered off, and solvent distilled off until crystallisation commenced. This and all subsequent operations were performed under nitrogen. The precipitate was filtered off, and washed with deoxygenated water, and then with ice-cold methanol.

Recrystallisation from light petroleum gave colourless prisms (620 mg., 90%), m.p. 119-121°, of 1-methyl-3,6-di-t-butyl-2-naphthol (67), $\lambda_{max.}$(EtOH) 235(4.8), 259(sh.), 269(3.63), 279(3.66), 289(sh.), 321(3.27), 334(3.31) nm.

$\nu_{max.}$(CCl_4) 3615 (OH), 1390 and 1362 (^tBu) cm^{-1}.

(KBr) 3600 (OH), 1389, 1365 and 1355 (^tBu), 812 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.2-2.7, multiplet, 4H (aromatics), 4.65, broad singlet, 1H, (O<u>H</u>), disappears with D_2O, 7.54, singlet, 3H (-C<u>H</u>$_3$), 8.50 and 8.62, 2 singlets, 18H (-C(C<u>H</u>$_3$)$_3$).

m/e 270 (M^+, 90), 255 (100), 286 (trace impurity).

O-methylation of 1-methyl-3,6-di-t-butyl-2-naphthol (67).

Freshly prepared naphthol (67) (270 mg., 1 mmole), was methylated in dmso, using sodium hydride and methyl iodide. The product was a pale yellow oil (306 mg.). T.l.c. (10% chloroform-petrol) indicated the presence of two components. Vacuum distillation gave a colourless solid which crystallised as prisms from methanol-water, (210 mg., 74%), m.p. 70-71°, of 1-methyl-3,6-di-t-butyl-2-methoxynaphthalene.

$\lambda_{max.}$(EtOH) 234(5.0), 271(sh.), 280(3.73), 290(sh.), 312(2.97), 326.5(3.06) nm.

$\nu_{max.}$(KBr) 1390, 1355, (^tBu), 812 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.1-2.7, multiplet, 4H (Aromatics), 6.20, singlet, 3H ($-OCH_3$), 7.44, singlet, 3H ($Ar-CH_3$), 8.52 and 8.60, two singlets, 18H, ($-C(CH_3)_3$). No significant change was detected in the n.m.r. spectrum at - 120°.

m/e 284 (M^+, 91), 269 (100).

Required for $C_{20}H_{28}O$: C 84.45% , H 9.92%

Found : C 84.66% , H 9.97% .

Oxygenation of 1-methyl-3,6-di-t-butyl-2-naphthol (67).

The naphthol (67) was found to be unstable to atmospheric oxygen, breaking down to give three components separable by t.l.c. (20% EtOAc-petrol).

A pure sample of the naphthol (810 mg., 3 mmole) was dissolved in dry benzene (15 ml), and quantitatively oxygenated. (Theoretical uptake = 67 ml) in the dark.

After 14 ± 2 hours 33 ml had been taken up.

After 36 ± 5 hours 62 ml had been taken up, and no further uptake was detected.

Removal of solvent gave a solid which crystallised as pale yellow prisms from benzene-light petroleum (no heat) (765 mg., 85%), m.p. 139-142°, assigned the structure 1-hydroperoxy-1-methyl-3,6-di-t-butyl-2(1H)-naphthalenone (81).

$\lambda_{max.}$ (EtOH) 237(4.2), 245(sh.), 317(3.75) nm.

$\nu_{max.}$ (CCl_4) 3500 (OH), 1678 (conj. C=O), 1390 and 1360 (^tBu), 835 (2 adj. arom.H) cm^{-1}.

(KBr) 1662 (conj. C=O), 1385, 1365 (^tBu), 825 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 0.75, v. broad singlet, 1H ($-OOH$, D_2O exchange), 2.3-2.85, multiplet, 4H, (aromatics and $-CH=C-C=O$), 8.53, singlet, 3H (isolated $-CH_3$), 8.67 and 8.70, two singlets, 18H ($-C(CH_3)_3$).

m/e 302 (M^+, trace), 284 (12), 201 (100).

Required for $C_{19}H_{26}O_3$: C 75.46% , H 8.67%

Found : C 75.47% , H 8.76% .

T.l.c. of the mother liquors showed three components, identical to those produced in greater quantity when the naphthol was exposed to atmospheric oxygen. Preparative t.l.c. gave a component much less polar than the hydroperoxide (81) (30 mg.), giving pale yellow microcrystals from methanol, m.p. 145-155°, which were identical in all respects (including mixed m.p.) to samples of the spirochroman (74) obtained in previous experiments.

The second component, a colourless solid, gave needles from chloroform-petrol (15 mg.), m.p. 152-155°, which dissolved in aqueous sodium bicarbonate with effervescence. This was α-t-butyl-2-acetyl-5-t-butyl-cinnamic acid (82).

$\lambda_{max.}$(EtOH) 256(sh.), 295(3.38) nm.

$\nu_{max.}$(CCl_4) 3510 (non-bonded OH), 3500-2500 (H bonded OH - intramolecular), 1755 (weak, acid C=O monomer), 1735 (hemiacetal form), 1690 and 1685 (acid dimer C=O and CH_3-C=O) cm^{-1}.

(KBr) 3500-2200 (H bonded OH), 1688 and 1678 (acid C=O and CH_3-C=O), 1625 (C=C), 833 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.27-2.80, multiplet, 3H, (Aromatics), 3.10, singlet, 1H, (-C<u>H</u>=C-CO_2H), 7.47, singlet, 3H (C<u>H</u>$_3$-C=O), 8.73, singlet, 18H, (accidentally coincident -C(C<u>H</u>$_3$)$_3$).

m/e 287 (M^+- CH_3, trace), 284 (M^+- H_2O, trace), 257 (M^+-CO_2H, 25), 245 (M^+- ^tBu, 100).

Required for $C_{19}H_{26}O_3$: C 75.46% , H 8.67%

Found : C 75.60% , H 8.73% .

<u>Oxygenation of 1-methyl-3,6-di-t-butyl-2-naphthol (67) in the presence of triphenylphosphine</u>.

A sample of the naphthol (67) was oxygenated in benzene in the presence of 1 mole of triphenylphosphine. After 48 hours, no significant uptake had been detected.

N.m.r. of the reaction mixture indicated that <u>ca</u>. 10% of the

starting naphthol had reacted to give another compound. P.l.c. (10% EtOAc/Petrol) gave an impure sample of 1-hydroxy-1-methyl-3,6-di-t-butyl-2(1H)-naphthalenone (85) which was prepared independently by the action of dimethyl sulphide on the hydroperoxide (81) in anhydrous ether.

$\lambda_{max.}$(EtOH) 312(4.03), 243(4.33) nm.

$\nu_{max.}$(Nujol) 3470 (OH), 1670 (conj. C=O). 1385, 1360 (^{t}Bu), 830, (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.4-2.9, 4H (Aromatics and -CH=C-C=O). 6.05, broad singlet, 1H (OH, D_2O exchange), 8.50, singlet, 3H (isolated CH_3), 8.64 and 8.67, singlets, 18H ($-C(CH_3)_3$).

m/e 286 (M^+).

Preparation of 2-hydroxy-2-methyl-3,6-di-t-butyl-1(2H)-naphthalenone (87) from the quinone (10).

3,6-Di-t-butyl-1,2-naphthaquinone (270 mg., 1 mmole) was dissolved in anhydrous ether (10 ml), and added dropwise with stirring to a solution of methyl magnesium iodide (1.5 mmole) in anhydrous ether (15 ml). The mixture was refluxed for three hours under nitrogen. A solution of ammonium chloride was carefully added to the cooled, stirring reaction mixture, and the organic layer separated off. The aqueous layer was extracted with ether (2 x 10 ml), and the combined ether extracts were washed, dried, and solvent was removed to give a yellow oil (285 mg.). Preparative chromatography (20% EtOAc-petrol) gave the hydroxy naphthalenone (87) as a colourless oil (190 mg., 66%), the remaining material being unreacted quinone.

$\lambda_{max.}$(EtOH) 225, 232(sh.), 273, 303(sh.) nm.

$\nu_{max.}$(liquid film) 3550 (OH), 1682 (conj. C=O), 1624 (conj. C=C), 835 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.5-2.9, multiplet, 3H (aromatics), 3.87, singlet, 1H, (-CH=C-C(CH_3)OH), 7.92, broad singlet, 1H (-OH, D_2O exchange), 8.55,

singlet, 3H (isolated -$C\underline{H}_3$), 8.63 and 8.70, singlets, 18H (-$C(C\underline{H}_3)_3$).

m/e 286 (M^+).

1-Morpholinomethyl-6-t-butyl-2-naphthol.

The naphthol was prepared from 6-t-butyl-2-naphthol[2] by a procedure identical to that used to prepare 1-morpholinomethyl-3,6-di-t-butyl-2-naphthol (above).

Recrystallisation from ethanol gave silvery plates (85% yield), m.p. 155-157°.

$\lambda_{max.}$(EtOH) 232.5(4.8), 257(sh.), 266.5(3.59), 276.5(3.64), 287(3.46), 326(sh.), 338(3.35), nm.

$\nu_{max.}$($CHCl_3$) 3200-2300 (intramolecular H bonded O$\underline{H}$) cm^{-1}.

(KBr) 815 and 810 (2 sets of 2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.13-3.02, multiplet, 5H (Aromatics), 5.86, singlet, 2H, (Ar-$C\underline{H}_2$-N), 6.20, broad triplet, J = 5 Hz., 4H ($C\underline{H}_2$-O-$C\underline{H}_2$), 7.33, broad triplet, J = 5 Hz., 4H ($C\underline{H}_2$-N-$C\underline{H}_2$), 8.60, singlet, 9H (($C\underline{H}_3)_3$C-), (OH signal not detected).

m/e 299 (M^+).

1-Methyl-6-t-butyl-2-naphthol (89).

1-Morpholinomethyl-6-t-butyl-2-naphthol (0.9 g., 3 mmole) was dissolved in the minimum quantity of anhydrous methanol (120 ml), and 10% palladium on charcoal catalyst (90 mg.) added.

The mixture was then stirred in a hydrogenation apparatus, the uptake of hydrogen being recorded. (Theoretical uptake 67 ml). After 30 minutes, the uptake of hydrogen ceased, 67 ml having been absorbed. The reaction mixture was filtered, and solvent evaporated off. The resulting material was taken up in ether, and the ether solution washed with water, dried, and solvent removed to give a solid which was recrystallised from petroleum (60-80°) to give colourless fibrous needles (640 mg., 100%), m.p. 110-112°, of 1-methyl-6-t-butyl-2-naphthol (89),

$\lambda_{max.}$(EtOH) 232(4.81), 258(sh.), 267(3.66), 276.5(3.73), 287(sh.), 328(sh.), 338(3.41) nm.

$\nu_{max.}$(CCl_4) 3615 (OH) cm^{-1}.

(KBr) 885 (isolated arom.H), 820 and 805 (2 sets of 2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.05-2.48, multiplet, 4H (4 arom.H), 3.02, doublet, J = 9 Hz., 1H (aromatic H_3), 5.20, broad singlet, 1H (O$\underline{H}$ D_2O exchange), 7.45, singlet, 3H, (Ar-C$\underline{H}_3$), 8.60, singlet, 9H (($C\underline{H}_3$)$_3$C-).

m/e 214 (40), 199 (100).

Required for $C_{15}H_{18}O$: C 84.07% , H 8.47%

Found : C 83.83% , H 8.54% .

Oxygenation of 1-methyl-6-t-butyl-2-naphthol (89).

A benzene solution of (89) was stirred in an oxygen atmosphere for three days. No uptake of oxygen was recorded, and a quantitative recovery of the naphthol was achieved, and although a slight discolouration had occurred, no other species was detected.

1-Phenyl-2-naphthol (90, R = H).

1-Iodo-2-naphthol was prepared in 70% yield, m.p. 92-93°, (lit.[72(c)] 92-93°) by the literature method[72(c)].

Freshly prepared 1-iodo-2-naphthol (1.08 g., 4 mmole) was dissolved in pure, dry benzene (200 ml), degassed at the water pump, and placed in a photolysis apparatus with a stirrer. The system was flushed with nitrogen, and irradiated for 21 hours using a medium pressure mercury vapour lamp. The reaction mixture was washed with 10% sodium meta-bisulphite and then with water, dried, and solvent removed. The resulting oil (0.93 g.) was subjected to preparative t.l.c. (15% $CHCl_3$-petrol) from which three components were isolated.

The least polar band gave colourless needles from methanol-water (0.37 g., 42%), m.p. 77.5-78.5°, (lit. 65-67° [15(a)], 81-83° [15(b)]), of 1-phenyl-2-naphthol. Mixed m.p. with authentic samples from another

source[74] were not depressed.

$\lambda_{max.}$(EtOH) 231(4.7), 268(sh.), 279(3.74), 289.5(sh.), 326(sh.), 334(3.50) nm.

$\nu_{max.}$(CCl_4) 3560 (OH) cm^{-1}.

(KBr) 1612, 1591, 1494 (arom. C=C), 820 (2 adj. arom.H), 765, 755, (5 adj. arom.H, and 4 adj. arom. H) cm^{-1}.

τ($CDCl_3$) 2.1-2.9, multiplet, 11H (Aromatics), 4.87, broad singlet, 1H, (O<u>H</u>), D_2O exchange.

m/e 220 (M^+).

Required for $C_{16}H_{12}O$: C 87.25% , H 5.49%

Found : C 87.23% , H 5.70% .

The band of intermediate polarity (490 mg.) was unambiguously identified as starting material. The band of highest polarity (56 mg.) gave pale brown crystals from chloroform-petrol, m.p. 215-217° (lit.[16] 216-218°) of 1,1'-binaphthol-2,2', identical in all respects (including mixed m.p.) to an authentic sample made by ferricyanide oxidation of 2-naphthol.

<u>Oxygenation of 1-phenyl-2-naphthol</u>.

1-Phenyl-2-naphthol was stirred in benzene in an oxygen atmosphere for 5 days. No uptake of oxygen was recorded, and a quantitative recovery of unreacted starting material was achieved. The addition of cobalt III acetylacetonate did not result in any reaction.

<u>1-Phenyl-3,6-di-t-butyl-2-naphthol (90, R = ^tBu)</u>.

1-Iodo-3,6-di-t-butyl-2-naphthol was prepared by the method used to prepare the parent 1-iodo-2-naphthol[72(c)] in 92% yield from 3,6-di-t-butyl-2-naphthol, and gave pale yellow needles from methanol-water, m.p. 85-87° (decomposition).

$\lambda_{max.}$(EtOH) 237, 272(sh.), 282, 292(sh.), 321, 335 nm.

$\nu_{max.}$(Nujol) 3550 (OH), 835 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.1-2.6, multiplet, 4H (aromatics), 4.00, singlet, 1H, (-O<u>H</u>, D_2O exchange), 8.60 and 8.50, singlets, 18H, (-C($C\underline{H}_3$)$_3$).

The iodonaphthol (1.9 g., 0.005 mole) was dissolved in benzene (250 ml) and photolysed for forty hours under dry nitrogen.

Preparative chromatography of the product mixture (15% $CHCl_3$-petrol) gave three identifiable components, although traces of many other components were detected.

The least polar band (160 mg., 13%) gave colourless plates from methanol, m.p. 332-334° (lit.[20] 331-333°), of 1,1'-di-(3,6-di-t-butyl-2-naphthol) (11).

$\lambda_{max.}$(EtOH) 232, 268(sh.), 278, 288(sh.), 320, 334 nm.

$\nu_{max.}$(Nujol) 3550 (OH), 830 (2 adj. arom.H) cm^{-1}.

τ($CDCl_3$) 2.0-3.15, multiplet, 8H (Aromatics), 4.68, singlet, 2H, (2 O<u>H</u>, D_2O exchange), 8.45 and 8.64, singlets, 36H (-C($C\underline{H}_3$)$_3$).

This was identical in all respects to a sample of the binaphthol prepared by ferricyanide oxidative coupling of 3,6-di-t-butyl-2-naphthol[23].

The band of intermediate polarity (420 mg., 25%) gave colourless prisms from methanol-chloroform, m.p. 180-182°, of 1-phenyl-3,6-di-t-butyl-2-naphthol (90, R = ^tBu).

$\lambda_{max.}$(EtOH) 234(4.8), 269(3.79), 278.5(3.83), 288(sh.), 322(3.44), 334(3.55) nm.

$\nu_{max.}$(CCl_4) 3530 (OH), 820 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.2-2.9, multiplet, 9H (Aromatics), 4.53, singlet, 1H, (-O<u>H</u> , D_2O exchange), 8.62 and 8.47, singlets 18H (-C($C\underline{H}_3$)$_3$), m/e 332 (M^+).

Required for $C_{24}H_{28}O$: C 86.70% , H 8.49%

Found : C 87.03% , H 8.65% .

The band of highest polarity (40 mg.) was not investigated.

Oxygenation of 1-phenyl-3,6-di-t-butyl-2-naphthol (90, R = ^{t}Bu).

The naphthol was dissolved in benzene and oxygenated under standard conditions for seven days. No uptake of oxygen was recorded, and, although a trace of a more polar component was detected on t.l.c., recrystallisation gave a quantitative recovery of starting material.

1-Bromo-3,6-di-t-butyl-2-naphthol.

This was prepared in 98% yield by treatment of 3,6-di-t-butyl-2-naphthol[2] with one mole of bromine in carbon tetrachloride, giving pale yellow needles from methanol, m.p. 70-71°.

$\lambda_{max.}$(EtOH) 235(4.7), 260(sh.), 269(3.68), 279(3.72), 289(3,57), 320(3.28), 333(3.41) nm.

$\nu_{max.}$(Nujol) 3500 (OH), 820 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.0-2.6, multiplet, 4H, (Aromatics), 3.84, singlet, 1H, (-OH, D_2O exchange), 8.62 and 8.49, singlets, 18H ($-C(CH_3)_3$).

Oxygenation of 1-iodo-, and 1-bromo-3,6-di-t-butyl-2-naphthol.

No oxidation products were detected when benzene solutions were oxygenated for 5 days.

1,8-Dimethyl-2-naphthol (107).

2-Methoxy-1,8-naphthalic anhydride (95).

3-Methoxyacenaphthene quinone was prepared in 78% yield from 2-methoxynaphthalene and diphenyloxalimide chloride by the method of Staudinger et al.[85] and gave yellow plates from acetic acid, m.p. 224-6°, (lit.[85] 224-6°).

2-Methoxy-1,8-naphthalic anhydride (95) was prepared from the acenaphthene quinone by treatment with alkaline hydrogen peroxide in ethanol in 86% yield[86]. Recrystallisation from acetic acid gave deep yellow microcrystals, m.p. 255-256° (lit.[86(a)] 255°). Recrystallisation from a large volume of ethanol (95%) gave colourless needles,

m.p. 261-263° (lit.[86(b)] 261-262°).

$\nu_{max.}$(Nujol) 1772, 1735; 825 (2 adj. arom.H), 750 (3 adj. arom.H).

T.l.c. (5% MeOH/$CHCl_3$) indicated that the material was pure.

Attempted preparation of 1,8-dimethyl-2-methoxynaphthalene by a direct route.

The naphthalic anhydride (228 mg., 1 mmole) was suspended in acetonitrile (5 ml), and trichlorosilane (1.8 g., 12 mmole) added. The mixture was refluxed under dry nitrogen for one hour.

Tri-n-propylamine (0.7 ml, 5.3 mmole) was added to the cooled reaction mixture, keeping the temperature below 15°. The mixture was then refluxed for 16 hours, cooled and ether (10 ml) added. The solution was filtered (to remove amine hydrochloride), and solvent removed. The residue was taken up in methanol (2 ml), and the solution refluxed for one hour. Claisen's alkali (2 ml) was then added to the cooled mixture, which was refluxed for a further 19 hours.

The cooled reaction mixture was diluted with water (10 ml), and extracted with ether (3 x 10 ml). The ether extracts were washed with dilute hydrochloric acid, and then with water to neutrality, dried, and solvent removed to give a brown polymeric oil (130 mg). Preparative t.l.c. (30% EtOAc-petrol) gave a colourless solid which gave needles from ether-light petroleum (60 mg., 30%), m.p. 62-63°, of 4-methoxy--1H,3H-naphtho(1,8-c,d)pyran (96).

$\lambda_{max.}$(EtOH) 232(4.8), 278(sh.), 286(3.75), 297(3.68), 326(3.27), 339(3.31) nm.

$\nu_{max.}$(CCl_4) 2835, 2820 ($-CH_2-O-CH_2-$ and $O-CH_3$), 1625, 1600, 1510, (Arom. C=C) cm^{-1}.

(Nujol) 830 (2 adj. arom.H), 770 (3 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.25-2.95, multiplet, 5H (Aromatics), 4.94 and 5.04, singlets, 4H ($-C\underline{H}_2-O-C\underline{H}_2-$), 6.12, singlet, 3H ($-OC\underline{H}_3$).

m/e 200 (M^+).

No less polar product was detected. The pyran (96) was found to be unstable to oxygen. Several more polar products were detected on t.l.c. after a benzene solution had been oxygenated for 24 hours. These could not be formed in sufficient quantity to be characterised.

1,8-Di(hydroxymethyl)2-methoxynaphthalene (98).

2-Methoxy-1,8-naphthalic anhydride (5.7 g., 0.025M) was suspended in anhydrous benzene (100 ml), and anhydrous ether (50 ml). LAH (2.3 g., 0.06 mole) was added, and the mixture was refluxed under dry nitrogen for two days, ether (25 ml) being added after 24 hours.

The reaction mixture was allowed to cool, and excess LAH was destroyed by careful addition of ethyl acetate to the stirred solution. A saturated aqueous solution of sodium sulphate was then added, and the organic layer separated off. The aqueous suspension of aluminium salts was extracted several times with hot ethyl acetate. The combined organic extracts were washed with dilute sodium hydroxide, and then with water, dried, and solvent removed to give a pale yellow solid. Recrystallisation from ethyl acetate-petrol gave pale yellow prisms (3.3 g., 61%), m.p. 132-134° of 1,8-di(hydroxymethyl)2-methoxynaphthalene (98),

$\nu_{max.}$ (Nujol) 3300 (H bonded OH), 828 (2 adj. arom.H), 775 (3 adj. arom. H) cm^{-1}.

τ (C_5D_5N) 4.03 and 4.10, singlets, 4H, ($-C\underline{H}_2OH$), 6.20, singlet, 3H ($-OC\underline{H}_3$).

Dilute hydrochloric acid was added to the aqueous residue, and the bulk was extracted with ether (3 times). The combined extracts were washed, dried, and solvent removed to give a pale yellow oil. Recrystallisation from ether-light petroleum gave colourless needles, m.p. 62-63° (0.95 g., 19%) of the naphthopyran (96), identical in all respects to a sample obtained from the chlorosilane reduction (above).

Treatment of 2-methoxy-1,8-naphthalic anhydride (95) with sodium dihydro-bis(2-methoxyethoxy) aluminate (SDA).

The anhydride (95) (228 mg., 1 mmole) was finely ground and suspended in anhydrous benzene (20 ml), and SDA (70% w/v solution in benzene, 6 mmole) added to the stirred suspension under dry nitrogen. The resulting deep yellow, homogeneous solution was refluxed for two hours.

The cooled, dark green reaction mixture was diluted with 5M aqueous sodium hydroxide, and extracted thoroughly with hot ethyl acetate. The combined organic extracts were washed with water, dried, and solvent removed. Recrystallisation from ethyl acetate-light petroleum gave pale yellow prisms, m.p. 132-134° of 1,8-di(hydroxymethyl)-2-methoxy-naphthalene (98) (maximum yield 30%), identical in all respects to a sample obtained by LAH reduction of (95). On occasions, the isolated yield was considerably lower.

T.l.c. (30% EtOAc-petrol) indicated that a second, less polar component was present in substantial quantity. This is described below.

The anhydride (95) (228 mg., 1 mmole) was treated with SDA in refluxing xylene for 2 hours as above. The cooled, dark green reaction mixture was carefully diluted with 3M hydrochloric acid with stirring. The pale yellow organic layer was separated off, and the aqueous layer extracted with ether (twice). The combined organic extracts were washed with water, and then with dilute sodium hydroxide, and finally with water to neutrality. The solution was dried, and solvent removed to give a pale yellow oil (170 mg.).

Preparative chromatography (25% EtOAc-petrol) gave two major components, although traces of other, highly polar components were present.

The less polar band (r.f. 0.55, 75 mg., 38%) gave colourless needles from light petroleum, m.p. 62-63°, identical in all respects

to the naphthopyran (96) previously prepared by reductive silylation of the anhydride, (95). The more polar band (r.f. 0.25, 40 mg.) was a colourless, low melting solid, (m.p. ca. 60-70°).

$\lambda_{max.}$(EtOH) 233, 276(sh.), 286.5, 297, 326, 335(sh.) nm.

$\nu_{max.}$(Nujol) 3400 (OH), 1720 (lactone C=O), 1615, 1600, (Arom. C=C), 835 (2 adj. arom.H), 765 (3 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.2-2.9, multiplet, 5H (Aromatics), 4.83, singlet, 2H, (Ar-CH_2-OH), 6.10, singlet, 3H (-OCH_3), 7.20, singlet, 3H (Ar-CH_3), 8.25, broad singlet, 1H (-CH_2OH, disappears with D_2O), (also a small singlet at 4.17 (lactone -CH_2)).

This was an inseparable mixture of ca. 90% (by n.m.r.) of 1-methyl-8-hydroxymethyl-2-methoxynaphthalene (99) and the 2-methoxy-1,8-naphthalide (101).

No further investigation of this mixture was undertaken.

By prolonged refluxing (up to 22 hours) of the naphthalic anhydride (95) in benzene with a five molar excess of SDA, the yield of the naphthopyran (96) could be increased to 45%, but this resulted in extensive polymerisation, and the production of many unidentified components.

Treatment of the naphthopyran (96) with SDA.

The naphthopyran (96) (200 mg., 1 mmole) was dissolved in anhydrous xylene (20 ml), and SDA (1.1 ml of 70% w/v solution in benzene, 1 mmole) syringed into the stirring solution. The solution which immediately turns a dark green colour, was then refluxed under dry nitrogen, the reaction being monitored by t.l.c.

After four hours, no starting material remained. The solvent was then distilled off under reduced pressure, and the residue dissolved in ether (50 ml). Dilute sodium hydroxide solution was carefully added, and the mixture transferred to a separating funnel and shaken. The aqueous layer was extracted with a further portion of ether, and

the ethereal extracts washed to neutrality, dried, and the solvent removed to give a brown oil (190 mg.).

T.l.c. (50% benzene-petrol) indicated the presence of the desired 1,8-dimethyl-2-methoxynaphthalene (105) along with more polar components, one less polar component, and some polymeric material.

P.l.c. (50% benzene-petrol) gave two major fractions. The less polar of these was a low melting solid (purple stain with ceric sulphate) (50 mg., 32%) whose structure was confirmed to be 1,8-dimethylnaphthalene m.p. (methanol-water) 61-63°, colourless plates (lit.[84] 63°),

$\lambda_{max.}$(EtOH) 228(4.91), 276(sh.), 285(3.80), 293(sh.), 347(2.89) nm.

$\nu_{max.}$(Nujol) 1605, 1595, (Ar C=C), 780 (3 adj. arom.H) cm^{-1}.

$\tau(CDCl_3)$ 2.33-2.90, multiplet, 6H, (Aromatics), 7.07, singlet, 6H, (Ar-$\underline{CH}_3$).

m/e 156 (M^+).

The more polar component was a colourless oil with identical spectral characteristics to reference samples of 1,8-dimethyl-2-methoxy-naphthalene (105) (reported fully below) (65 mg., 35%).

The remainder of the material consisted of an orange, intractible oil containing at least three components of high polarity.

Treatment of the anhydride (95) with SDA under forcing conditions.

2-Methoxy-1,8-naphthalic anhydride (460 mg., 2 mmole) was added with stirring to a solution of SDA (8 mmole) in dry xylene (20 ml). The anhydride dissolved with effervescence to give a dark green solution. This solution was refluxed for 6 hours under dry nitrogen, and the solvent was then distilled off under reduced pressure.

The residue was taken up in ether (50 ml), and 5M sodium hydroxide solution (50 ml) slowly added with stirring. The aqueous layer was extracted with two further portions of ether, and the combined extracts washed to neutrality with water, dried, and the solvent removed to give a dark red oil (450 mg.)

Chromatography on silica eluted with petrol, and subsequently with 5% benzene-petrol, gave 1,8-dimethylnaphthalene (130 mg., 42%), and 1,8-dimethyl-2-methoxynaphthalene (105) (210 mg.), the complete separation of which proved extremely difficult by chromatography.

The methoxynaphthalene was purified by fractional distillation (b.p. 85-90°/0.05 mm), giving a colourless oil (190 mg., 50%) identical in all respects to reference samples (see below). The material balance in this experiment consisted of polymers, which were produced in considerable quantity in all runs.

A similar mixture was obtained by treating 1,8-di(hydroxymethyl)-2-methoxynaphthalene (98) with SDA under the same conditions.

Treatment of the anhydride (95) with a five molar excess of SDA in refluxing toluene (internal temperature 110°) for three to six hours gave a lower isolated yield (maximum 35%) of the desired 1,8-dimethyl-2-methoxynaphthalene, along with substantial amounts (up to 30% isolated yield) of 1,8-dimethylnaphthalene. Several more polar components were detected on t.l.c. but were not investigated.

Treatment of 1,8-dimethyl-2-methoxynaphthalene (105) with SDA.

The methoxynaphthalene (105) (90 mg., 0.5mmole) was dissolved in anhydrous xylene (5 ml) and SDA solution in benzene (0.5 mmole) syringed into the flask.

The solution was refluxed for four hours under dry nitrogen, and then the solvent was removed, and the reaction mixture worked up using 5M sodium hydroxide solution as before to give a pale yellow oil (85 mg.) containing ca. 30% of 1,8-dimethylnaphthalene (n.m.r. and g.l.c. estimation), starting material (ca. 70%) and traces of polymeric material.

Treatment of other 2-methoxynaphthalenes with SDA in refluxing xylene is fully reported in the discussion section.

1-Methyl-2-naphthol.

Treatment of 1-formyl-2-naphthol with SDA in refluxing xylene for two hours according to the method of Cěrny et al.[92] gave 1-methyl-2-naphthol (95%), m.p. 109-110° (lit.[1,2] 109-110°), identical in all respects to an authentic sample.

2-Hydroxy-1,8-naphthalic anhydride (106).

2-Methoxy-1,8-naphthalic anhydride (95) (2.28 g., 10 mmole) was added to a 45% w/v solution of hydrogen bromide in glacial acetic acid (40 ml), and water (20 ml), and the solution was refluxed under nitrogen for three hours.

The cooled reaction mixture was diluted with water (20 ml), and the product precipitated out as a pale yellow solid, which was filtered off, and washed thoroughly with water. T.l.c. (5% methanol-chloroform) indicated the complete disappearance of starting material. (Shorter reaction times give some starting material).

Recrystallisation from acetone gave pale yellow fibrous needles (0.9 g., 42%), m.p. 249-251° (lit.[97] 245-6°),
$\nu_{max.}$(Nujol) 1765, 1720, (anhydride C=O), 805 (2 adj. arom.H), 750, (3 adj. arom.H), 3600-2500 (H-bonded OH), cm^{-1}.

The residue (1.1 g.) was also a pale yellow solid, but had different spectral characteristics. Recrystallisation from ethanol-water gave pale yellow prisms of 7-hydroxy-1-naphthoic acid (108) (1.05 g., 56%), m.p. 255-8° (lit.[108] 255-6°).
$\lambda_{max.}$(EtOH) 232(4.80), 292(3.67), 304(sh.), 324(sh.), 342(3.73) nm.
$\nu_{max.}$(Nujol) 3600-2200 (CO_2H and H-bonded OH), 1695 (acid C=O), 840, (2 adj. arom.H), 760 (3 adj. arom.H) cm^{-1}.
m/e 188 (M^+).

The reaction was repeated in the absence of water, in order to avoid decarboxylation of the anhydride (106), but complete demethylation could not be achieved. The use of pyridine hydrochloride produced a polymeric tar.

1,8-Dimethyl-2-naphthol (107) from 2-hydroxy-1,8-naphthalic anhydride (106).

2-Hydroxy-1,8-naphthalic anhydride (216 mg., 1 mmole) was finely ground and suspended in anhydrous xylene (10 ml). A solution of SDA (11 mmole) in benzene was added slowly, and the substrate dissolved with effervescence to give an orange solution. This was refluxed (internal temperature 141°) under dry nitrogen for three hours, aliquots being taken at regular intervals. The cooled reaction mixture was diluted with ether (30 ml), and dilute sulphuric acid carefully added with stirring, maintaining an atmosphere of nitrogen. The aqueous layer was extracted twice with ether, and the combined organic extracts washed to neutrality, dried, and the ether removed by distillation under nitrogen. Addition of light petroleum to the remaining solution in xylene gave a yellow precipitate, which was filtered off and recrystallised from light petroleum to give 1,8-dimethyl-2-naphthol (110 mg., 64%) as pale yellow needles, m.p. 90-94° (decomposition), whose spectral characteristics were similar to a reference sample from another source (below), but which contained traces of the hydroperoxide (109).

Isolation of absolutely pure naphthol from this reaction was never achieved, owing to the prolonged work-up, and the necessity to remove by-products. All samples contained traces of the hydroperoxide and could not therefore be used for rigorous comparison with pure samples obtained from another source (below).

Oxygenation of impure 1,8-dimethyl-2-naphthol (from above).

Samples obtained from the above reaction absorbed ca. 60-80% of the theoretical volume of oxygen, the reaction being completed after 15 ± 5 hours, and the only isolated product being the hydroperoxide (109) although traces of the other components discussed below were detected. In general impure samples of the naphthol (107) were oxygenated at a slower rate than pure samples.

8-Methyl-2-naphthol (110) from 7-hydroxy-1-naphthoic acid (108).

7-Hydroxy-1-naphthoic acid (940 mg., 5 mmole) was finely ground and suspended in anhydrous xylene (30 ml), and SDA solution (7 ml, 25 mmole) was added with stirring. Benzene was distilled off, and the homogeneous solution refluxed under dry nitrogen for six hours. Treatment of the cooled reaction mixture with dilute sulphuric acid, followed by extraction with ether and removal of most of the solvent as previously described, gave a pale yellow solution in xylene.

Addition of light petroleum gave a golden precipitate, which was filtered off, and recrystallised from EtOAc/petrol to give yellow plates m.p. 164-6° (650 mg., 75%), of 8-hydroxymethyl-2-naphthol (111), $\lambda_{max.}$(EtOH) 229(4.82), 268(3.61), 278(3.73), 289.5(3.66), 320(sh.), 332.5(3.43) nm.

$\nu_{max.}$(Nujol) 3400 (non-bonded OH), and 3500-2600 (H-bonded OH), 1620 and 1595 (arom. C=C), 855 (isolated arom.H), 825 (2 adj. arom.H), 750 (3 adj. arom.H) cm^{-1}.

τ (D_6dmso) 0.30, singlet, 1H (Ar-O<u>H</u>, D_2O exchange), 2.2-3.0, multiplet, 6H, (aromatics), 4.80, triplet, J = 4.5 Hz., 1H (CH_2-O<u>H</u>, D_2O exchange), 5.18, doublet, J = 4.5 Hz., 2H (C<u>H</u>$_2$-OH).

τ (C_5D_5N) 1.5-2.8, multiplet, (aromatics and solvent), 4.57, singlet, 2H, (C<u>H</u>$_2$-OH).

m/e 174 (M^+).

The mother liquors contained a less polar component, and removal of solvent under reduced pressure gave a low melting solid (130 mg., 16%) recrystallised from methanol-water as colourless needles, m.p. 70-71°, (lit.[98] 70-71°), assigned the structure 8-methyl-2-naphthol (110) based on the following data.

$\lambda_{max.}$(EtOH) 228(4.79), 269(3.66), 278.5(3.76), 290(3.68), 322(sh.), 333(3.37) nm.

(cf. 1-Methyl-2-naphthol,

$\lambda_{max.}$(EtOH) 231(4.84), 270(3.71), 280(3.80), 291(3.71), 325(3.30), 335(3.40) nm.).

$\nu_{max.}$(Nujol) 3300 (H-bonded OH), 855 (isolated Ar-H), 825 (2 adj. arom.H), 750 (3 adjacent arom.H) cm^{-1}.

τ ($CDCl_3$) 2.2-3.10, multiplet, 6H (Aromatics), 4.86, broad singlet, 1H, (OH, D_2O exchange), 7.43, singlet, 3H, (Ar-CH_3). m/e158 (M^+)

8-Methyl-2-naphthol (110) from 8-hydroxymethyl-2-naphthol (111).

8-Hydroxymethyl-2-naphthol (174 mg., 1 mmole) was dissolved in methanol, and 10% palladium-charcoal catalyst (20 mg.) was added. The solution was then stirred under an atmosphere of hydrogen, the uptake being recorded. After 70 minutes, the uptake of hydrogen ceased, 19 ml having been taken up. (Theoretical absorption 22 ml). The catalyst was filtered off, the solution dried, and solvent removed to give a pale yellow solid, recrystallised from methanol/water to give colourless needles (160 mg., 100%) of 8-methyl-2-naphthol, identical in all respects to samples obtained above.

The attempted preparation of 1,8-dimethyl-2-methoxynaphthalene (105) from the naphthopyran (96).

(a) Hydrogenolysis.

Prolonged hydrogenation of (96) over a 10% palladium-charcoal catalyst in methanol resulted in the recovery of pure starting material. The addition of catalytic amounts of perchloric acid, or the use of glacial acetic acid containing a trace of perchloric acid as catalyst did not result in conversion to the desired product. The reaction was also attempted employing Adam's catalyst in methanol containing a trace of concentrated hydrochloric acid.

(b) Lithium aluminium hydride - aluminium chloride.

The naphthopyran (200 mg., 1 mmole) was dissolved in anhydrous ether (10 ml), and added to a cooled solution of LAH (38 mg., 1 mmole)

and aluminium chloride (266 mg., 2 mmole) which had previously been stirred for 30 minutes at 0°.

The mixture was refluxed under nitrogen for 24 hours. Ethyl acetate was added to the cooled reaction mixture, and then dilute hydrochloric acid. Extraction with ether, and work-up in the usual manner gave an intractible oil containing at least four components (t.l.c. 30% EtOAc-petrol), and a large proportion of highly polar material. None of the desired product was detected in the n.m.r..

The reaction was repeated using a 1 : 1 mixture of LAH and aluminium chloride with no success.

When the reaction was attempted at room temperature for 24 hours, the product consisted of some phenolic material, but mainly of starting material.

Hydrogenolysis of 1,8-di(hydroxymethyl)-2-methoxynaphthalene (98).

(a) The diol (98) (55 mg., 0.25 mmole) was dissolved in ethyl acetate (5 ml), and 10% palladium-charcoal catalyst (10 mg.) added. The mixture was quantitatively hydrogenated at room temperature under a slight positive pressure of hydrogen. (Theoretical uptake of hydrogen for hydrogenolysis of both C-O bonds = 11 ml).

After 10 hours, 2 ml of hydrogen had been taken up.

After 26 hours, 13 ml of hydrogen had been taken up.

The reaction mixture was filtered, dried, and solvent was removed to give a colourless semi-crystalline oil (42 mg.). T.l.c. (50% EtOAc-petrol) indicated that no starting material remained, and two less polar components had been produced.

Preparative chromatography (50% EtOAc-petrol) gave a colourless oil (r.f. 0.7), (15 mg.), which was assigned the structure 1,8-dimethyl-5,6,7,8-tetrahydro-2-methoxynaphthalene (112) on the basis of the following data.

$\lambda_{max.}$ (EtOH) 287(3.20), 282(sh.), 278(3.21) nm.

$\nu_{max.}$(liquid film) 1600, 1580 (arom. C=C), 795 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.98 and 3.26, AB quartet, J_{AB} = 9 Hz., 2H (aromatics), 6.20, singlet, 3H ($-OC\underline{H}_3$), 6.5-7.5, multiplet, 3H ($CH_3-C\underline{H}-Ar$ and $-C\underline{H}_2-Ar$), 7.80, singlet, 3H ($C\underline{H}_3-Ar$), 8.10-8.33, multiplet, 4H, ($-CH(CH_3)-C\underline{H}_2-C\underline{H}_2-CH_2-Ar$), 8.85, doublet, J = 7.5 Hz., 3H ($C\underline{H}_3-CH$).

m/e 190 (M^+).

The second more polar component gave colourless needles from light petroleum (23 mg.), m.p.111-112°, and was assigned the structure 8-hydroxymethyl-1-methyl-5,6,7,8-tetrahydro-2-methoxynaphthalene (113),

$\lambda_{max.}$(EtOH) 278.5(3.27), 282.5(sh.), 287(3.26) nm.

$\nu_{max.}$(CCl_4) 3630 (OH), 1595, 1580 (ArC=C) cm^{-1}.

(KBr) 802 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 3.10 and 3.32, AB quartet, J_{AB} = 8 Hz., 2H, (Aromatics), 6.22, singlet, 3H ($-OC\underline{H}_3$), 6.30-6.42, multiplet, 2H ($HO-C\underline{H}_2-CH$, non-equivalent), 6.70-6.95, multiplet, 1H ($HO-CH_2-C\underline{H}-$), 7.25, broad triplet, J = 5 Hz., ($-CH_2-C\underline{H}_2-Ar$), 7.78, singlet, 3H ($C\underline{H}_3-Ar$), 8.0-8.4, multiplet, 4H ($-C\underline{H}_2-C\underline{H}_2-CH_2-Ar$), 8.42, broad singlet, 1H ($-O\underline{H}$, D_2O exchange).

m/e 206 (M^+).

(b) The diol (98) (436 mg., 2 mmole) was dissolved in the minimum quantity of methanol (30 ml), and 10% palladium-charcoal (40 mg.) added. The solution was quantitatively hydrogenated at room temperature. (Theoretical uptake of hydrogen for the production of 1,8-dimethyl-2-methoxynaphthalene = 90 ml).

After 30 minutes, 90 ml of hydrogen had been absorbed.

After 10 hours, 114 ml of hydrogen had been absorbed.

The solution was filtered, dried, and the solvent was removed. Preparative t.l.c. (50% EtOAc/petrol) gave two fractions. The less polar fraction (r.f. 0.85) (254 mg., 67%) was identical in all respects to the dimethyltetrahydronaphthalene (112) obtained above. The more polar fraction (r.f. 0.51) gave needles from petrol (82 mg., 20%),

m.p. 110-111°, identical in all respects to the hydroxymethyl-tetrahydronaphthalenes (113) obtained above.

(c) The reaction was repeated on the diol (436 mg., 2 mmole) as above. When 90 ml of hydrogen had been taken up (30 minutes), the reaction was stopped. Preparative t.l.c. (30% benzene-petrol) gave four fractions.

The least polar fraction (20 mg.) was identical in all respects to the dimethyltetrahydronaphthalene (112) obtained previously. The second fraction (r.f. 0.80, 220 mg.), a colourless oil, consisted of ca. 5% of the dimethyltetrahydro compound (112) and 1,8-dimethyl-2-methoxynaphthalene (105) (estimated by g.l.c.) This could not be further purified by chromatography, or by fractional distillation. The third fraction (r.f. 0.50, 60 mg.) was a colourless solid identical in all respects to the hydroxymethyltetrahydronaphthalene (113). The fourth fraction (r.f. 0.14, 30 mg.) gave pale yellow crystals from ether-petrol, m.p. 110-120°. Spectral data were consistent with the structure 1,8-di(hydroxymethyl)-5,6,7,8-tetrahydro-2-methoxynaphthalene (114).

$\lambda_{max.}$(EtOH) 279, 283(sh.), 288 nm.

$\nu_{max.}$(Nujol) 3330 (H-bonded OH), 1600, 1590 (ArC=C), 1250 (Ar-OCH_3), 795 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.86 and 3.20, AB quartet, J_{AB} = 8 Hz., 2H (Aromatics), 5.22, doublet, J = 6 Hz., 2H (-HO-$C\underline{H}_2$-Ar), 6.16, singlet, 3H, (-$OC\underline{H}_3$), 6.35-6.80, multiplet, 3H (HO-$C\underline{H}_2$-$C\underline{H}$-Ar), 7.22, broad triplet, J = 6 Hz., 2H (-CH_2-$C\underline{H}_2$-Ar), 7.2, 2H (-O$\underline{H}$, D_2O exchange), 7.9-8.4, multiplet, 4H (-$C\underline{H}_2$-$C\underline{H}_2$-CH_2-Ar).

m/e 222 (M^+).

No further investigation of this compound was undertaken.

The dimethylmethoxynaphthalene (105) could be purified by low temperature crystallisation (DriKold/acetone bath) from pentane, giving colourless microcrystals, m.p. ca. 5° (180 mg., 50%).

$\lambda_{max.}$(EtOH) 232(4.8), 278(sh.), 286(3.75), 297(3.68), 326(3.27), 339(3.31) nm.

$\nu_{max.}$ (liquid film) 1615, 1600, 1510 (ArC=C), 815 (2 adj., arom.H), 755 (3 adj. arom.H) cm^{-1}.

τ($CDCl_3$) 2.30-2.90, multiplet, 5H (Aromatics), 6.10, singlet, 3H, ($-OC\underline{H}_3$), 7.23 and 7.10, singlets 6H ($Ar-C\underline{H}_3$).

m/e 186 (43), 171 (100).

Required for $C_{13}H_{14}O$: C 83.83% , H 7.58%

Found : C 84.00% , H 7.69% .

(G.l.c. 2½% SE 30, 200°, retention times : (112) = 3 minutes, (105) = 4.5 minutes.)

Attempted re-aromatisation of the dimethyltetrahydronaphthalene (112).

(a) The tetrahydronaphthalene (112) (190 mg., 1 mmole) was dissolved in dry benzene (5 ml), and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) (500 mg., 2.2 mmole) added. The solution was refluxed for a total of 24 hours, at the end of which time a trace of a less polar component remained. All attempts to attain a quantitative conversion to 1,8-dimethyl-2-methoxy-naphthalene failed. The product was diluted with petrol to precipitate the oxidising agent and the hydroquinone by-product, and subsequent chromatography on silica eluted with petrol, gave the dimethylmethoxynaphthalene (105) contaminated with about 10% (estimated by g.l.c) of a dihydronaphthalene.

Treatment of mixtures with DDQ under varying conditions did not produce the pure product.

(b) The tetrahydronaphthalene (112) (190 mg., 1 mmole) was dissolved in dry toluene (25 ml), and 10% palladium-charcoal (25 mg.) was added. The solution was refluxed for a total of ten hours, a stream of dry nitrogen being bubbled through the solution.

The reaction mixture was filtered, and solvent removed to give the dimethylmethoxynaphthalene (105) (190 mg.) contaminated with a dihydro-derivative (ca. 8-10% by g.l.c.).

The reaction was repeated in refluxing xylene with a similar

result.

The dihydronaphthalene contaminant (detected in m.s. as an M+2 peak) was not isolated.

1,8-Dimethyl-2-naphthol (107).

To 1,8-dimethyl-2-methoxynaphthalene (105) (930 mg., 5 mmole) was added a 45% w/v solution of HBr (15 ml), and redistilled, deoxygenated water (15 ml). The mixture was refluxed under nitrogen for 40 minutes. The cooled reaction mixture was diluted with water (25 ml), and extracted under an atmosphere of nitrogen with ether (3 x 20 ml). The combined ethereal extracts were washed with water, saturated sodium bicarbonate solution and finally with saturated brine, dried, and solvent distilled off under nitrogen to give a pale yellow solid (860 mg., 100%). Recrystallisation from ether-light petroleum gave colourless needles (780 mg., 91%), m.p. 92-95° (decomposition), of 1,8-dimethyl-2-naphthol (107),

$\lambda_{max.}$(EtOH) 339, 328.5, 295.5, 284, 274, 234 nm.

$\nu_{max.}$(Nujol) 3400, (broad, OH), 830 (2 adj. arom.H), 760 (3 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.5-3.2, multiplet, 5H, (Aromatics), 5.20, broad singlet, 1H, (O$\underline{H}$, D_2O exchange), 7.28 and 7.13, singlets, 6H (aromatic C$\underline{H}_3$'s).

Longer reaction times result in polymerisation.

Treatment of the naphthol (107) with acetic anhydride in anhydrous pyridine at room temperature for twelve hours gave a quantitative yield of 2-acetoxy-1,8-dimethylnaphthalene, which gives colourless prisms from light petroleum (40-60°) m.p. 60-61.5°,

$\lambda_{max.}$(EtOH) 228(4.9), 275(sh.), 283(3.77), 292(sh.), 303(sh.), 325(2.92) nm.

$\nu_{max.}$(Nujol) 1760 (CH_3COO-), 820 (2 adj. arom.H), 755 (3 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 2.2-3.0, multiplet, 5H (Aromatics), 7.10 and 7.33, singlets, 6H (Ar-C$\underline{H}_3$), 7.65, singlet, 3H, (C$\underline{H}_3$COO-).

m/e 214 (M^+, 20), 172 (M - ketene, 100), 157 (M - (ketene + CH_3), 28).

Required for $C_{14}H_{14}O_2$: C 78.48 % , H 6.59%

Found : C 78.10% , H 6.61% .

Oxygenation of 1,8-dimethyl-2-naphthol (107).

Pure 1,8-dimethyl-2-naphthol (516 mg., 3 mmole) was dissolved in anhydrous benzene (15 ml), and oxygenated under standard conditions, the uptake of oxygen being recorded at regular intervals. (Theoretical uptake = 67 ml).

After 3 ± 0.2 hours, 33 ml had been absorbed.

After 12 ± 2 hours, 65 ml had been absorbed, and no further uptake of oxygen was detected. (Results averaged over three experiments.)

Removal of solvent gave a yellow solid (610 mg.), recrystallised from benzene-light petroleum (60-80°) to give colourless prisms, (570 mg., 94%) of 1-hydroperoxy-1,8-dimethyl-2(1H)-naphthalenone (109), m.p. 144-6° (decomposition),

$\lambda_{max.}$ (EtOH) 235(3.92), 241(3.92), 317(3.82) nm.

$\nu_{max.}$ (CCl_4) 3500 (OH), 1680 (conj. C=O) cm^{-1}.

(KBr) 1660, 800 (3 adj. arom.H), 765 (cis-disubstituted double bond) cm^{-1}.

τ ($CDCl_3$) 0.97, broad singlet, 1H (-OOH, D_2O exchange), 2.62, doublet, J = 10 Hz., 1H (CH=CH-C=O), 2.70-2.93, multiplet, 3H (Aromatics), 3.85, doublet, J = 10 Hz., 1H (CH=CH-C=O), 7.33, singlet, 3H (CH_3-Ar), 8.47, singlet, 3H (CH_3-CR_2OOH).

m/e 204 (M^+), 187 (M - OH), 172 (M - MeOH).

Required for $C_{12}H_{12}O_3$: C 70.58% , H 5.92%

Found : C 70.46% , H 6.13% .

Preparative chromatography (20% EtOAc-petrol) of the mother liquors (30 mg.) gave three components.

The least polar component (10 mg.) gave pale yellow plates from methanol, m.p. 155-157° (decomposition), and is thought to be the quinone methide dimer (116).

$\lambda_{max.}$ (EtOH) 235(4.8), 288(sh.), 299(3.99), 320(sh.), 336(sh.) nm.

$\nu_{max.}$(KBr) 1680 (conj. C=O), 820 (2 adj. arom.H), 760 (3 adj. arom.H) cm^{-1}.

m/e 340 (M^+, 14), 171 (100), 157 (70), 129(100).

This compound was not obtained in sufficient quantity to be unambiguously characterised.

The second component (12 mg.) was identical in all respects to the hydroperoxide (109).

The most polar component (ca. 10 mg.) was never isolated in sufficient quantity for characterisation. It failed to stain on silica plates when developed with ceric (typical of an acid), and was thought to be the acetylcinnamic acid (117),

$\lambda_{max.}$(EtOH) 263 nm.

$\nu_{max.}$(CCl_4) 3500-2600 (H-bonded OH), 1700 (C=O) cm^{-1}.

The compound dissolved in aqueous sodium bicarbonate with effervescence.

1-Isopropyl-2-naphthol (119).

This was prepared by isopropylation of sodium 2-naphthoxide in anhydrous toluene in the manner reported[2].

The naphthol was isolated in a pure state by fractional distillation (b.p. 98-104°/0.01 mm.). The distillate was taken up in ether, washed with aqueous sodium hydroxide, and then with water, dried, and solvent removed. Three crystallisations from benzene-light petroleum gave colourless needles, m.p. 72-74° (lit.[4,5] 72-74°) (55%). The spectral characteristics were identical to those reported for this naphthol[2].

Oxygenation of 1-isopropyl-2-naphthol (119).

A pure sample of the naphthol (119) (560 mg., 3 mmole) was dissolved in anhydrous benzene (15 ml), and oxygenated under standard conditions.

After 4 ± 0.5 hours, 33 ml of oxygen had been absorbed.

After 16 ± 2 hours, 67 ml of oxygen had been absorbed.

A plot of oxygen uptake versus time in one of these experiments is

shown in Fig. A of the Appendix.

Removal of solvent and recrystallisation from benzene gave 1-hydroperoxy-1-isopropyl-2(1H)-naphthalenone (120) (590 mg., 90%), m.p. 135-137° (lit.[5,6] 135-137°), whose spectral characteristics were identical to those reported[2,6] for this compound.

Oxygenation of the naphthol (119) in the presence of one mole of triphenylphosphine proceeded extremely slowly. After seven days, some unreacted starting material was still present. The product, isolated by preparative chromatography, was the known[2] 1-hydroxy-1-isopropyl-2(1H)-naphthalenone (40), which could be prepared in high yield from the hydroperoxide (120) by treatment with dimethyl sulphide in ether.

6-Bromo-1-isopropyl-2-naphthol (121).

(a) By bromination of 1-isopropyl-2-naphthol (119).

Freshly crystallised 1-isopropyl-2-naphthol (560 mg., 3 mmole) was taken up in glacial acetic acid (10 ml), and a standard solution of bromine in acetic acid (3.2 ml, 3 mmole) was added dropwise with stirring over thirty minutes under dry nitrogen.

After standing at room temperature for 12 hours, water (50 ml) was added, and the solution extracted with ether (3 x 20 ml). The combined extracts were washed with water, aqueous sodium bicarbonate, dried, and solvent removed to give an orange oil, which could not be induced to crystallise. This was taken up in ether, and washed with dilute aqueous sodium hydroxide, and then with Claisen's alkali.

The Claisen's alkali extracts were acidified and extracted with ether. The ether extracts were washed, dried, and solvent removed. Recrystallisation from benzene-petrol gave pale brown needles (180 mg., 15%), m.p. 70-77° of impure 6-bromo-1-isopropyl-2-naphthol (121).

The original ether extracts (base insoluble) were washed, dried, and solvent removed to give impure 1-bromo-1-isopropyl-2(1H)-naphthalenone (122), which could not be purified.

$\lambda_{max.}$(EtOH) 240, 315 nm.

$\nu_{max.}$(liquid film) 3400 (OH of the naphthol (121)), 1690 (conj. C=O) cm^{-1}.

τ ($CDCl_3$) 1.9-3.1, multiplet (Aromatics and C<u>H</u>=CH-C=O), 4.06, doublet, J = 10 Hz., 1H (CH=C<u>H</u>-C=O), 7.60, heptet, J = 6.5 Hz., 1H (-C<u>H</u>$(CH_3)_2$), 9.03, doublet, J = 6.5 Hz., 6H (-CH($C\underline{H}_3$)$_2$).

All spectra contained bands attributable to the naphthol (121).

The bromonaphthalenone (122) was taken up in a solution of hydrogen bromide in glacial acetic acid, and refluxed for twelve hours. Water was added, and the solution extracted with ether. T.l.c. indicated that both (121) and (122) were present in substantial quantity.

Treatment of this mixture with acetic anhydride in anhydrous pyridine followed by fractional crystallisation gave 2-acetoxy-6-bromo-1-isopropylnaphthalene (310 mg., 23%) which gave colourless fibrous needles from light petroleum, m.p. 88.5-90.5°,

$\lambda_{max.}$(EtOH) 232(4.84), 270(sh.), 279(3.87), 290(sh.), 311(3.06), 326(3.02) nm.

$\nu_{max.}$(KBr) 1758 (CH_3COO), 900 (1 isolated arom.H), 820 (2 adj. arom.H), 815 (2 adj. arom.H) cm^{-1}.

τ($CDCl_3$) 1.9-3.0, multiplet, 5H (Aromatics), 6.27, heptet, J = 7Hz., 1H (-C<u>H</u>$(CH_3)_2$), 7.64, singlet, 3H ($C\underline{H}_3$-C=O), 8.55, doublet, J = 7 Hz., 6H (-CH($C\underline{H}_3$)$_2$).

m/e 306, 308 (M^+).

Required for $C_{15}H_{15}O_2Br$: C 58.66% , H 4.92% , Br 26.01%

Found : C 58.80% , H 5.00% , Br 26.25% .

<u>6-Bromo-1-isopropyl-2-naphthol from 6-bromo-2-naphthol</u>.

6-Bromo-2-naphthol[105] (22.3 g., 0.1 mole) was dissolved in a solution of sodium methoxide, prepared by adding sodium (2.4 g., 0.1 mole) to anhydrous methanol (70 ml). The methanol was removed under reduced pressure, and anhydrous toluene (50 ml) added. The toluene was removed under reduced pressure, and this process of adding and removing toluene

repeated a further three times to remove traces of methanol.

To the residual colourless sodium 6-bromo-2-naphthoxide was added anhydrous toluene (75 ml) and then 2-bromopropane (10 ml). The mixture was refluxed under dry nitrogen (internal temperature 125-130°) for twenty four hours, a further three 10 ml portions of 2-bromopropane being added at approximately six hour intervals.

To the cooled reaction mixture was added water, and the toluene layer separated. The aqueous layer was then extracted with ether (twice) and the combined organic extracts washed with 1M sodium hydroxide solution.

The aqueous layers were combined and acidified, and the resulting precipitate filtered off, washed with water, and dried to give 6-bromo-2-naphthol (16.5 g., 74%).

The organic extracts were then extracted with Claisen's alkali (2 x 25 ml) under an atmosphere of nitrogen. The alkaline extracts were carefully acidified, cooled in an ice bath, and extracted ether (three times). The combined ether extracts were washed to neutrality, dried, and solvent removed to give a brown oil (3.8 g.), consisting mainly of 6-bromo-1-isopropyl-2-naphthol (121).

Purification was achieved by fractional distillation (b.p. 127-130°/ 0.015 mm.), followed by recrystallisation from light petroleum to give yellow prisms (2.4 g., 9%), m.p. 74-77° of 6-bromo-1-isopropyl-2-naphthol (121),

$\lambda_{max.}$(EtOH) 237(4.9), 273(3.63), 283(3.71), 294(3.58), 234(3.34), 245(3.36) nm.

$\nu_{max.}$(Nujol) 3400, broad,(H-bonded OH), 885 (isolated aromatic H), 820 (2 adj. arom.H), 805 (2 adj. arom.H) cm^{-1}.

τ ($CDCl_3$) 1.93-3.10, multiplet, 5H (Aromatics), 5.13, singlet, 1H (-O<u>H</u>, D_2O exchange), 6.13, septet, J = 6.5 Hz., 1H ($(CH_3)_2$<u>C</u>H-), 8.50, doublet, J = 6.5 Hz., 6H ($(C\underline{H}_3)_2$CH-).

6-Bromo-1-isopropyl-2-acetoxynaphthalene was prepared from this naphthol as described previously to give a sample identical in all respects to that prepared by an alternative route.

Oxygenation of 6-bromo-1-isopropyl-2-naphthol (121).

Freshly crystallised bromonaphthol (121) (795 mg., 3 mmole) was dissolved in dry benzene (15 ml) and oxygenated under standard conditions, the uptake of oxygen being recorded at regular intervals. (Theoretical uptake = 67 ml).

After 25 ± 2 hours, 33 ml had been taken up.

After 80 ± 5 hours, 65 ml had been taken up, and no further uptake was detected.

The solvent was removed under reduced pressure to give a yellow solid. Recrystallisation from benzene-light petroleum gave pale yellow needles (885 mg., 100%), m.p. 137-140° (decomposition) of 6-bromo-1-hydroperoxy-1-isopropyl-2(1H)-naphthalenone (124),

$\lambda_{max.}$(EtOH) 239(sh.), 245(4.44), 306(3.88) nm.

$\nu_{max.}$(CCl_4) 3500 (OH), 1680 (conj. C=O) cm^{-1}.

(KBr) 1665 (conj. C=O), 815 (2 adj. arom.H), 890 (isolated arom.H) cm^{-1},

τ ($CDCl_3$) 0.54, S, 1H (OO<u>H</u>, D_2O exchange), 2.4-2.5, multiplet, 2H, (Aromatics H_7 and H_8), 2.54, doublet, J_{meta} = 1 Hz., 1H (Aromatic, H_5), 2.70, doublet, J = 10 Hz., 1H (C<u>H</u>=CH-C=O), 3.82, doublet, J = 10 Hz., 1H (CH=C<u>H</u>-C=O), 7.87, septet, J = 7 Hz., ($(CH_3)_2$C<u>H</u>-), 9.12 and 9.14, two doublets, J = 7 Hz., 6H (non-equivalent C<u>H</u>$_3$'s).

m/e 296 and 298 (M^+).

Required for $C_{13}H_{13}O_3Br$: C 52.52% , H 4.41% , Br 26.88%

Found : C 52.41% , H 4.74% , Br 27.40% .

The oxygenation was repeated on a sample prepared from the treatment of pure 2-acetoxy-1-bromo-1-isopropylnaphthalene with LAH in anhydrous ether under dry nitrogen (1 hour reflux), giving the same results within the limits of experimental error.

APPENDIX

Table 1

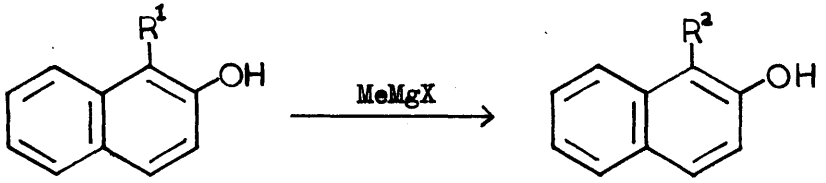
Substituted 2-naphthol	Time taken for :- Uptake of 0.5 moles of oxygen per mole. (hours)	Time taken for :- Complete Aut-oxidation (hours)	Isolated yield of Hydro-peroxide (%)	Chemical Shift of H-8 (τ)
1-methyl	------	------	----	ca 7.85
1-isopropyl	4 ± 0.5	16 ± 2	90	8.08
	2 ± 0.5 ×	14 ± 2 ×		
1-isopropyl-6-bromo	25 ± 2	80 ± 5	100	7.95
1-t-butyl	≤10 min.	0.5 ± 0.1	85	8.41
1-t-pentyl	≤10 min.	0.5 ± 0.1	95	8.37
1-methyl-3,6-di-t-butyl	14 ± 2	36 ± 5	85	ca 7.8
bisnaphthylmethane (72)	10 ± 2 min †	1 ± 0.1 †	----	8.11 *
1,8-dimethyl	3 ± 0.2	12 ± 2	94	----

× This experiment was carried out in diffuse sunlight on a bright day.

† This experiment was carried out in ethyl acetate-benzene solution.

* The downfield shift of this proton may be a result of mutual deshielding by the two naphthalene systems.

Table 2



(see experimental section for detailed reaction conditions)

Substrate	Reagent(s)	Temperature T°	Reaction time at T° (hours)	Product Proportions (%)* R^2 = $C(CH_3)_2OH$	$COCH_3$	$C(CH_3)=CH_2$	$C(CH_3)_3$	
$R^1 = CO_2Me$	MeMgI or MeMgBr	110°	17	ca. 1	14	57	28	
$R^1 = CO_2Me$	MeMgI	130°	22	---	13	65	22	
$R^1 = CO_2Me$	MeMgI	130°	42	---	trace	70	30	X
$R^1 = CO_2Me$	MeMgI, $^nBu_2O$	142°	24	6	12	78	4	
$R^1 = CO_2Me$	MeMgI	90°	28	75	13	12	----	
$R^1 = CO_2Me$	MeMgI/$AlCl_3$ (12 : 1)	110°	22	4	14	62	20	X

continued over

Table 2 continued

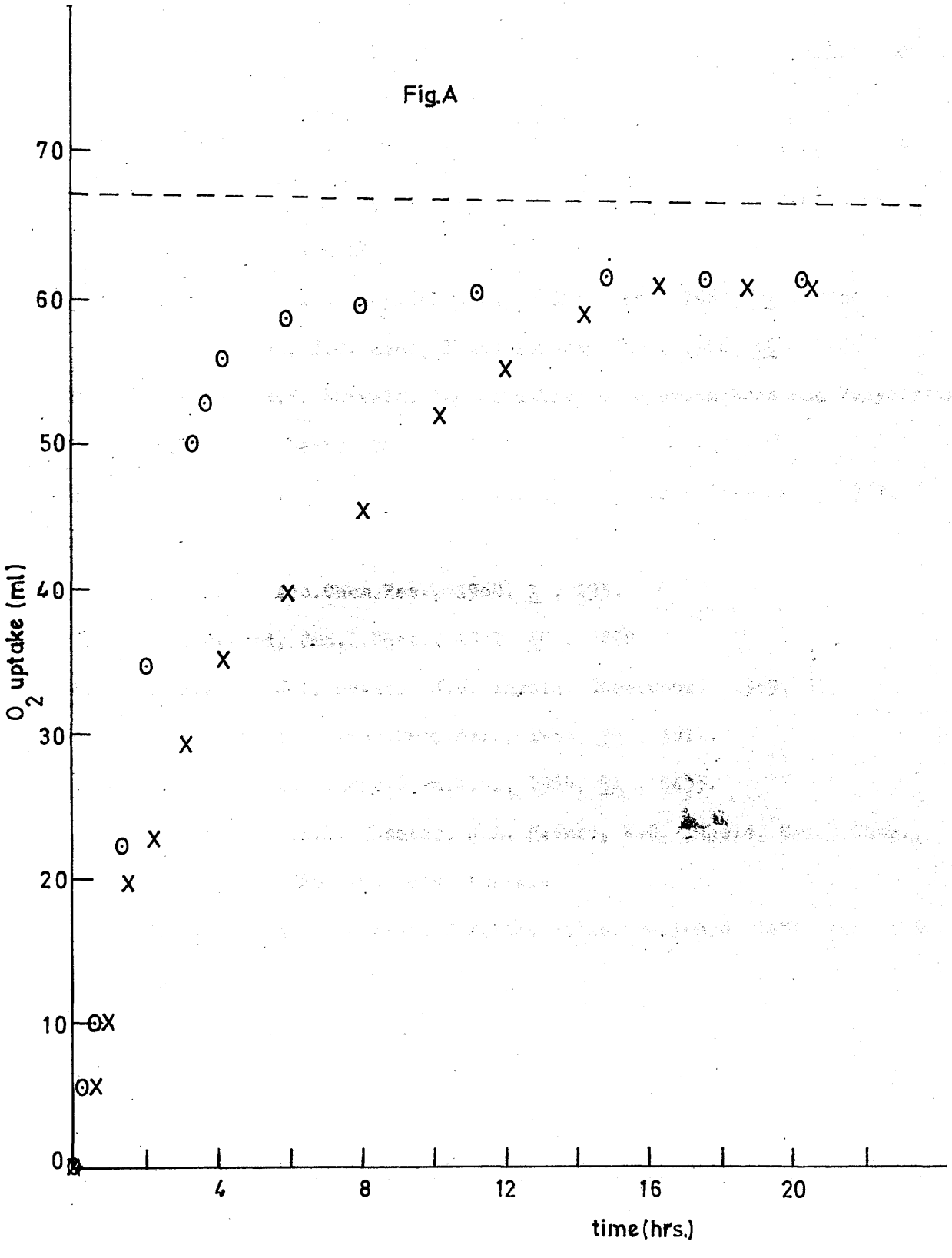
$R^1 = CO_2Me$	MeLi	130°	22	45	35	20	----
1-Acetyl-2-methoxy-naphthalene	MeMgI	110°	20	3	14	65	18
$R^1 = CO_2Me$	(1) MeMgI (2) MeI/dmso	110°	18	----	12 †	57 †	31 † (25% isolated yield)
$R^1 = CO_2Me$	(1) MeMgI (2) MeI/dmso	130°	40	----	----	70 †	30 † (18% isolated yield)

* Relative product ratios, estimated by n.m.r..

† Isolated as a mixture of the methyl ethers.

× Extensive polymerisation.

Autoxidation of 1-isopropyl-2-naphthol (119).



⊙ = Autoxidation in diffuse sunlight.

X = Autoxidation in dark.

INTRODUCTION REFERENCES.

1.(a) J.K. Kochi (Ed.), 'Free Radicals', Interscience, 1973, Vol.II, Ch.I.

(b) J. Betts, Quart.Rev., 1971, 25 , 265.

(c) G. Scott, 'Atmospheric Oxidation and Antioxidants', Elsevier, 1965.

(d) W.O. Lundberg (Ed.), 'Autoxidation and Antioxidants', Interscience, 1961, Vols.I and II.

2. A. Bromberg, K.A. Muszket, J.Amer.Chem.Soc., 1969, 91 , 2860.

3. D.J. Carlson, J.C. Robb, Trans.Faraday Soc., 1966, 62 , 3403.

4. L. Reich, S.S. Stivala, 'Autoxidation of Hydrocarbons and Polyolefins', Dekker, New York, 1969.

5. E.G. Janzen, F.J. Johnston, C.A. Ayers, J.Amer.Chem.Soc., 1967, 89 , 1176.

6. F.R. Mayo, Acc.Chem.Res., 1968, 1 , 193.

7. J.A. Howard, Can.J.Chem., 1972, 50 , 2298.

8. K. Adamic, J.A. Howard, K.U. Ingold, Chem.Comm., 1969, 505.

9. G.A. Russell, J.Amer.Chem.Soc., 1957, 79 , 3871.

10. R.E. Kellogg, J.Amer.Chem.Soc., 1969, 91 , 5433.

11. S. Korcek, J.H.B. Chenier, J.A. Howard, K.U. Ingold, Can.J.Chem., 1972, 50 , 2285, and refs. therein.

12. D. Swern (Ed.), 'Organic Peroxides', Interscience, 1971, pps. 106-127.

13. L.R. Mahoney, M.A. Da Rooge, J.Amer.Chem.Soc., 1970, 92 , 4063.

14. J.A. Howard, Adv.Free Rad.Chem., 1972, 4 , 49.

15. G.S. Hammond, J.Amer.Chem.Soc., 1955, 77 , 334.

16. K.U. Ingold, Acc.Chem.Res., 1969, 2 , 1, and refs. therein.

17. J.A. Howard, S. Korcek, Can.J.Chem., 1970, 48 , 2165.

18. M. Ballester, Pure and Appl.Chem., 1967, 15 , 123.

19. J.A. Howard, K.U. Ingold, Can.J.Chem., 1970, 48 , 873.

20. V.V. Voronenkov, A.N. Vinogradov, V.A. Belyaev, Russ.Chem.Rev., 1970, 39 , 944.

21. see D.C. Nonhebel, J.C. Walton, 'Free Radical Chemistry', Cambridge Univ.Press, 1974, Ch.4, for a review of this subject.

22. A.J. Dobbs, B.C. Gilbert, R.O.C. Norman, J.Chem.Soc. (A), 1971, 124.

23. R. Caputo, L. Previtera, P. Monaco, L. Mangoni, Tetrahedron, 1974, 30 , 963.

24. E.R. Altwicker, Chem.Rev., 1967, 67 , 475.

25. A.R. Battersby, W.I. Taylor, 'Oxidative Coupling of Phenols', Arnold, 1967.

26. H.R. Gersmann, A.F. Bickel, J.Chem.Soc., 1962, 2356, and refs. therein.

27. G.A. Nikiforov, V.V. Ershov, Russ.Chem.Rev., 1970, 39 , 644.

28. M.S. Kharasch, B.S. Joshi, J.Org.Chem., 1957, 22 , 1439.

29. V.V. Ershov, A.A. Volod'kin, Chem.Abs., 1962, 57 , 12337c.

30. B. Miller, J.Amer.Chem.Soc., 1967, 89 , 1685.

31. T. Matsuura, K. Ogura, J.Amer.Chem.Soc., 1967, 89 , 3846.

32. T. Matsuura, K. Ogura, Tetrahedron, 1968, 24 , 6167.

33. H. Bredereck, G. Bauer, Ann., 1970, 739 , 117.

34. C. Bischoff, A. Reiche, Zeitchrift Chem., 1968, 8 , 384.

35. G. Wojack, Ber., 1938, 71 , 1102.

36. J.J. Artus, J.J. Bonet, A.E. Pẽna, Chem.Comm., 1973, 579.

37. V. Balasubramaniyan, Chem.Rev., 1966, 66 , 567.

38. D. Bright, I.E. Maxwell, J. deBoer, J.C.S. Perkin II, 1973, 2101, and refs. therein.

39. A. Saika, A. Kawamori, R. Takagi, J.Mag.Res., 1972, 7 , 324.

40. J.B. Robert, J.S. Sherfinski, R.E. Marsh, J.D. Roberts, J.Org.Chem., 1974, 39 , 1152.

41. H. Van Bekkum, T,J. Nieuwstad, J. Van Barneveld, P. Klapwijk, B.M. Wepster, Rec.Trav.Chim., 1969, 88 , 1028, and refs. therein.

42. A. Maunschreck, L. Ernst, Chem.Ber., 1971, 104 , 228.

43. J.E. Anderson, R.W. Franck, W.L. Mandella, J.Amer.Chem.Soc., 1972, 94 , 4608, and refs. therein.

44. H.O. House, D.G. Koepsill, W.J. Campbell, J.Org.Chem., 1972, 37 , 1003.

45. A. Reiser, T.R. Wright, J.Chem.Phys., 1973, 59 , 3433.

46. W.L. Mandella, R.W. Franck, J.Amer.Chem.Soc., 1973, 95 , 971, and refs. therein.

47. H.H. Wasserman, D.L. Larsen, Chem.Comm., 1972, 253.

48. C.K. Bradsher, N.A. Porter, T.G. Wallis, J.Org.Chem., 1974, 39 , 1172.

49. D.L. Fields, T.H. Regan, J.Org.Chem., 1971, 36 , 2986.

50. A. Schonberg, A. Mustafa, A.F. Shalaby, J.Amer.Chem.Soc., 1955, 77 , 5756.

51. M. Bosco, L. Forlani, P.E. Todesco, J.Chem.Soc. (B), 1970, 1742.

52. M. Schach von Wittenau, J.Org.Chem., 1964, 29 , 2746; A.I. Scott, C.J. Bedford, J.Amer.Chem.Soc., 1962, 84 , 2271.

53. R.W. Franck, K. Yanagi, J.Org.Chem., 1968, 33 , 811.

54. C. Dufraisse, A. Etienne, J. Rigaudy, Bull.Soc.Chim.France, 1948, 804, and refs. therein.

55. Y. Ogata, Y. Kosugi, K. Nate, Tetrahedron, 1971, 27 , 2705.

56. J. Carnduff, Ph.D. Thesis, Univ. of Glasgow, 1963.

57. D.G. Leppard, Ph.D. Thesis, University of ~~Glasgow~~ Dundee, 1969.

58. J. Carnduff, D.G. Leppard, Chem.Comm., 1969, 829.

59. W. Brackmann, E. Havinga, Rec.Trav.Chim., 1955, 74 , 1021.

60. K. Fries, Ber., 1914, 47 , 1193.

DISCUSSION REFERENCES.

1. V.S. Gandhi, H. Mori, E. Schwenk, Chem.Pharm.Bull.Japan, 1964, 12 , 112 and refs. therein.
2. D.G. Leppard, Ph.D. Thesis, Univ. of ~~Glasgow,~~ Dundee 1969.
3.(a) M.L. Khorana, S.H. Pandit, Indian J.Chem., 1963, 1 , 489.
   (b) K. Fries, Annalen, 1924, 439 , 232.
4. K. Takeda, H. Osaka, J.Pharm.Soc.Japan, 1955, 75 , 210.
5. J. Carnduff, Ph.D. Thesis, Univ. of Glasgow, 1963.
6. J. Carnduff, D.G. Leppard, Chem.Comm., 1967, 829.
7. E. Wenkert, R.D. Youssefych, R.G. Lewis, J.Amer.Chem.Soc., 1960, 82 , 4675.
8. K. Gulati, S. Seth, K. Venkataraman, J.Prakt.Chem., 1933, 47 , 177;
   B.C. McKusick, J.Amer.Chem.Soc., 1948, 70 , 2196.
9. A. Belorossova, V. Epshstein, L. Angert, Uch.Zap.Yaroslavsk. Teknol.Inst., 1962, 8 , 123.
10. B. Alberti, Annalen, 1926, 450 , 304.
11. L. Claisen, Ber., 1912, 45 , 3160.
12. V.A. Zagoreosky, J.Gen.Chem.(U.S.S.R.), 1957, 27 , 3055.
13. A. Schonberg, A. Mustafa, A.F.A.M. Shalaby, J.Amer.Chem.Soc., 1955, 77 , 5756, and refs. therein.
14. D.R. Buckle, E.S. Waight, Chem.Comm., 1969, 922.
15.(a) W.A. Henderson, E.F. Ullman, J.Amer.Chem.Soc., 1965, 87 , 5424.
   (b) R. Huisgen, L.A. Feiler, P.Otto , Chem.Ber., 1969, 102 , 3405.
   (c) D.L. Fields, J.Org.Chem., 1971, 36 , 3002.
16. R. Pummerer, F. Frankfurter, Ber., 1919, 52 , 1403.
17. J. Green, D. McHall, Chem. and Ind., 1964, 43 , 1801.
18. R.W. Franck, K. Yanagi, J.Org.Chem., 1968, 33 , 811.

19. N.P. Buu-Hoi, H. LeBihan, F. Binon, P. Rayet, J.Org.Chem., 1950, 15 , 1060, and refs. therein.

20. A. Reiker, N. Zeller, K. Schurr, E. Muller, Annalen, 1966, 697 , 1.

21. G.A. Razuvaev, M.L. Khidekel, V.B. Berlina, Dokl.Akad.Nauk., U.S.S.R., 1962, 145 , 1071.

22. R.T. Ferris, D. Hamer, J.Chem.Soc., 1960, 1409.

23. P.A. Brady, J. Carnduff, D.G. Leppard, Tet.Let., 1972, 4183.

24. T. Kauffmann, Angew.Ch.Int.Ed., 1974, 291, and refs. therein.

25. E. Illingworth, A.T. Peters, J.Chem.Soc., 1951, 1602.

26. J.W. Cook, C.A. Lawrence, J.Chem.Soc., 1936, 1431.

27. R.G. Kadesch, J.Amer.Chem.Soc., 1944, 66 , 1207.

28. F. Snyckers, H. Zollinger, Helv.Chim.Acta., 1970, 1294.

29. C. Gardner, H.B. Boyles, J.Amer.Chem.Soc., 1951, 73 , 870.

30. H.C. Brown, C.P. Garg, J.Amer.Chem.Soc., 1961, 83 , 2951.

31. H. VanBekkum, T.J. Nieuwstad, J. VanBarnevald, P. Klapwijk, B.M. Wepster, Rec.Trav.Chim., 1969, 88 , 1028.

32. D. Bryce-Smith, J.Chem.Soc., 1956, 1603.

33. J.W. Burnham, W.P. Duncan, E.J. Eisenbraun, Org.Prep.Proc.Int., 1973, 5 , 285.

34. Elsevier's Encyclopaedia, Series III, 12B , 2374.

35. J. Kahovec, J. Pospisil, Chem. and Ind., 1969, 489, and refs. therein.

36. P.L. Julian, W.G. Gist, J.Amer.Chem.Soc., 1935, 57 , 2030.

37. A. Meisters, T. Mole, Chem.Comm., 1972, 595.
J.K. Kochi, R.G. Salomon, J.Org.Chem., 1973, 38 , 3715.

38. B.M. Trost, M.Preckel, J.Amer.Chem.Soc., 1973, 95 , 7862, and refs. therein.

39. I.M. Hunsberger, J.Amer.Chem.Soc., 1950, 72 , 5626.

40. T. Severin, I. Ipach, Synthesis, 1973, 796.

41. D. Swern (Ed.), 'Organic Peroxides', Interscience, Vol.II, 1970.

42. J. Carnduff, D.G. Leppard, Chem.Comm., 1971, 975.

43. R.B. Marks, B.Sc. Thesis, Univ. of Glasgow, 1972.

44. S. Danilov, E. V. Danilova, Ber., 1934, 67 , 24.

45. M. Nakamura, M. Oki, Tet.Let., 1973 (10), 727.

46. W.J. LeNoble, Synthesis, 1970, 1 , 1.

47. R.W. Franck, E.G. Leser, J.Amer.Chem.Soc., 1969, 91 , 1577.

48. I thank Dr. J.E. Anderson, Univ. College, London, for carrying out this experiment.

49. J.E. Anderson, R.W. Franck, W.L. Mandella, J.Amer.Chem.Soc., 1972, 94 , 4608.

50. W.L. Mandella, R.W. Franck, J.Amer.Chem.Soc., 1973, 95 , 971.

51. D.L. Fields, T.H. Regan, J.Org.Chem., 1971, 36 , 2986.

52. G.I. Feutrill, R.N. Mirrington, Tet.Let., 1970, 1327, and refs. therein.

53. A.L. Wilds, W.B. McCormack, J.Amer.Chem.Soc., 1948, 70 , 4127; 'Methoden der Organische Chemie', Houben-Weyl, Meerwein, Muller, (Eds.), Vol. IV, 1964, p. 160.

54. E.R. Altwicker, Chem.Rev., 1967, 67 , 475.

55. D.R. Buckle, E.S. Waight, Chem.Comm., 1969, 922.

56. J. Carnduff, unpublished work.

57. G. Lock, Monatsh, 1954, 85 , 802.

58. A. Russell, L.B. Lockhart, Org.Synth., Coll. Vol. III, 463.

59. V.S. Gandhi, H. Mori, E. Schwenk, Chem.Pharm.Bull.Japan, 1964, 12 , 112.

60. S.V. Liebermann, E.C. Wagner, J.Org.Chem., 1949, 14 , 1008; R.L. Shriner, G.F. Grillot, W.O. Teeters, J.Amer.Chem.Soc., 1946, 68 , 946.

61. A. Shimomura, I.B. Cohen, J.Chem.Soc., 1921, 119 , 746; K. Fries, E. Hubner, Ber., 1906, 39 , 439.

62. A. Merijan, P.D. Gardner, J.Org.Chem., 1965, 30 , 3965.

63. P.D. Gardner, H.S. Rafsanjani, L. Rand, J.Amer.Chem.Soc., 1959, 81 , 3364.

64. M.S. Chauhan, F.M. Dean, D. Matkin, M.L. Robinson, J.C.S. Perkin I, 1973, 120.

65. R. Pummerer, E. Cherbuliez, Ber., 1919, 52 , 1392.

66. G. Catterall, Chem.Comm., 1974, 41.

67. H.-U. Wagner, R. Gomper, 'Chemistry of Quinones', Interscience, Ch. 18, 1145.

68. F. McCapra, Y.C. Chang, Chem.Comm., 1968, 22, and refs. therein.

69. H.O. House, D.G. Koepsill, W.J. Campbell, J.Org.Chem., 1972, 37 , 1003, and refs. therein.

70. D. Bright, I.E. Maxwell, J. DeBoer, J.C.S. Perkin II, 1973, 101.

71. J.S. Hastings, H.G. Heller, J.C.S. Perkin I, 1972, 1839.

72(a). J.E. Marsh, J.Chem.Soc., 1927, 3164.

(b) P.S. Varma, K. Rajah, J.Ind.Chem.Soc., 1933, 10 , 595.

(c) R. Meldola, J.Chem.Soc., 1885, 47 , 525.

73. P.G. Sammes, Synthesis, 1970, 636;
R.K. Sharma, N. Kharasch, Angew.Chemie, Int.Ed., 1968, 36.

74. I thank W.A. Henderson and D.L. Fields for providing samples of this compound.

75. A.L. Buchachenko, 'Stable Radicals', Consultants Bureau, New York, 1965, p. 90.

76. M.D. Jameson, B.R. Penfold, J.Chem.Soc., 1965, 528.

77. J. Parker, J. Vaughan, E. Wong, J.Org.Chem., 1958, 23 , 1373.

78. M. Sy, J. Oiry, Bull.Soc.chim.France, 1967, 10 , 3759;
M.L. Khorana, S.Y. Pandit, Ind.J.Chem., 1963, 1 , 489.

79. M.J. Gallagher, M.D. Sutherland, Austral.J.Chem., 1965, 18 , 1111.

80. W. Cocker, J. Chem.Soc., 1946, 36.

81. G. Traverso, Gazzeta Ch.Ital., 1966, 96 , 1186.

82. L. Ruzicka, K. Hofmann, H. Schellenberg, Helvetica. Chim. Acta., 1936, 19 , 1391.

83. Elsevier's Encyclopaedia, Series III, 13 , 133.

84(a) V. Boeckelheide, M. Goldman, J.Org.Chem., 1954, 19 , 575.

(b) R.E. Beyler, L.H. Sarett, J.Amer.Chem.Soc., 1952, 74 , 1406.

(c) W. Reid, H. Boden, Chem.Ber., 1958, 91 , 1354.

(d) W.J. Mitchell, R.D. Topsom, J. Vaughan, J.Chem.Soc., 1962, 2 , 2526.

(e) J.W. Burnham, E.J. Eisenbraun, Org.Prep.Proc.Int., 1972, 4 , 35.

85. H. Staudinger, H. Goldstein, E. Schlenker, Helvetica Chim.Acta, 1921, 4 , 342.

86(a) R.I. Davies, I.M. Heilbron, F. Irving, J.Chem.Soc., 1932, 2 , 275.

(b) J. Cason, A. Weiss, S.A. Monti, J.Org.Chem., 1968, 33 , 3404.

87. R.A. Benkeser, K.M. Foley, J.M. Gaul, G.S. Li, J.Amer.Chem.Soc., 1970, 92 , 3232.

88. K. Ramakrishnan, P. Bickart, Chem.Comm., 1972, 1338.

89. Cambrian Chemicals Ltd.

90. A. Reiche, H.E. Seyfarth, F. Brand, Annalen, 1969, 725 , 93.

91. J. Cason, D.M. Lynch, A. Weiss, J.Org.Chem., 1973, 38 , 1944.

92. M. Cěrny, J. Malèk, Coll.Czech.Chem.Comm., 1970, 35 , 3079.

93. J.H. Brewster, S.O. Osman, H.O. Beyer, H. Hopps, J.Org.Chem., 1964, 29 , 121.

94. C.T. West, S.J. Donnelly, D.A. Kovistra, M.P. Doyle, J.Org.Chem., 1973, 38 , 2675.

95. J. Carnduff, R.B. Marks, private communication.

96. J. Furukawa, K. Omura, O. Yamamoto, K. Ishikawa, Chem.Comm., 1974, 77.

97. Elsevier's Encyclopaedia, Series III, 12B , 4272.

98. Elsevier's Encyclopaedia, Series III, 12B , 1395.

99. R.L. Augustine, (Ed.), 'Reduction', Dekker, 1968.

100. A.L. Meyer, R.B. Turner, Tetrahedron, 1971, 27 , 2614, and refs. therein.

101. D. Walker, J.D. Hiebert, Chem.Rev., 1967, 67 , 153.

102. L.F. Feiser, M. Feiser, 'Reagents for Organic Synthesis', Wiley, 1967, p. 778 et seq..

103. H. Hellmann, J.L.W. Pohlmann, Annalen, 1961, 642 , 28;
L.I. Smith, J.W. Horner Jr., J.Amer.Chem.Soc., 1938, 60 , 676.

104. K. Fries, Schimmelschmidt, Annalen, 1930, 484, 290.

105. C.F. Koelsch, Org.Synth., Coll. Vol. III, 132.

106. M.D. Sevilla, G. Vincov, J.Phys.Chem., 1968, 72 , 3635.

107. H. Staudinger, W. Kries, W. Schilt, Helv.Ch.Acta, 1922, 5 , 243.

108. L.F. Feiser, H.L. Holmes, J.Amer.Chem.Soc., 1936, 58 , 2319.

109. Doddrell, J.C.S. Perkin II, 1973, 1333;
J.B. Stothers, 'C-13 N.M.R. Spectroscopy', Academic Press, 1972.