A Thesis entitled

Aspects of Phenol Oxidation

submitted to the

University of Glasgow

for the degree of Doctor of Philosophy

in the Faculty of Science

by

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November 1977

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I thank Dr. John Carnduff very much for his help and interest, Professor G.W. Kirby for the opportunity of carrying out this work and the University of Glasgow for a Glasgow University Studentship.

I am grateful to Mrs. Harkness for microanalyses, Mr. Ritchie for mass spectra and other members of the technical staff for their assistance.

I wish to thank Professor Dr. Ch. Rüchardt for his hospitality in the Department of Physical Organic Chemistry in the University of Freiburg during the tenure of an exchange scholarship from Glasgow University/DAAD.

I thank Mrs. Jeanette Docherty for typing this thesis.

CONTENTS

Summary

In an extension of previous studies on the rate of autoxidation of 1-alkyl-2-naphthols, the synthesis and study of a series of related 1-aralkyl-2-naphthols was undertaken. Preparation of 1-trityl-2-naphthol from o-naphthofuchsone was reinvestigated. Initial attempts to prepare o-naphthofuchsone by reaction of 2-naphthol with Ph_2CCl_2 in the presence of $AlCl_3$ led to formation of 12-phenyl-12H-benzo[a]xanthene. A successful preparation involved the dehydration of 1-diphenylhydroxy c methyl-2-naphthol which was prepared in high yield from the methyl ester of 2-hydroxy-1-naphthoic acid by reaction with PhMgBr. Reaction of the stable o-quinone methide with PhMgBr gave 1-trityl-2-naphthol. The related 1-(1,1-diphenylethyl)- and diphenylmethyl-2-naphthol were prepared from o-naphthofuchsone by reaction with MeMgI and $NaBH_4$ respectively. None of these three naphthols showed any tendency to autoxidise although they were considered to experience an unfavourable peri interaction the magnitude of which would be similar to, if not greater than, that in related 1-alkyl-2-naphthols which had proved to be highly susceptible to autoxidation. The solution IR spectra of these three compounds revealed that there was total intramolecular hydrogen bonding in each case. The previously studied 1-benzyl-2-naphthol which is also stable to autoxidation under the standard conditions showed approximately one third of the molecules had intramolecularly H-bonded hydroxyl groups. Prolonged treatment of 1-benzyl-2-naphthol with oxygen with or without a catalytic amount of $Co(acac)_3$ led to the formation of 1-benzyl-1-(1-benzyl-2-naphthyloxy)naphthalen-2(1H)-one and a mixture of ketol isomers, 1-benzyl-1-hydroxynaphthalen-2(1H)-one and 2-benzyl-2-hydroxynaphthalen-1(2H)-one. The identity of these species was confirmed by the

independent synthesis of the dimer by potassium ferricyanide oxidation of 1-benzyl-2-naphthol and of the ketol mixture by sodium periodate oxidation and by Wessely oxidation of 1-benzyl-2-naphthol. Attempts to oxidise 1-benzyl-2-naphthol to an o-quinone methide using dichlorodicyanobenzoquinone led to the formation of the above O-C dimer.

Attempts to prepare the benzoate of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one repeatedly led to the isolation of 1-benzoyloxy-1-isopropoxynaphthalen-2(1H)-one. Thermolysis of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one itself proceeds by a radical pathway with evolution of a gas.

The latter part of the thesis describes work intended to explore the range of application and the stereospecificity of various reagents which epoxidise α,β-unsaturated ketones in which the faces of the enone are not equivalent. Three enone types were investigated - 1-alkyl-1-hydroxynaphthalen-2(1H)-ones, 4-hydroxy-2,4,6-trialkylcyclohexadienones and 4-alkyl-4-hydroxynaphthalen-1(4H)-one. Preparation of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one was achieved by autoxidation of 1-isopropyl-2-naphthol followed by reduction of the hydroperoxide by dimethyl sulphide. 1-Hydroxy-1-methylnaphthalen-2(1H)-one was prepared by chromium trioxide or peroxyacetic acid oxidation of 1-methyl-2-naphthol. On heating with molybdenum hexacarbonyl both these ketols undergo ketol rearrangement, the latter more slowly than the former, and in both cases this rearrangement precludes epoxidation by t-butyl hydroperoxide catalysed by $Mo(CO)_6$. 1-Hydroxy-1-isopropylnaphthalen-2(1H)-one was reduced to a single diol by sodium borohydride. Reaction of the diol with t-BuOOH and $VO(acac)_2$ or with m-chloroperoxybenzoic acid led to a mixture of hydroxyketones containing an epoxide which is probably 2-hydroxy-2-isopropylnaphthalen-2(1H)-one-3,4-epoxide formed after unexpected oxidation of the diol and ketol rearrangement.

The *in situ* generation of singlet oxygen, using CeO_2 and H_2O_2, provides a convenient route to hydroperoxycyclohexadienones from mesitol and 2,6-di-t-butyl-4-methylphenol. Attempts to prepare 4-hydroperoxy-2,4,6-tri-t-butylcyclohexadienone by this method led to recovery of starting material. 2,6-Di-t-butyl-4-hydroperoxy-4-methylcyclohexadienone was also prepared by base-catalysed oxygenation. Reduction of these hydroperoxides with dimethyl sulphide gave the corresponding hydroxydienones. Attempted epoxidation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexadienone with t-butyl hydroperoxide and $Mo(CO)_6$ led to a complex mixture which showed evidence for the presence of an epoxide but which could not be separated. Attempted epoxidation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexadienone and 4-hydroxy-2,4,6-trimethylcyclohexadienone with alkaline hydrogen peroxide were unsuccessful. Epoxidation of 4-hydroxy-4-methylnaphthalen-1(4H)-one, prepared by singlet oxygen oxidation of 4-methyl-1-naphthol followed by reduction, with both alkaline hydrogen peroxide and *m*-chloroperoxybenzoic acid led to the same epoxide, both reactions proceeding with high stereoselectivity.

The discussion of these new results is preceeded by an Introduction reviewing previous work on phenol oxidations of various types and enone epoxidations with particular regard to steric control.

INTRODUCTION

1. Phenol Oxidation

The oxidation of phenols can be effected by a variety of oxidising agents and allows facile conversion to compounds of many different types. Improved separation techniques, a more sophisticated understanding of the factors which influence the product distribution, the identification of phenol coupling in the biosynthesis of different classes of natural products, and the industrial importance of anti-oxidants have all guaranteed continuing interest in the chemistry of phenol oxidation.

Under the heading of phenol oxidation several discrete subgroups can be identified. Of these, the following have been selected for detailed consideration because of their relevance to the work being presented in this thesis.

1) Autoxidation - the reaction of a substance with triplet molecular oxygen, $^3O_2$, at moderate temperatures. Studies are mainly carried out in inert solvents, with or without radical catalysts.

2) Base-catalysed autoxidation in which $^3O_2$ reacts with the phenoxide anion.

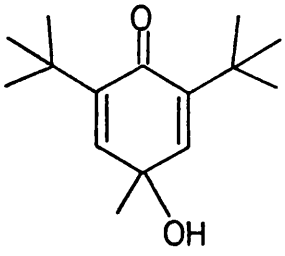
3) Reaction with singlet oxygen, $^1O_2$, by mechanisms quite different from those with triplet oxygen.

4) Phenol oxidative coupling, with many oxidising agents and giving rise to a variety of dimeric substances derived from the phenoxy radical is probably the most investigated area of phenol oxidation.

5) Dehydrogenation of certain types of phenol to quinone methides

which may or may not be isolated.

6) Hydroxylation of certain phenols by any of a host of oxidising agents to give o- and p-quinols (hydroxycyclohexadienones).



1) Autoxidation. This process can be either an undesirable reaction of industrial importance (causing the deterioration of rubber, the rancidification of natural oils, etc.) or a reaction of industrial utility (providing an efficient synthetic route to phenol and acetone from cumene and also providing the radical species necessary for the drying of paints and varnishes). The subject of autoxidation has been comprehensively reviewed[1] and the proposed mechanism can be described by the following general scheme.

Initiation : production of free radicals $R^{\bullet}$

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

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

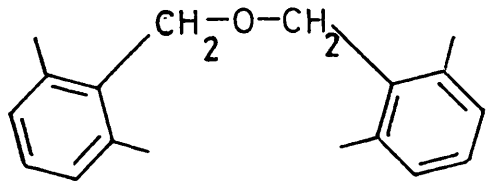
Termination: $2R^{\bullet} \longrightarrow R\text{-}R$

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

$2ROO^{\bullet} \longrightarrow O_2 + ROOR$

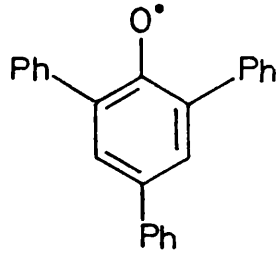
or $ROO^{\bullet} + AH \longrightarrow ROOH + A^{\bullet}$ (a non-propagative radical)

The rate determining propagation reaction for most organic compounds is the reaction between peroxy radical and substrate. Thus steric and electronic factors which weaken or strengthen the R-H bond can have a very significant effect on the rate of autoxidation. For example, the methylene groups of the hindered ether

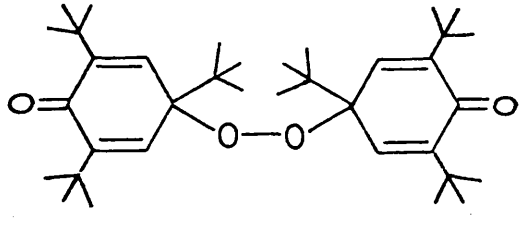


are fifteen times less reactive than those of dibenzyl ether towards the $HOO^{\bullet}$ radical[2] and o-substituted alkyl benzenes autoxidise more slowly than p-isomers.

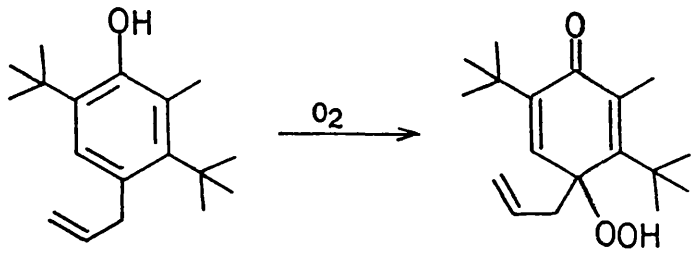
In the case of phenol autoxidation, phenoxy radicals are formed as a result of $H^{\bullet}$ abstraction from the hydroxyl group. Sterically accessible phenoxy radicals readily form stable O-C and C-C dimers, more hindered species may form dimers which partially dissociate in solution, for example, the triphenylphenoxy radical.[3]



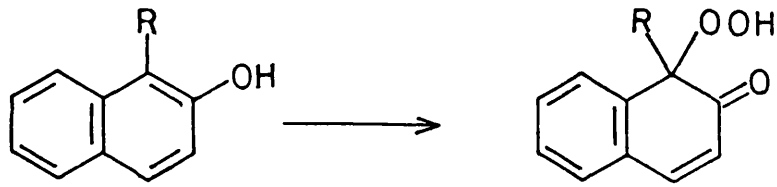
In certain extreme cases, the radical may exhibit a high degree of stability. For example, 2,4,6-tri-t-butylphenoxy radical, in the absence of O_2, is stable in solution and as a crystalline solid.[4] With O_2, the peroxide is formed.[5]



Some phenols autoxidise to ketohydroperoxides. For example, 4-allyl-2,5-di-t-butyl-6-methylphenol.[6]



Certain 1-alkyl-2-naphthols are known to autoxidise to give hydroperoxynaphthalenones

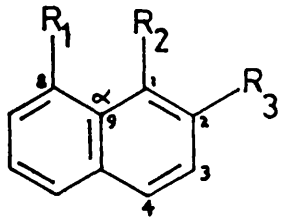


if the alkyl group is secondary or tertiary.[7,8]

R	Rate of reaction
t-butyl t-pentyl	rapid, complete conversion after 0.5h.
isopropyl cyclohexyl	slower, complete conversion after 20h.
benzyl methyl	no reaction under the conditions of the reaction.

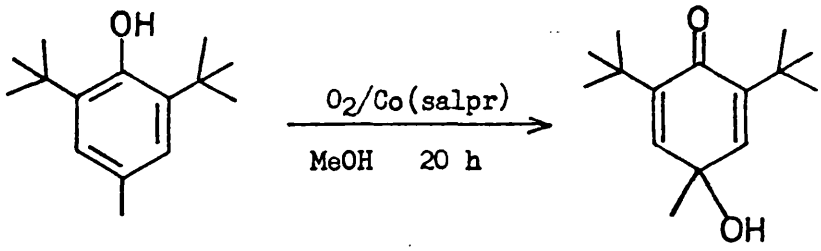
As can be seen from the table, the rate of autoxidation of the 1-alkyl-2-naphthols in this series increases with the bulk of the alkyl group and this was attributed to the increased strain in the phenol, due to the peri-interaction. Although it is still not clear how the strain increases the rate, the presence of strain in the substituted naphthols is proved by X-ray studies[9] on the series of compounds in the following table which show increasing distortion of the skeleton intended to reduce the van der Waals repulsion between the peri substituents. The most significant distortion observed is

a splaying apart of the ring system, separating C_1 and C_8, and one indicator of this is the 1 - 9 - 8 angle (α).

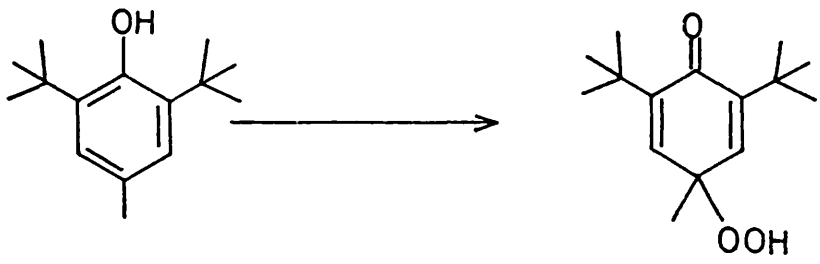


R_1	R_2	R_3	α
H	H	H	120.2°
H	Me	OAc	122.3°
H	Pr^i	OAc	123.2°
Me	Me	OAc	125.9°

Catalysts have often been used to promote autoxidation. For example, the presence of cobalt(III) acetylacetonate, $Co(acac)_3$, increases the rate of autoxidation of 1-isopropyl-2-naphthol[10] presumably by increasing the concentration of naphthoxy radicals. Other cobalt complexes have been used to catalyse autoxidation. One example is the autoxidation of 2,6-di-t-butyl-4-methylphenol using Co(salpr).[11] The temperature of the reaction has an effect on the product obtained.



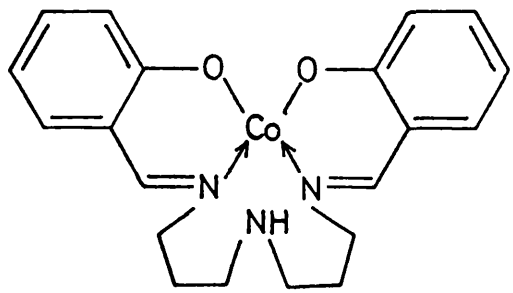
96% at room temperature



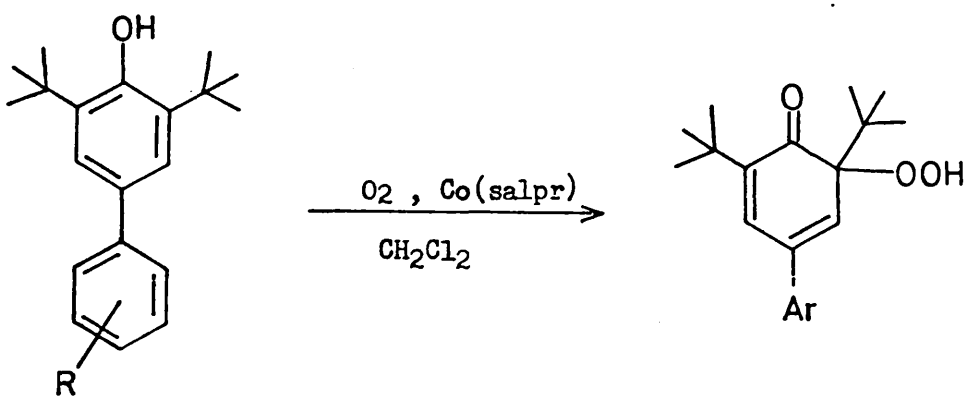
80% at 10°C

(salpr) = bis(3-salicylideneaminopropyl)amine

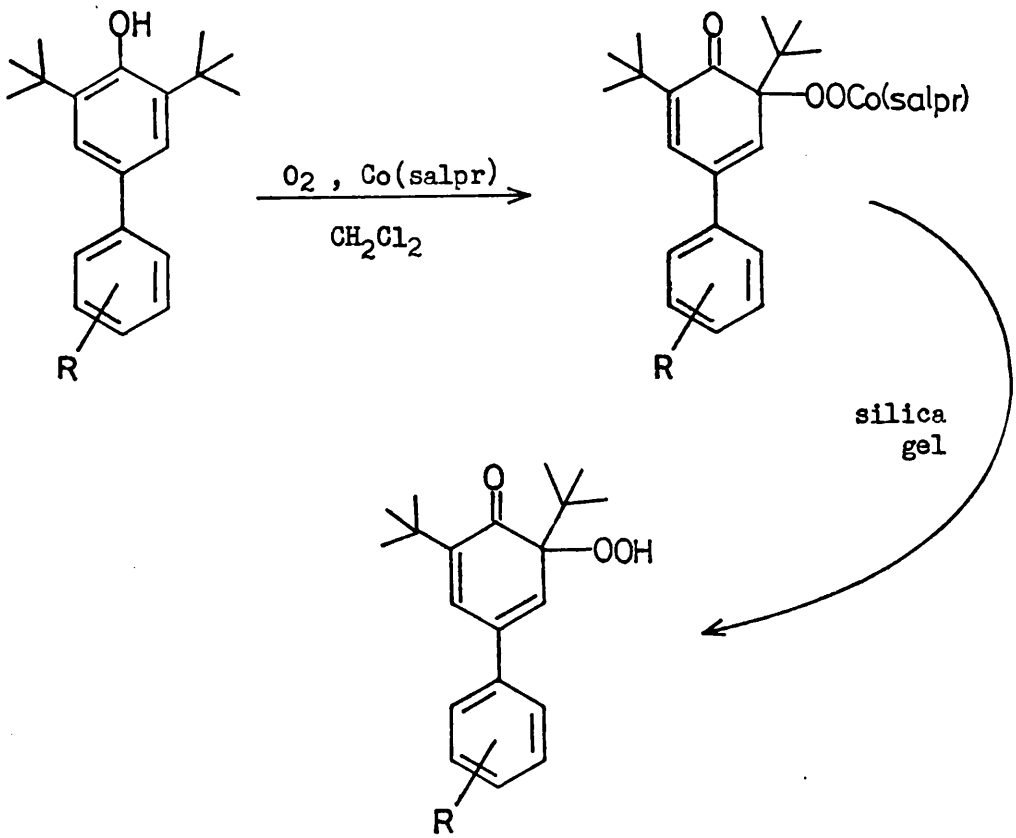
Co(salpr) =



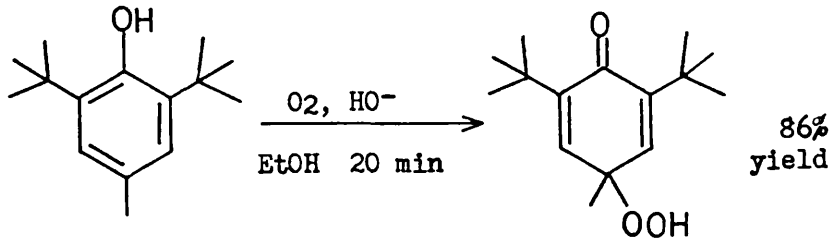
When 4-aryl-2,6-di-t-butylphenols are autoxidised using the same catalyst,[12a] the corresponding 4-aryl-2,6-di-t-butyl-6-hydroperoxy-1-oxo-cyclohexadienes are formed.



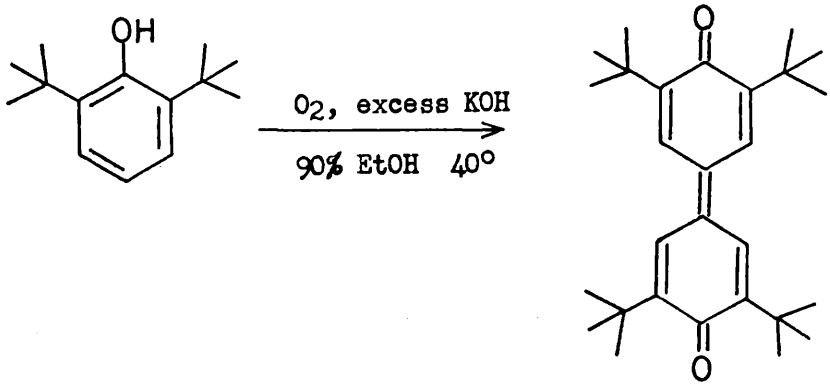
This reaction has been shown to involve an intermediate peroxycobalt complex which can be isolated as a crystalline solid and is converted on silica to the hydroperoxide.[12b]

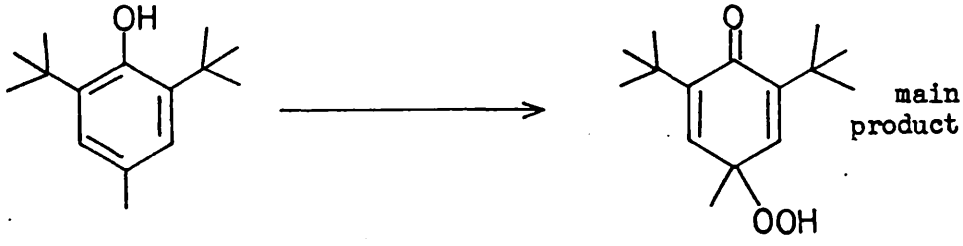


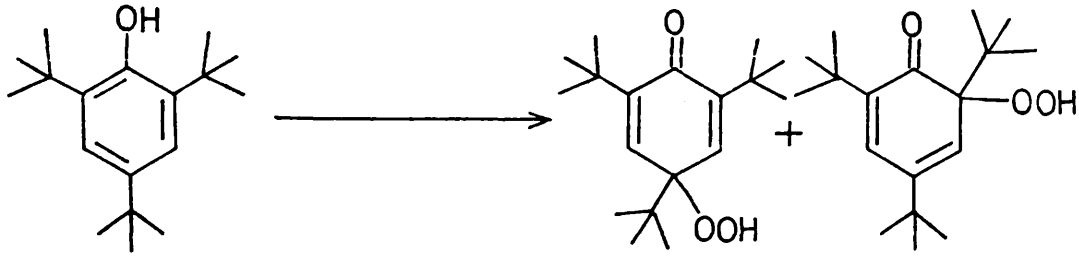
2) Base-catalysed autoxidation. A variety of molecules are susceptible to base-catalysed autoxidation.[13] Phenols have been observed to give rise to many different types of product.[13,14] In particular, some highly hindered phenols are converted to hydroperoxides when treated, in alkaline solution, with oxygen. For example, 2,6-di-t-butyl-4-methylphenol in basic ethanolic solution is rapidly converted to the 4-hydroperoxy-cyclohexadienone.[15]



Autoxidation of the related series, 2,6-di-t-butylphenol, 2,6-di-t-butyl-4-methylphenol, and 2,4,6-tri-t-butylphenol shows that steric accessibility can play some part in determining the products obtained.

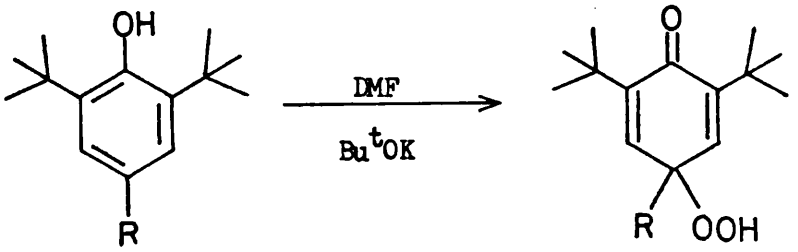




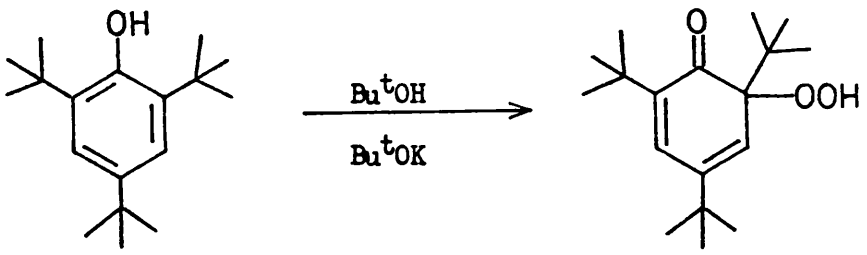


total 75%

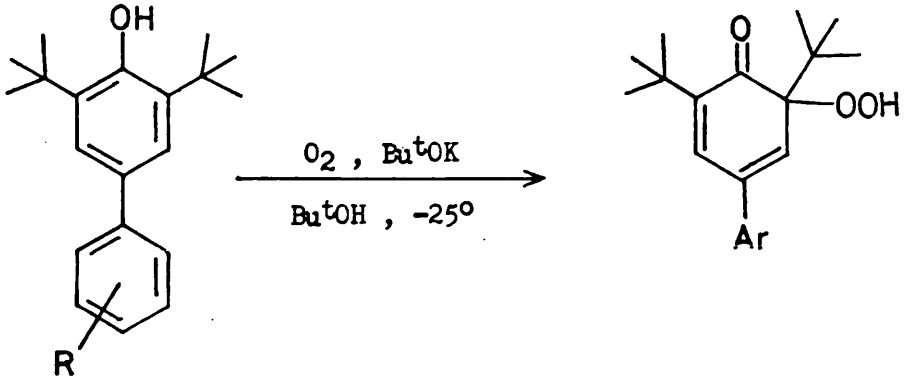
Solvent can also exert a potent effect on the course of the reaction. In the potassium t-butoxide-catalysed oxygenation of 2,4,6-tri-t-butylphenol in hexamethylphosphoric triamide (HMPA) or dimethylformamide (DMF) molecular oxygen attacks only the p-position[17] whereas in t-butanol (Bu^tOH) it attacks only the o-position.[18]



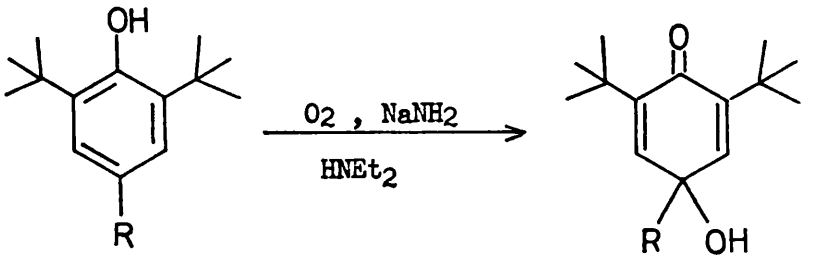
R = Bu^t, Pr^i, Et, Me



In the corresponding 4-aryl-2,6-di-t-butylphenol series, although these compounds are not oxygenated in the presence of Bu^tOK in DMF, HMPA, or methanol, they are attacked by oxygen, at the o-position in Bu^tOH.[19]



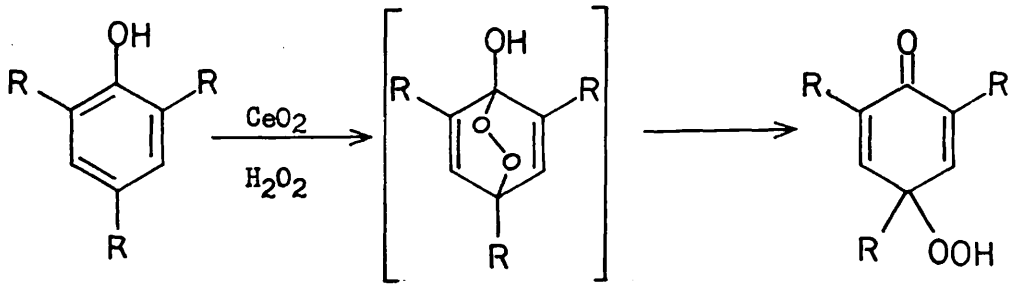
Base catalysed autoxidation of certain 4-alkyl-2,6-di-t-butylphenols with sodamide in diethylamine affords the corresponding p-quinols in a one step synthesis.[20]



R = Bu^t, Pr^i, Et, Me

The mechanism of these base catalysed autoxidation has been the subject of controversy. Recent results[21] involving both 4-alkyl- and 4-aryl-2,6-di-t-butylphenols strongly suggest an ionic mechanism, even though the ionic mechanism had been previously rejected, by reason of the violation of the spin conservation rule, in favour of a radical mechanism.

3) Reaction with singlet oxygen. The electronically excited metastable singlet oxygen, $^1O_2$, has been of interest, physically, synthetically, and biologically.[22] It can be made chemically, or photochemically and is a potent dienophile. The in situ generation of $^1O_2$ from hydrogen peroxide and cerium(IV) oxide provides a method for the synthesis of 4-hydroperoxycyclohexadienones from suitable phenols. p-Cresols, mesitol, and 2,6-di-t-butyl-4-methylphenol all give the corresponding 4-hydroperoxycyclohexadienone in good yield.[23]

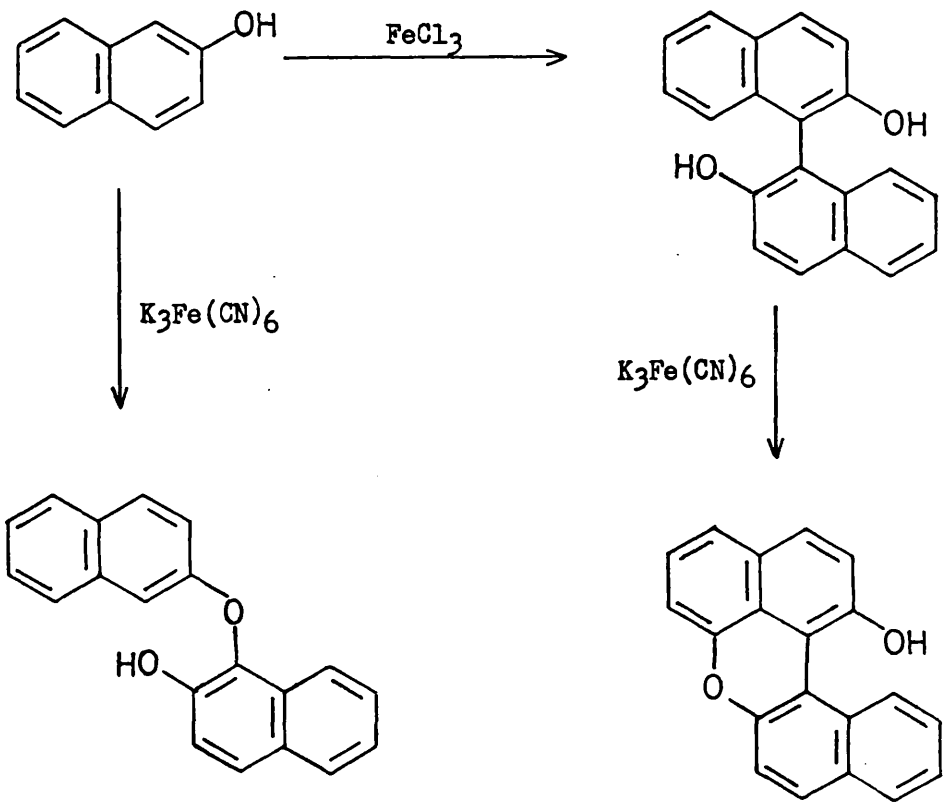


Several other transition metal - hydrogen peroxide systems have been employed for the oxidation of phenols. Thus mesitol, and 2,4,6-tri-t-butylphenol when treated with titanium tetrachloride or dichlorocyclopentadienyltitanium(IV) and hydrogen peroxide afford the corresponding 4-hydroperoxycyclohexadienones.[24] Molybdenum(VI) is also an effective reagent for these reactions.[24,25] Decomposition of H_2O_2 by other transition metal ions (Co^{II}, Fe^{II}, Fe^{III}, Cu^{I}, and Cu^{II}) in the presence of 2,4-di-t-butyl-4-methylphenol gave the p-hydroperoxycyclohexadienone.[26] The intermediacy of singlet oxygen has not been proven in these latter cases.

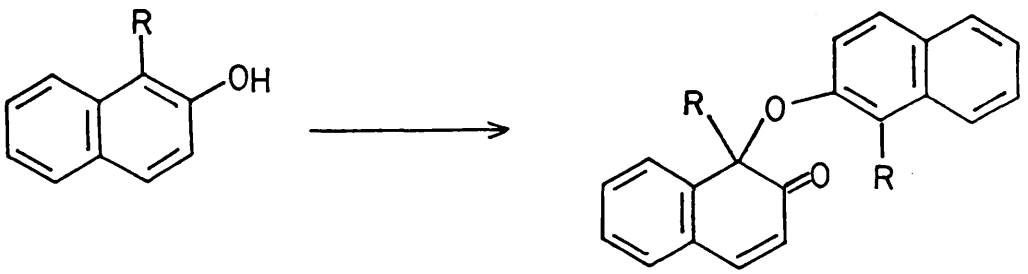
4) Phenol oxidative coupling. It has been well known for a very long time that in the presence of a variety of chemical and biological oxidants, phenol molecules combine to form many different products arising from either C-C or C-O coupling.[27] Simple phenols may link ortho and / or para to the hydroxy group of another unit to yield several possible dimers. These can be further oxidised to produce trimers, polymers, and quinonoid - type structures. Intramolecular, as well as intermolecular, coupling may occur in more complex polyhydroxy compounds. Almost every possible oxidising agent has been used to try to couple phenols oxidatively. Examples include potassium ferricyanide,[28] ferric chloride, manganese dioxide, lead dioxide, silver oxide, mercuric oxide, hexachloroiridate(IV),[29] vanadium(IV) tetrachloride,

vanadium(V) oxytrichloride,[30] thallium(III) trifluoroacetate.[31]

Some of these oxidants behave in a predictable way, at least within certain well studied systems. For instance, in the oxidation of 2-naphthol, the course of the reaction can be influenced by the choice of the oxidising agent.[32]



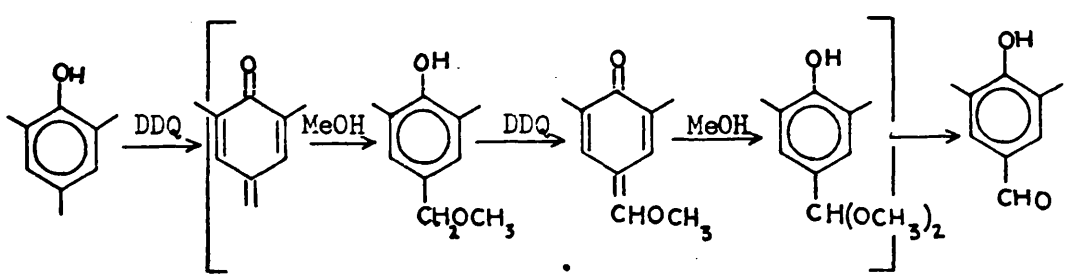
Here oxidation by potassium ferricyanide gives the O-C dimer, whereas use of ferric chloride promotes the formation of the C-C dimer. Similarly, studies of the oxidation of 1-alkyl-2-naphthols with potassium ferricyanide show that the O-C dimer is formed preferentially in each case.[7]



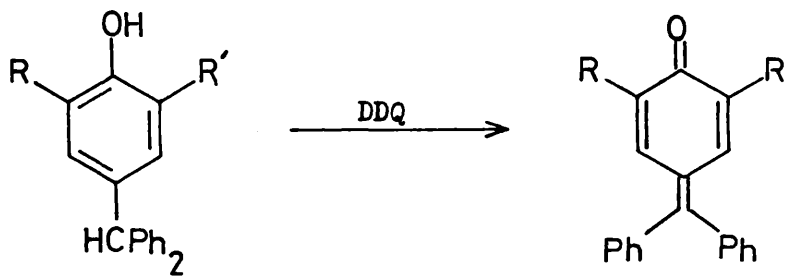
where R = Me, Et, Pr^i.

In the majority of cases the mechanism of these coupling reactions involves simply the dimerisation of phenoxy radicals generated by oxidation of the phenol although, in a few cases, a different route to the same type of product is followed.[27c]

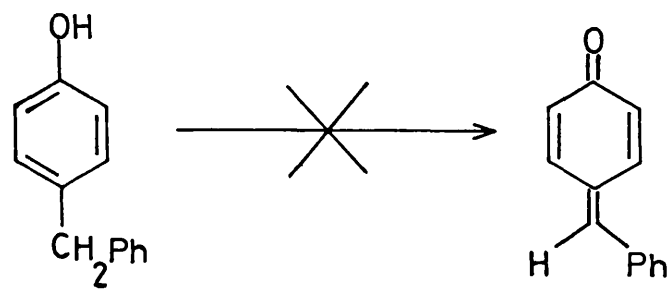
5) Dehydrogenation. Many oxidising agents can cause dehydrogenation of organic substances, including phenols, giving rise, by net loss of two hydrogen atoms, to a variety of products (eg. quinones and quinone methides), and sometimes, by net loss of one hydrogen atom to compounds resulting from the coupling process referred to in sub-section 4. Quinone methides can be formed by dehydrogenation of phenols with o- or p-alkyl groups containing one benzylic hydrogen atom. Quinone methides are usually reactive and undergo cycloaddition and addition of nucleophiles. They have been postulated as intermediates in several chemical reactions. For example, the oxidation of mesitol with 2,3-dichloro-5,6-dicyano-1, 4-benzoquinone (DDQ),[33] is thought to proceed by dehydrogenation to a p-quinone methide followed by reaction with solvent.



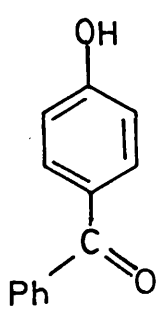
Stable quinone methides are, however, products in the reaction of DDQ with a series of 4-hydroxy-triphenylmethanes.



Attempted synthesis of a quinone methide stabilised by only one phenyl group was unsuccessful.

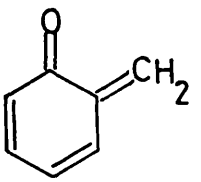


The isolated product was



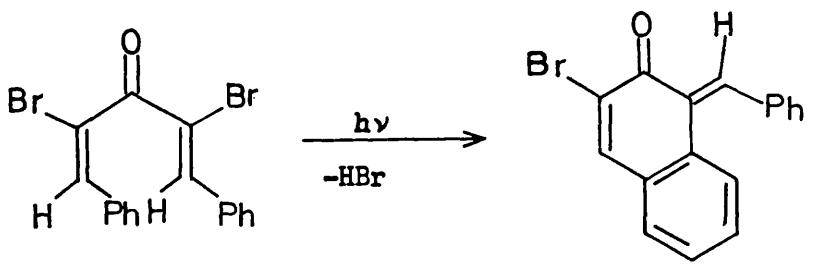
i.e. the same type of compound as was isolated from the mesitol reaction. In general, quinone methides can be stabilised by extending the conjugated system and by introducing bulky substituents

which inhibit addition or cycloaddition reactions. o-Quinone methides are also usually unstable, but can be detected by spectroscopic techniques.[34] They have been invoked as intermediates in several chemical reactions[35] and their presence has been deduced by trapping with suitable reagents.[36] The parent of this family of compounds, o-quinone methide,

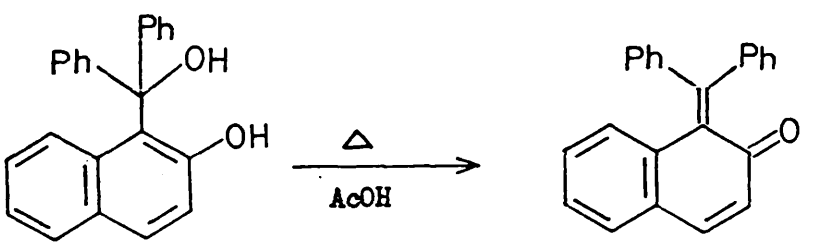


is reported to be a stable, monomeric species at - 196°C.[37]

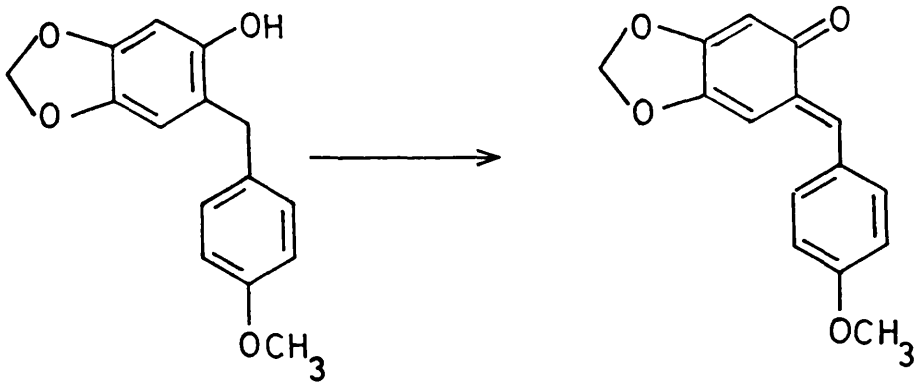
o-Quinone methides stable at room temperature have been reported. 1-Benzylidene-3-bromonaphthalen-2(1H)-one is reported to be formed from cis, trans-α,α'-dibromo-dibenzylideneacetone by elimination of hydrogen bromide.[38]



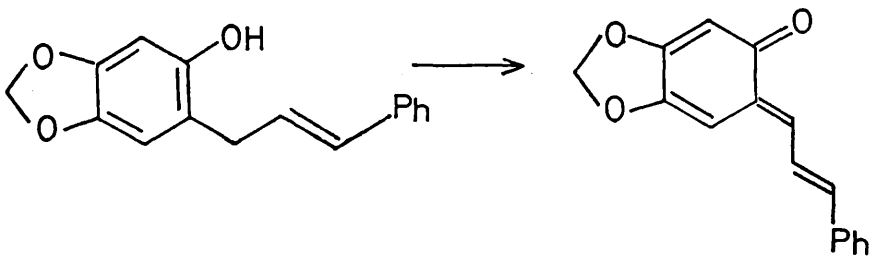
The stable o-naphthofuchsone was obtained, as orange red crystals, by heating the corresponding diphenylcarbinol in glacial acetic acid.[39]



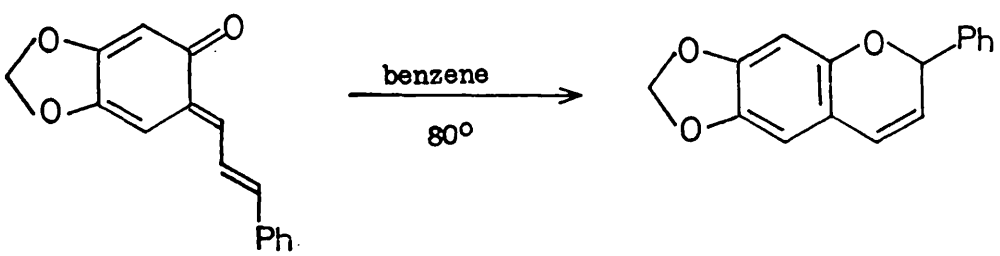
Silver oxide oxidation of 2-(4-methoxybenzyl)-4,5-methylene-dioxyphenol leads to the formation of a stable quinone methide



and similarly 2-cinnamyl-sesamol is converted quantitatively to the corresponding orange-red crystalline quinone methide which is also stable.

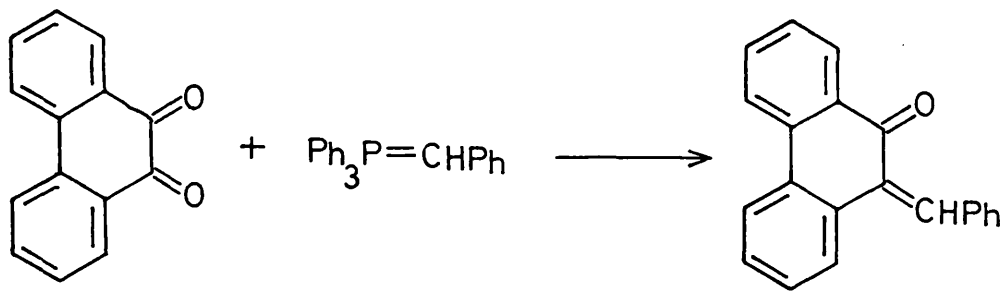


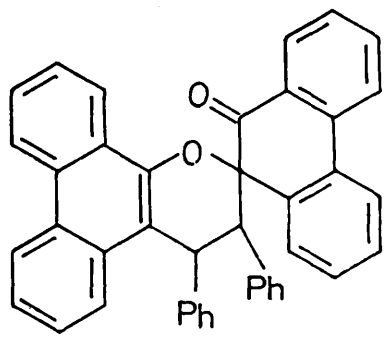
In boiling benzene, however, the 6-cinnamylidene-3,4-methylene-dioxycyclohexa-2,4-dienone is converted to the colourless 6,7-methylenedioxyflav-3-ene.[40]



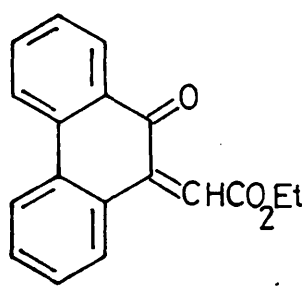
Again, the fact that electronegative and/or bulky substituents help to stabilise quinone methides can be inferred from the reported

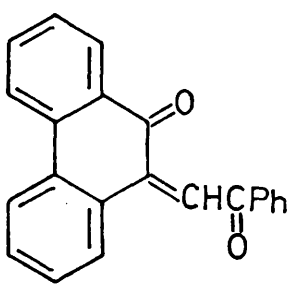
relative stability of products obtained from the reaction of 9,10-phenanthrenequinone with various ylides.

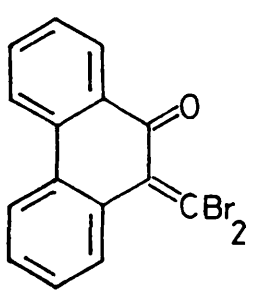


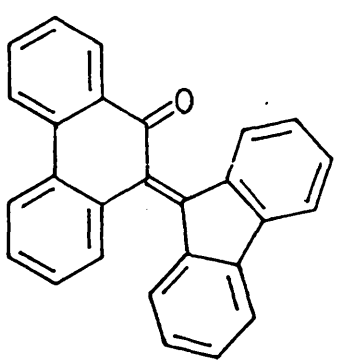


As shown, the 10-benzylidene-9-phenanthrone is unstable and undergoes rapid dimerisation. By suitable choice of reagent, the following compounds can be prepared from 9,10-phenanthrenequinone.



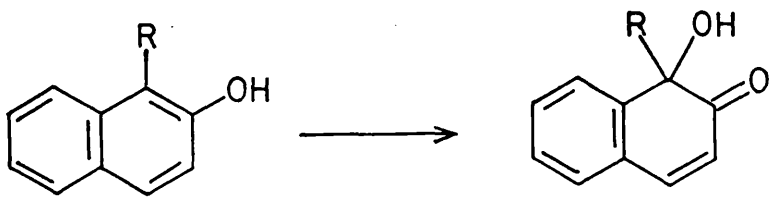






All of these are more stable than the 10-benzylidene-9-phenanthrone.[41]

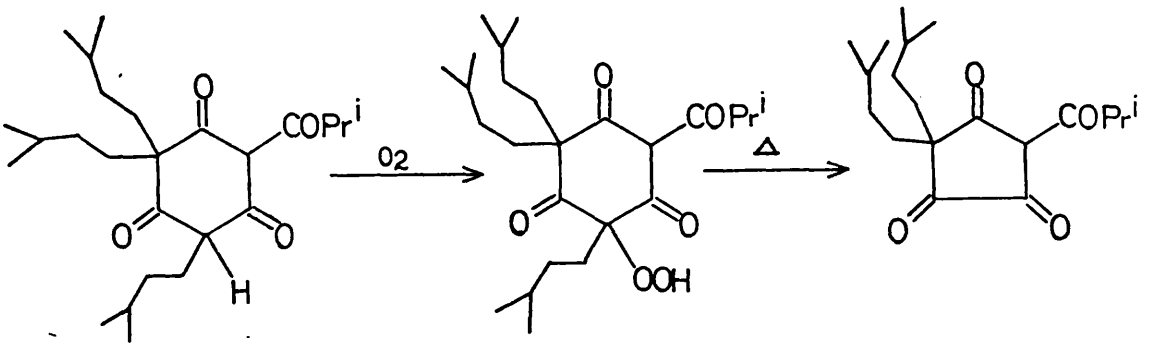
6) Hydroxylation of phenols. A variety of reagents is available for the hydroxylation of phenols to hydroxycyclohexadienones. Some of these involve electrophilic attack on the phenol, others involve pericyclic rearrangement. Some involve direct introduction of a hydroxyl group while with others the group introduced first (OAc, OCOPh, Br, NO_2) is easily converted to a hydroxyl group. The regiospecificity of electrophilic attack is often predictable. Thus 1-alkyl-2-naphthols are usually converted to 1-alkyl-1-hydroxy-2(1H)-naphthalenones.



Hydroxylation has been effected by chromium trioxide (CrO_3),[42] periodates (IO_4^-),[43,44] lead tetraacetate ($Pb(OAc)_4$),[44c] thallium trinitrate ($Tl(NO_3)_3.3H_2O$),[45] thallium oxide in perchloric acid ($Tl_2O_3/HClO_4$), diphenylselenenic anhydride ($(PhSeO)_2O$),[47] dibenzoyl peroxide $(PhCO)_2O_2$,[48] peracetic acid (CH_3CO_3H),[49] performic acid (HCO_3H),[50] bromine,[51] nitronium ion (NO_2^+),[51] superoxide ion (O_2^-).[52] An alternative route to hydroxycyclohexadienones involves the reduction of the hydroperoxydienones mentioned in sections I 1), 2), and 3), using mild reducing agents such as KOH/KI,[53] Me_2S/THF,[23] or Ph_3P.[54] Initially formed hydroperoxides are often converted to alcohols by base (cf. section II) and this may occur in the autoxidation reaction vessel, as in the base catalysed autoxidation of 4-alkyl-2,6-di-t-butylphenol with sodamide in diethylamine.[20]

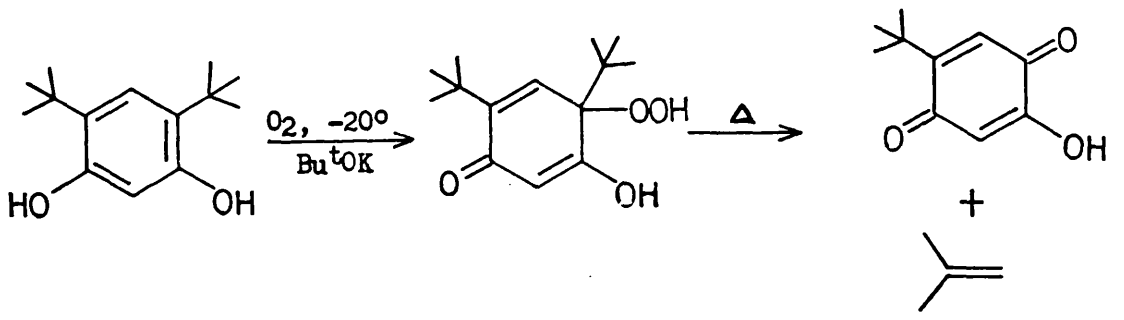
II Chemistry of Hydroperoxides.

1) Thermolysis. The thermal decomposition of hydroperoxides often leads to complex mixtures of products which are difficult to identify. There are, however, cases where products have been identified. These products are often the result of complex decompositions of the radicals, $RO^{\bullet}$ and $HO^{\bullet}$, which are the probable initial fragments. For example, the hydroperoxide obtained by autoxidation of hexahydrocolupulone decomposes on heating to give tetrahydrocohulupone.[55]

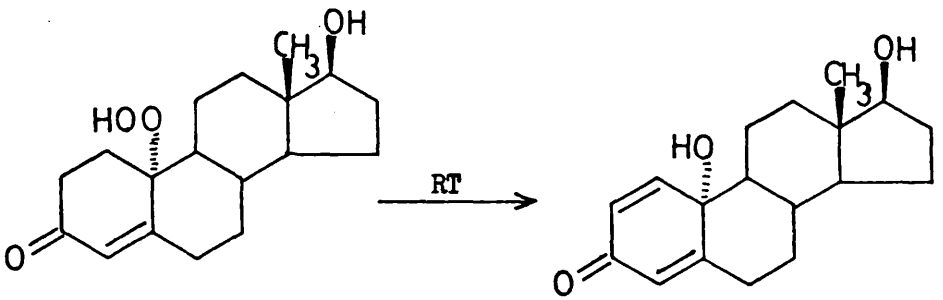


Clearly here, thermolysis has resulted in a fundamental change in the structure of the molecule. This is not always the case.

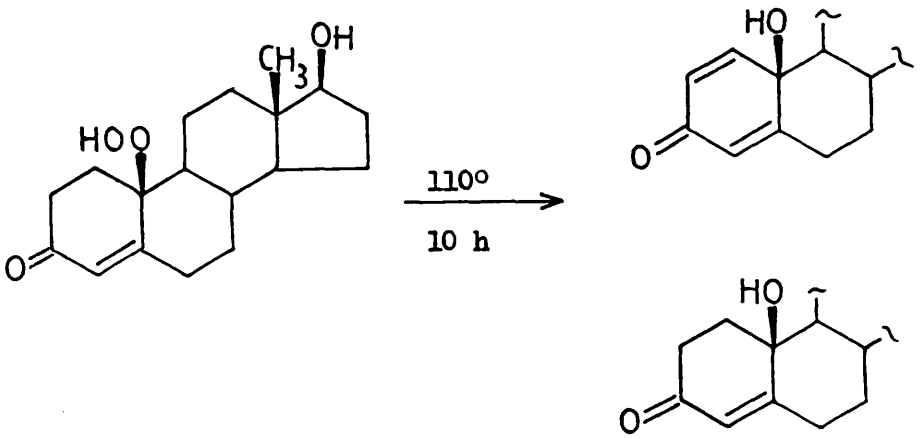
Thermolysis of the hydroperoxide obtained from low temperature, base-catalysed autoxidation of 4,6-di-t-butylresorcinol gives 5-hydroxy-2-t-butylbenzoquinone.[56]



Thermolysis of 10α-hydroperoxy-3-keto-17β-hydroxyestr-4-ene leads to the formation of the 10α-hydroxydienone.



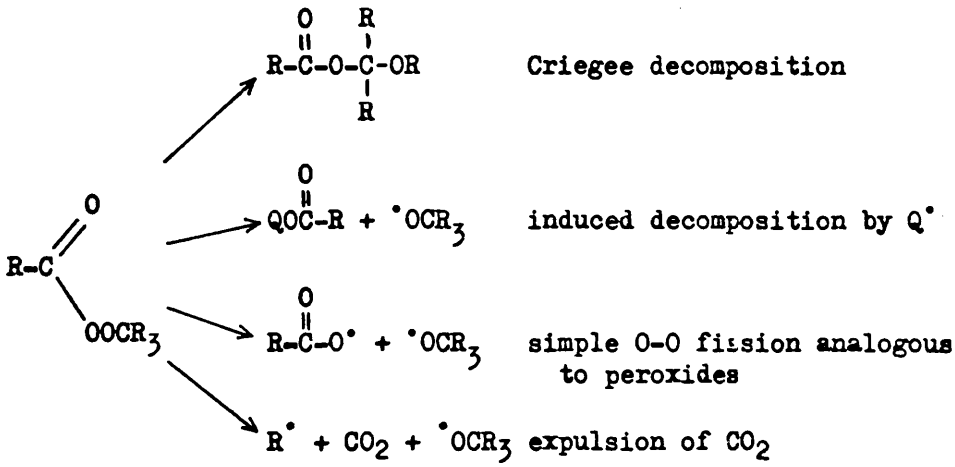
Whereas the epimeric 10β-hydroperoxide which is more stable, decomposes at higher temperatures to the 10β-hydroxydienone and also 10β-hydroxy-3-keto-17β-hydroxyestr-4-ene.[57]



α-Hydroperoxyketones have been reported to decompose on heating to give mainly carboxylic acids and ketones.[58]

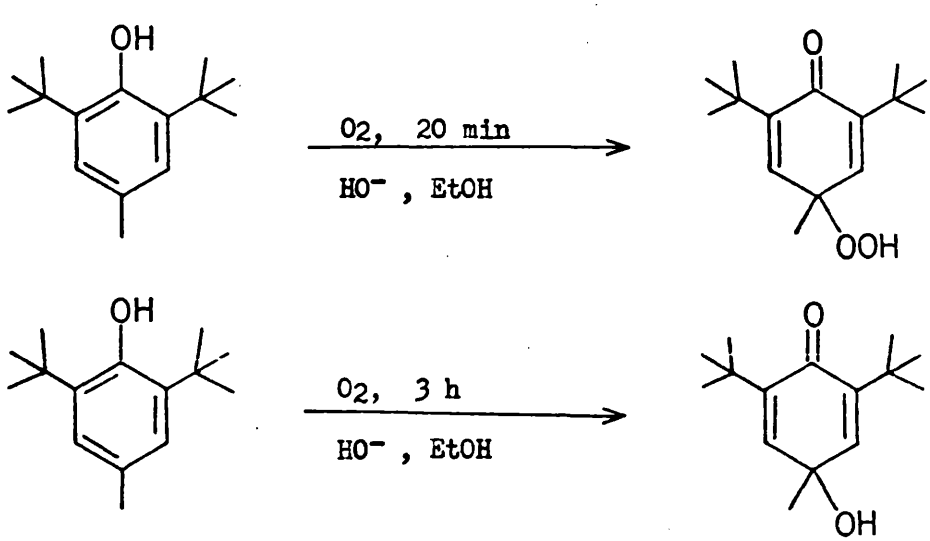
$$R_1C(=O)-CR_2R_3(OOH) \xrightarrow{\Delta} R_1COOH + R_2R_3CO$$

The thermolysis of derivatives of hydroperoxides has been studied since they often give less complex mixtures. For example, the thermal decomposition of peresters can in most cases be described by one of only four paths.

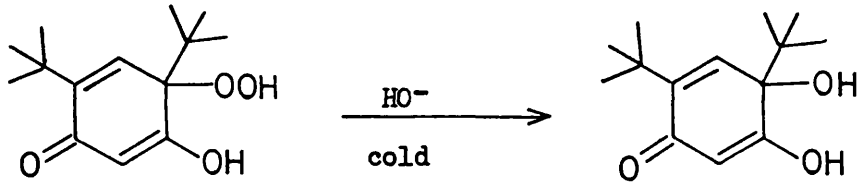


Studies of peresters, which decompose by this last mechanism, have been conducted in order to investigate the relationship between structure and reactivity in radical species.[59]

2) Base-catalysed reactions. Hydroperoxyketones and enones have been observed to decompose, in basic media, in a variety of ways. For example, the hydroperoxide can be converted to the corresponding alcohol, as in the base catalysed autoxidation of 2,6-di-t-butyl-4-methylphenol. The primary product was the hydroperoxide but if the reaction mixture was heated or left standing, the hydroperoxide decomposed. Within two or three hours there was complete loss of peroxide titre and about 45% of the hydroperoxide had been converted to the quinol.[15]

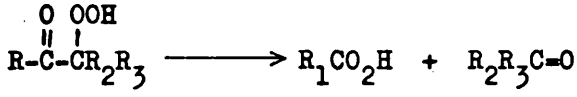


1-Hydroperoxy-6-hydroxy-1,3-di-t-butyl-cyclohexa-2,5-dien-4-one in cold alkaline solution is converted to the corresponding alcohol.[56]

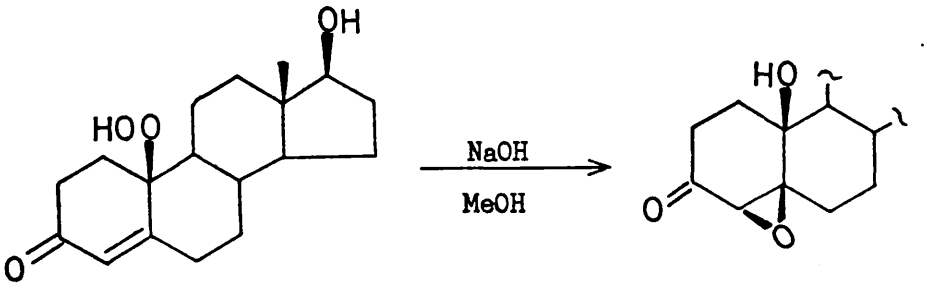


The mechanism of conversions of this type, from hydroperoxide to alcohol is not entirely clear but it may occur by substitution of ^{-}OH for ^{-}OOH or by loss of oxygen gas.[60]

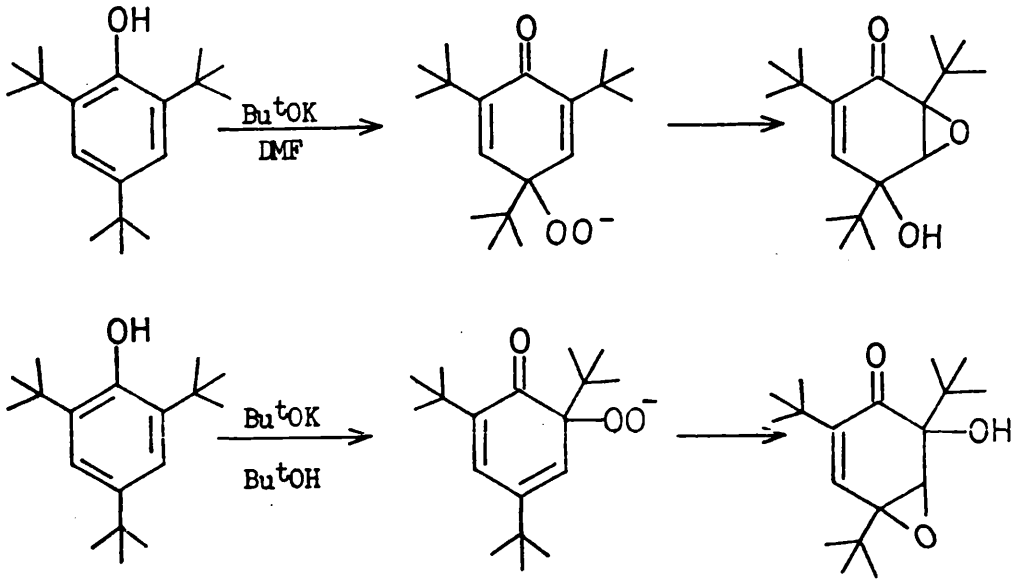
It is well known that α-hydroperoxyketones can be cleaved by base to give a ketone and an acid.[61]



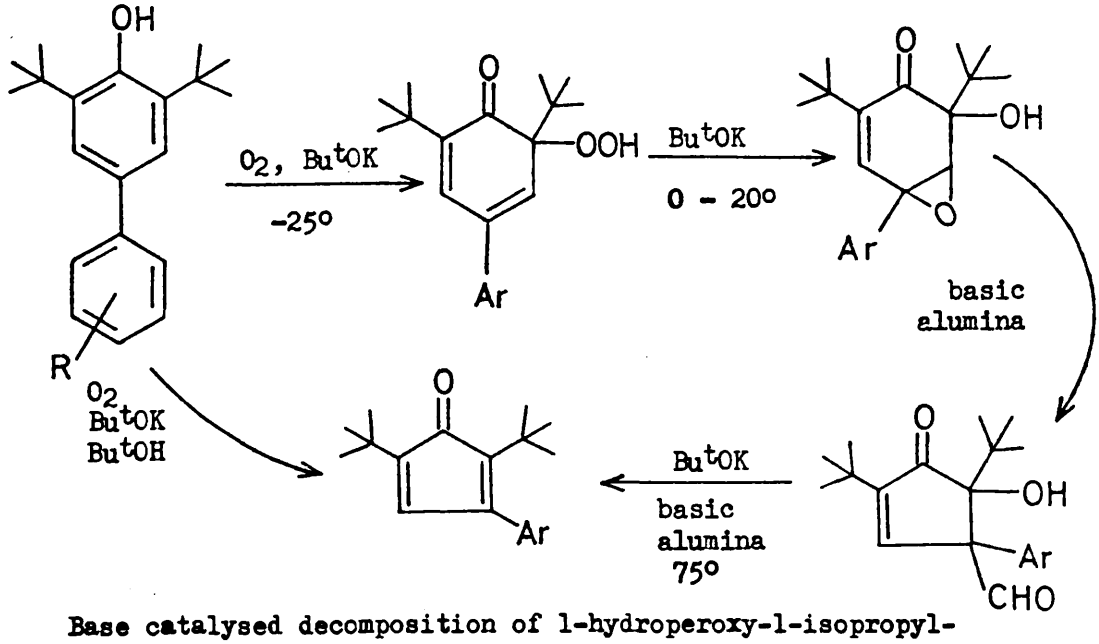
Of particular interest here is the observation that hydroperoxides can, in the presence of base, epoxidise enones.[62] If a molecule contains both the hydroperoxide function and an enone group then the molecule may either undergo intramolecular self-epoxidation giving an epoxy-oxo-alcohol or it may effect the epoxidation of another hydroperoxyenone molecule. This latter, intermolecular epoxidation, would give rise to an alcohol and a hydroperoxyepoxide. Epoxidations of this type, resulting from the decomposition of hydroperoxides in basic media, have been reported. For example 10β-hydroperoxy-3-keto-17β-hydroxyestr-4-ene is decomposed by methanolic sodium hydroxide to give an epoxy-oxo-alcohol in high yield by an intermolecular oxygen transfer. The epoxide and alcohol oxygen in the product were cis.[63]



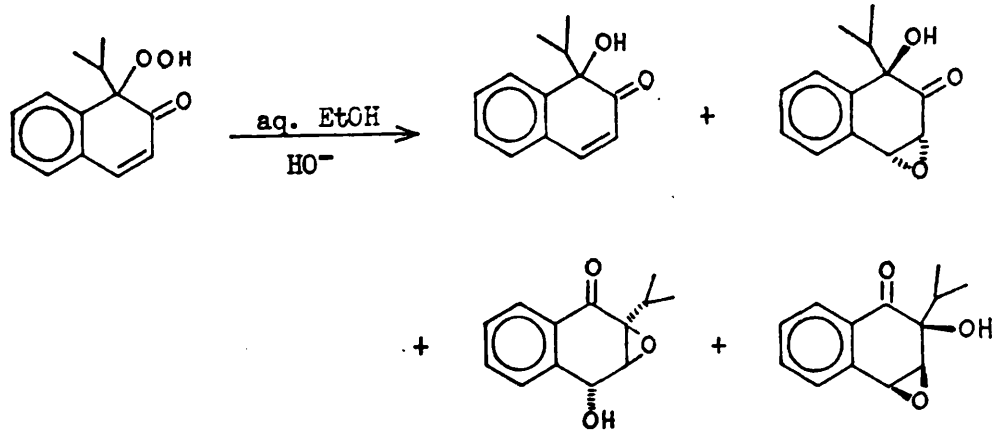
The potassium t-butoxide catalysed autoxidation of 4-alkyl- and 4-aryl-2,6-di-t-butylphenol is known to be strongly influenced by the solvent.[19a] In the case of 2,4,6-tri-t-butylphenol, in the presence of hexamethylphosphoric triamide (HMPA) or dimethyl formamide (DMF), molecular oxygen attacks only at the p-position, while in t-butanol, molecular oxygen attacks only at the o-position. The resulting hydroperoxides can be isolated when the reactions are performed at low temperatures.[11,18a] At room temperature and above, the hydroperoxy species are not isolated but decompose to give quinol epoxides.[17,18b]



An intramolecular self-epoxidation mechanism, with the hydroxyl and epoxide oxygens cis-disposed, was assumed. In the case of 4-aryl-2,6-di-t-butylphenol the product obtained from potassium t-butoxide-catalysed autoxidation is 3-aryl-2,5-di-t-butyl-2,4-cyclopentadienone.[19a] By repeating the reaction at low temperatures, intermediates species were isolated, which show that the mechanism of this reaction is consistent with the observations with the 4-alkyl-2,6-di-t-butylphenols.[19b]



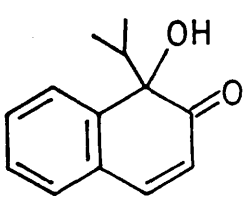
Base catalysed decomposition of 1-hydroperoxy-1-isopropyl-naphthalen-2(1H)-one has been shown to give the corresponding alcohol, the trans-epoxide of this enone, and two isomeric epoxides.[64]

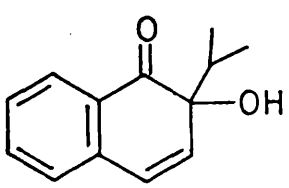


The stereoselectivity in this reaction is not as high as in the previous examples.[63,17,18b] Both epoxides, with the oxirane and the hydroxyl oxygens trans and cis to one another, seemed to be formed initially although both underwent further reaction. The mechanism of production of these epoxides, which are 5,6-epoxy-2-hydroxycyclohex-2-enones, as opposed to the 2,3-epoxy-4-hydroxycyclohex-5-enones above, is not known.

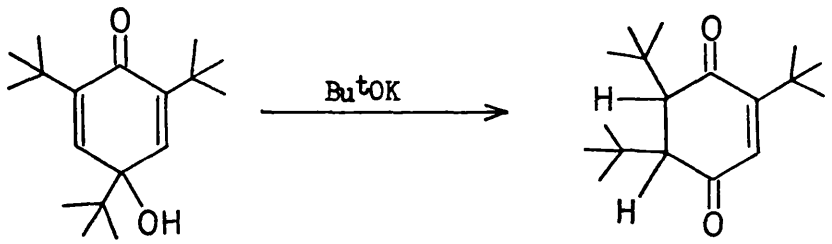
III Reactions of Hydroxycyclohexadienones.

Certain of the reactions of o- and p-hydroxycyclohexadienones are of particular interest here, since they limit the kind of molecules that can be isolated and the kinds of conditions that can be used. Typical reactions include rearrangements and dimerisations. The α-hydroxyketones can undergo the base-catalysed acyloin rearrangement (ketol rearrangement). For example, 1-hydroxy-1-isopropylnaphthalen-2(1H)-one, when treated with base, gives 2-hydroxy-2-isopropylnaphthalen-1(2H)-one.[10]

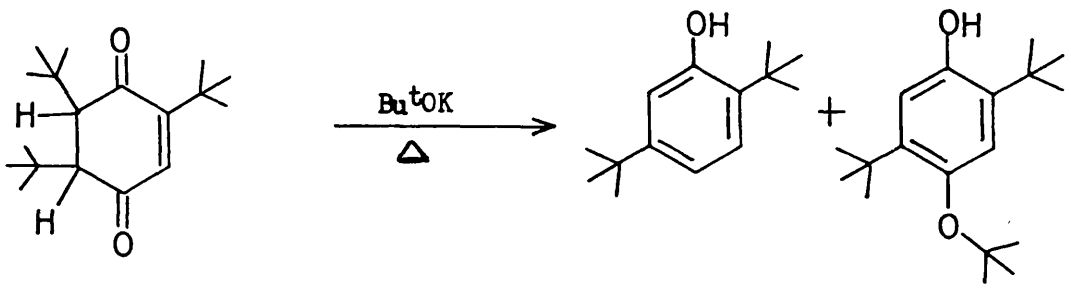




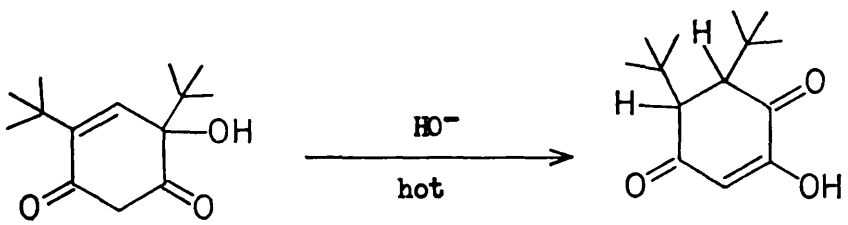
Similarly, p-quinols can undergo a vinylogous, base-catalysed, ketol rearrangement, again with the migration of an alkyl group to an adjacent carbon atom of the ring. For example, the p-quinol, obtained by the sodamide/diethylamine autoxidation of 2,4,6-tri-t-butylphenol, rearranges as shown when treated with base.[18a,65]



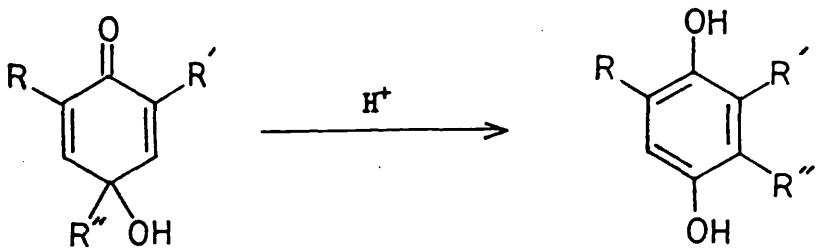
At higher temperatures, the reaction proceeds more quickly. Under these conditions, alkyl loss and further rearrangement may occur.[65]



1,6-Dihydroxy-1,3-di-t-butylcyclohexadi-2,5-en-4-one rearranges in a similar manner.[56]

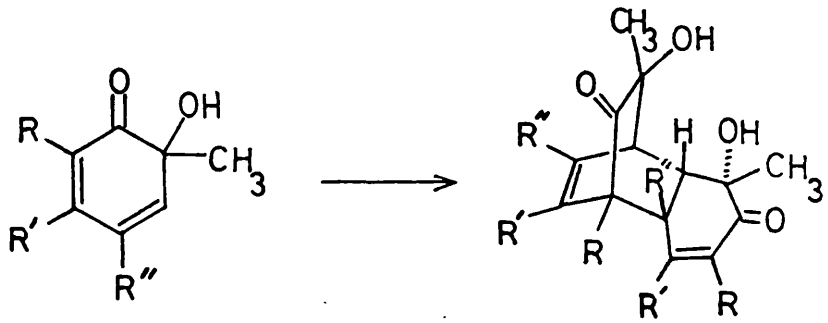


Quinols are also susceptible to the acid catalysed, dienonephenol rearrangement.[66]

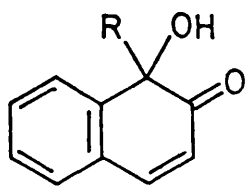


This rearrangement is well studied in strongly acidic media, but it can also occur under much milder conditions with non-protic acids.

Dimerisation by Diels-Alder addition usually prevents isolation of monocyclic o-quinols.



The stereospecificity and regiospecificity of this reaction have been studied in detail.[67] The benzo-analogues of o-quinols, for example the hydroxynaphthalenones,



do not dimerise.

IV Alkylphenols and Naphthols

All the relevant monocyclic phenols used by me are available commercially. Alkylnaphthols can be prepared by a variety of techniques which will be discussed in detail later. Some can be made from 2-naphthol by direct alkylation. For example, 1-benzyl-2-naphthol, 1-isopropyl-2-naphthol, and 6-trityl-2-naphthol can all be prepared in this way. Some are obtained via acylation followed by reduction. For example, 1-methyl-2-naphthol and 1-ethyl-2-naphthol can be prepared by reduction of 1-formyl- and 1-acetyl-2-naphthol respectively. Yet others are obtained by

manipulation of naphthalene systems which are already functionalised in other ways. Some of these syntheses are complicated multistep processes but two examples which are at least conceptually simple are the preparation of 1-t-butyl-2-naphthol and 1-trityl-2-naphthol by Grignard reaction, with methyl 2-hydroxy-1-naphthoate and o-naphthofuchsone respectively.

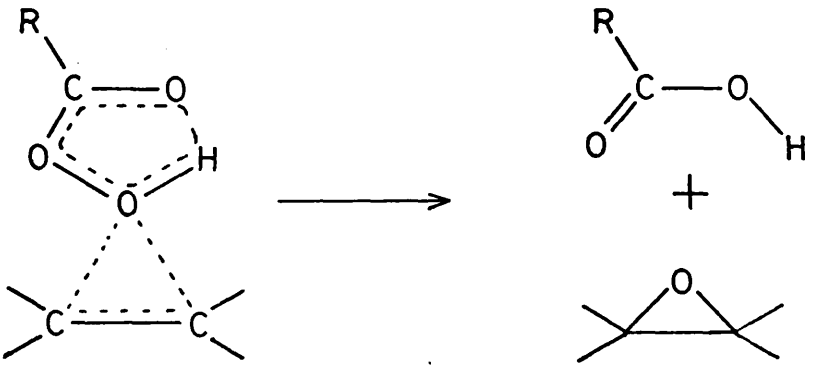
Alkyl phenols can also be prepared by hydroxylating suitably substituted aromatic compounds.

V Epoxidation

There is a variety of reagents which are available to effect the epoxidation of alkenes.[68]

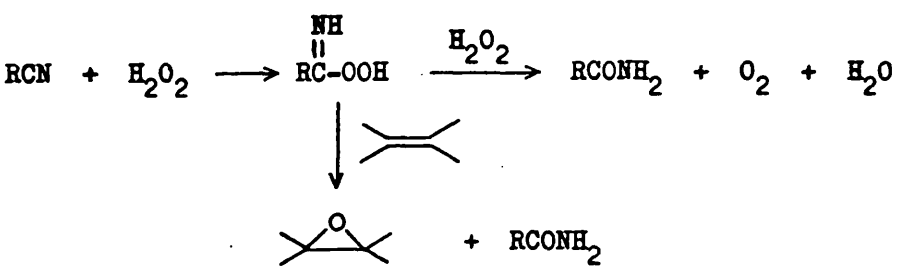
1) Peroxyacids. Many peroxyacids have been used as epoxidising agents. For example, peroxyacetic, peroxybenzoic, peroxymaleic peroxyphthalic, p-nitroperoxybenzoic, m-chloroperoxybenzoic, and trifluoroperoxyacetic acids have all been employed in epoxidation. This reaction is usually considered to involve initial addition of the electrophilic peroxyacid to the alkene. The electrophilic behaviour of the acid follows from the findings that peroxyacid epoxidations work best with electron-rich alkenes and an electron deficient peracid acyl group. By varying the ability of the rest of the molecule to withdraw electron density from the peroxyacid group these reagents can exhibit a varying degree of electron deficiency so that, even with an electron deficient double bond, it may be possible to find a suitable peroxyacid to effect epoxidation. A stepwise mechanism involving an initial α-hydroxycarbonium ion, an oxiranium ion, and final deprotonation, fails to explain the fact that, compounds resulting from rotation about the carbon-carbon bond in an α-hydroxycarbonium ion are never obtained, even in cases where

electron donating substituents could stabilise such a carbonium ion. The stereospecificity of this reaction may be accounted for by a cyclic transition state arising from attack of an intramolecularly hydrogen-bonded peroxyacid on the olefin.



This mechanism also has its weaknesses, in that it considers only unsolvated molecules and it fails to explain, for example, the specific influence of solvent, the selectivity of epoxidation as a function of the nature of the peracid, induced decomposition of peracids, and the formation of rearranged products concurrent with epoxidation. Elucidation of the mechanism of peroxyacid epoxidations is still the subject of investigation.[69]

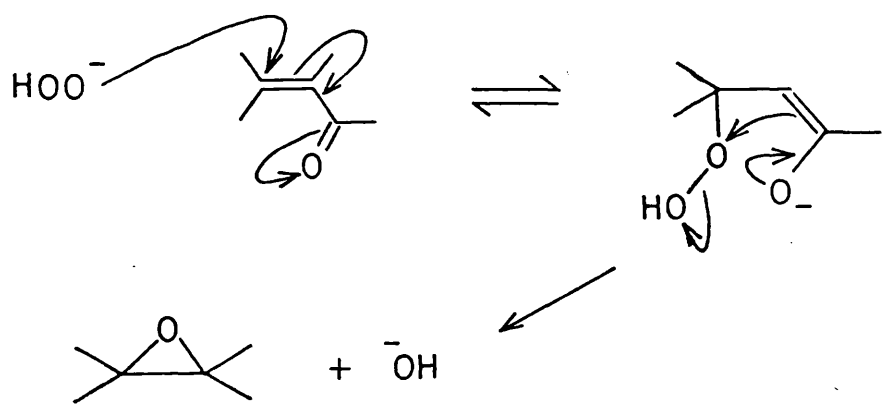
2) Peroxycarboximidic acid. Epoxides are formed when alkenes are treated with hydrogen peroxide in a medium consisting of a nitrile buffered at pH 8.[70] The reaction probably involves the formation of peroxycarboximidic acid.



The mechanism is presumably similar to that operating in the

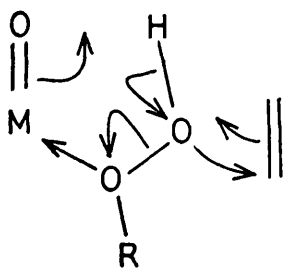
peracid epoxidations. Although this system is particularly useful if the substrate is acid-sensitive, peroxycarboximidic acids are more sensitive to steric congestion than peroxyacids.

3) Alkaline hydrogen peroxide. Compounds with electron deficient double bonds such as enones may react only slowly, or not at all, with the electrophilic peroxyacids. These compounds may undergo other reactions, for example Baeyer-Villiger oxidation, in competition with epoxidation. In these cases, base catalysed hydrogen peroxide epoxidation, the Weitz-Scheffer reaction,[71] is often successful. The reaction is thought to involve a Michael-type addition of the hydroperoxide anion to the conjugated system, followed by ring closure of the intermediate enolate anion with expulsion of ^{-}OH.



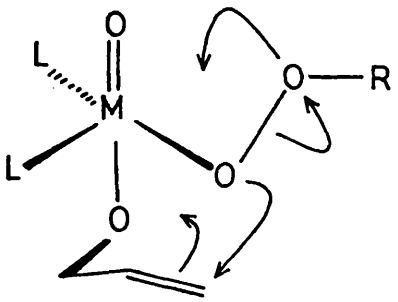
4) t-Butyl hydroperoxide. This reagent has been used instead of hydrogen peroxide in the epoxidation of enones. The use of this reagent allows the reaction to be carried out in homogeneous non-polar media, using for example Triton B as a catalyst.[62b] The greater bulk of the reagent sometimes leads to poorer yields, as compared with H_2O_2, in reactions where there are unfavourable steric interactions. It cannot, for example, be used to epoxidise cholest-4-en-3-one.

5) Hydroperoxide/transition metal system.[72] Certain transition metal compounds have been found to promote the epoxidation of alkenes by hydroperoxides. The most active catalysts are the hydrocarbon-soluble compounds of molybdenum but salts of vanadium, tungsten, and chromium have also been used to catalyse this reaction. Investigations into epoxidations with these systems have shown that the rate of epoxidation increases with the number of electron donating substituents attached to the double bond. The proposed mechanisms for these reactions can be divided into two types. The first, earlier, mechanism describes the reaction in terms of an initial co-ordination of the hydroperoxide with the transition metal catalyst, weakening of the oxygen-oxygen bond with a transfer of electron density to the metal, an increase in the electrophilic character of the hydroperoxide leading to rupture of the oxygen-oxygen bond as the alkene attacks the complexed hydroperoxide with, finally, deprotonation leading to epoxide.



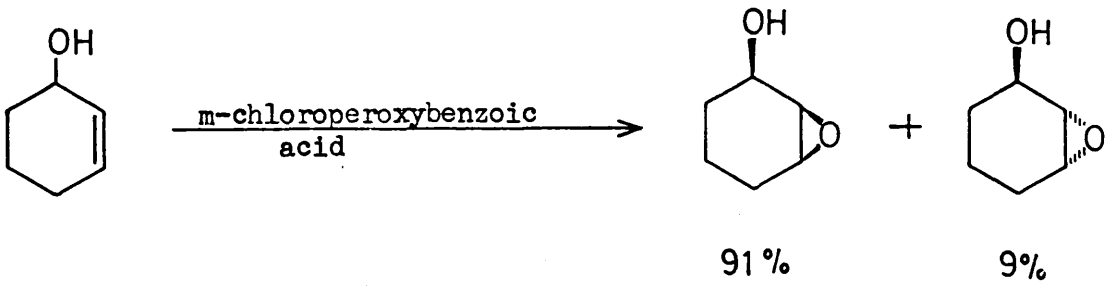
A more recent mechanism[73] tries to account for the great rate accelerations observed in epoxidations of allylic alcohols with these epoxidising systems. If the explanation for the rate increase lies in a complexing of the hydroxyl group of the alcohol then it is geometrically impossible for this to occur simultaneously with co-ordination of the oxygen proximal to the alkyl group of the

hydroperoxide and the approach of the alkene to the distal oxygen. The mechanism proposed involves the co-ordination of the oxygen distal to the alkyl group and subsequent oxygen transfer between the ligands.

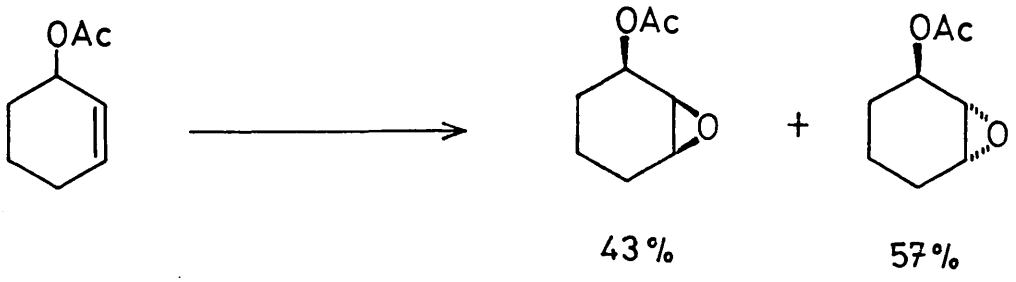


6) Stereoselectivity. In the epoxidation of cycloalkenes containing chiral carbons, since the two faces of these molecules are not equivalent, there is the possibility of the production of two diastereoisomeric epoxides. Much effort has been devoted to the elucidation of the factors which influence the stereoselectivity of epoxidation (for example, the identification of steric, conformational, and electronic effects). It is often extremely difficult to estimate the relative importance of these factors in any attempt to predict the stereospecificity of an epoxidising system on complex alkenes, although there are many examples of post facto rationalisations in terms of one factor outweighing another. However, in general terms, certain structural features often lead to stereospecificity. For example, peroxyacid epoxidation of hydroxyalkenes and unsaturated sterols occurs, in most simple cases, cis to the hydroxyl group, the rate of reaction being slower than for the corresponding alkene but much faster than for the corresponding allylic acetate. Cyclohex-2-en-1-ol is converted by peroxybenzoic acid to the cis epoxide, with little dependence on solvent or

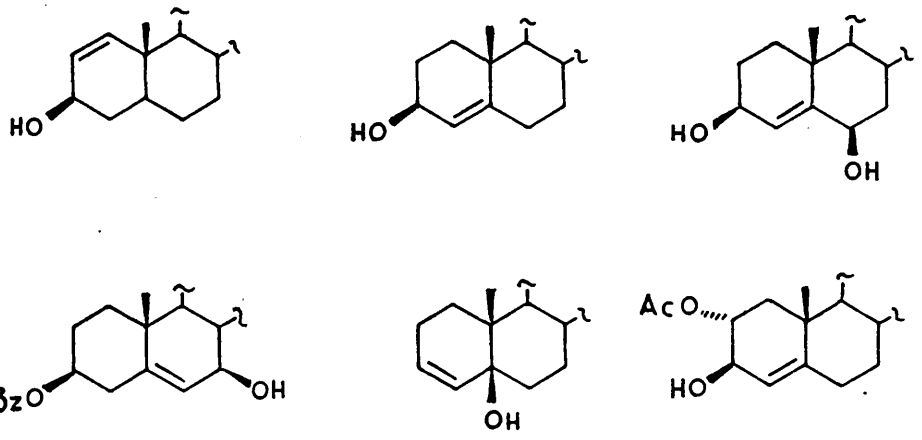
peroxyacid.[74]



The epoxidation of the corresponding acetate is much slower and does not lead to a great preponderance of either epoxide.



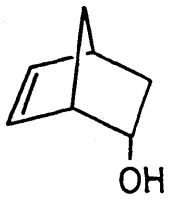
In the following cholestane derivatives,

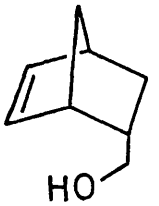


in contrast to the usual rule of α-attack by peroxyacids, there is a high or exclusive preference for β-epoxide formation.[75]

A hydroxyl group in the homoallylic postion or farther away from the double bond can exert an effect on the stereospecificity if, by hydrogen bonding with the peracid, it can bring the reagent more

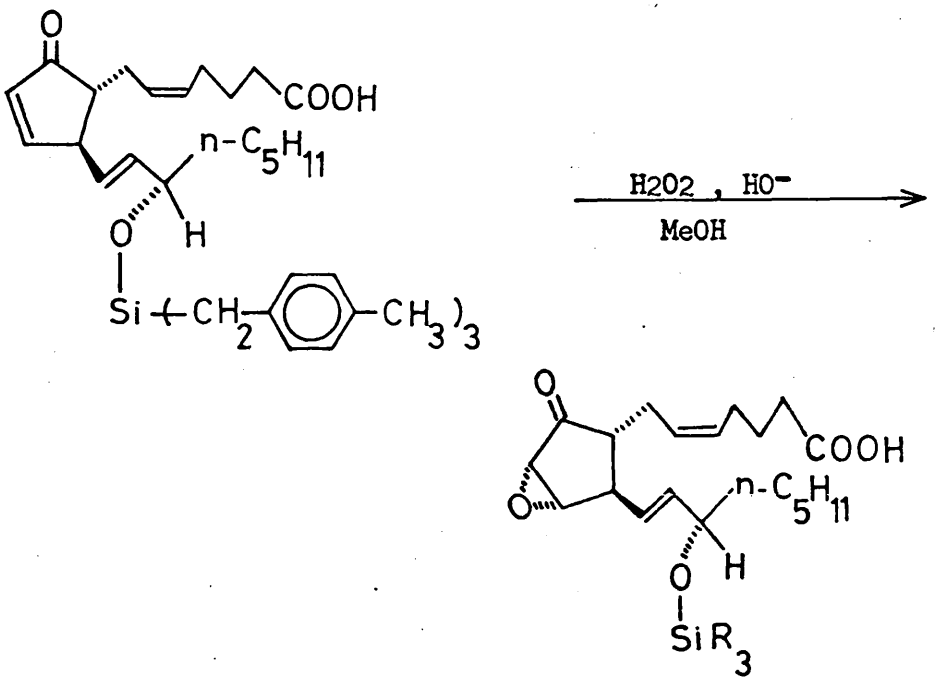
readily into contact with the double bond. Steric effects can interfere with the directing influence of the hydroxyl group even if it is favourably situated with respect to the double bond. The norbornene derivatives





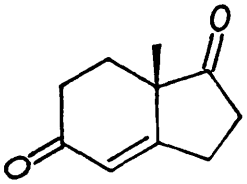
are attacked by peroxyacid entirely from the <u>exo</u> side because of the highly unfavourable nature of <u>endo</u> attack.[76]

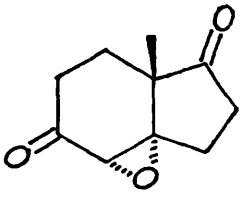
The stereospecificity of base-catalysed epoxidations of enones with hydrogen peroxide has also been interpreted in terms of steric, conformational, and electronic considerations. The presence of a large alkyl group can lead to epoxidation from the opposite face. For example, the $\Delta^{10,11}$ linkage in prostaglandin A_2 can be epoxidised with a high degree of stereoselectivity by converting the 15-hydroxyl group to the very bulky tri-<u>p</u>-xylylsilyl ether



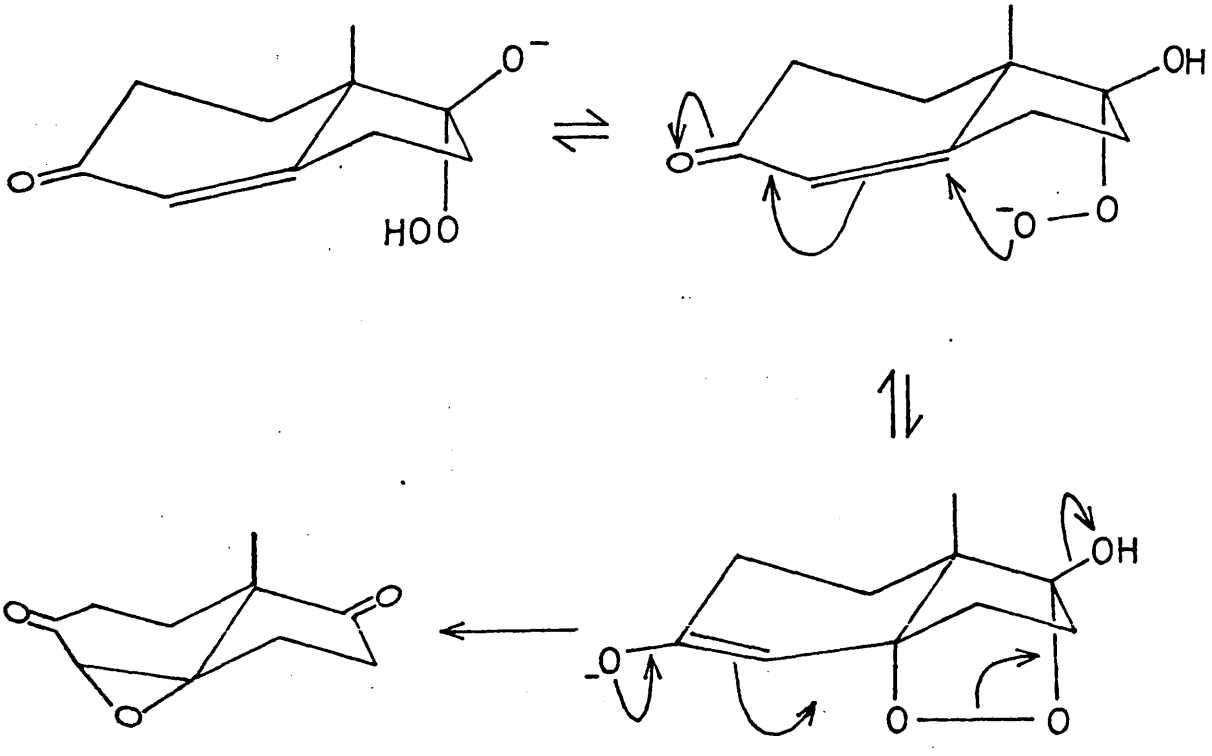
By blocking the approach of a reagent to the β-face in this way an $\alpha:\beta$ epoxide ratio of 94:6 was obtained.[77]

Intramolecular delivery has been used to explain the stereoselectivity of the base catalysed hydrogen peroxide epoxidation of 7,7a-dihydro-7a-β-methyl-indane-1,5(6H)-dione.[78]

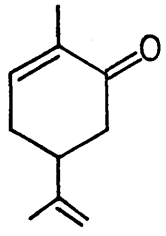
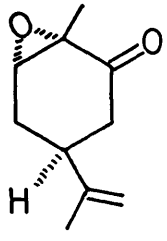




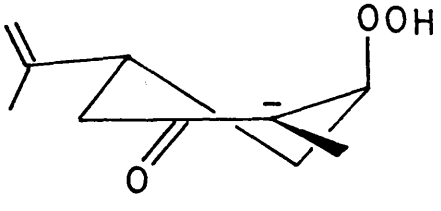
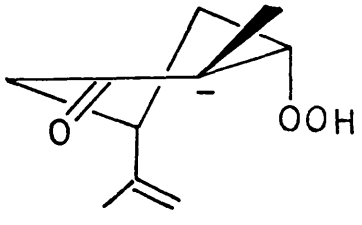
The trans-stereochemistry of the ring junction was indicated by comparison with the cis-epoxide, synthesised by a stereochemically unambiguous route. The proposed mechanism involved initial attack by the hydroperoxide anion at the less hindered face of the non-conjugated carbonyl followed by intramolecular delivery to the carbon of the enone.



Stereoselectivity has been observed in certain cyclohexenone epoxidations and has been explained in terms of the stereo-electronic requirement that the hydroperoxide group should be as nearly axial as possible so as to ensure colinearity of the O-O bond with the enolate π-orbital for the cyclisation step. For example, carvone gives only one epoxide.

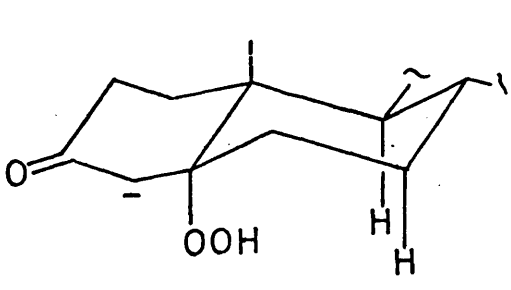
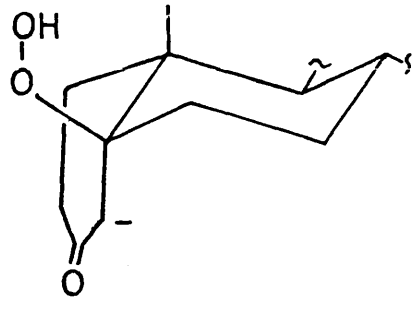



This can be rationalised by comparing the relative stability of the two axial conformations of the two anions which can be obtained by hydroperoxide attack on carvone.

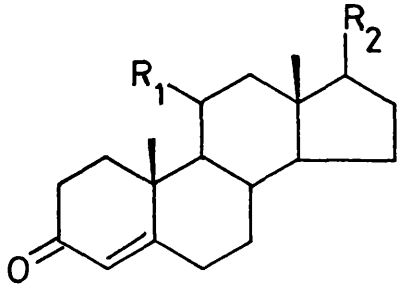
Of these the first, leading to the trans-epoxide, is the more stable.

It is less obvious why β-epoxides are the main or only products in the Weitz-Scheffer epoxidation of steroid 4-en-3-ones. In this system, the hydroperoxy group can assume the axial disposition with respect to ring A both in the 5α- and 5β-hydroperoxides.

Two effects could be responsible for this stereoselectivity. Stabilisation of the carbanion should be greater in the second than in the first compound since 5β-3-oxosteroids enolise preferentially towards C(4), and 5α-3-oxosteroids towards C(2). Also, in the transition state for ring closure, the departing $^{-}$OH must be anti to the enolate π-bond. Such a geometry will result in more unfavourable steric interactions in the 5α-structure (with the hydroperoxy group equatorial to ring B) than in the 5β-structure.

Remote polar substituents have been shown to have an effect on the steric course of the Weitz-Scheffer epoxidation of steroid 4-en-3-ones.[79] Polar substituents at C(11) or C(17) can

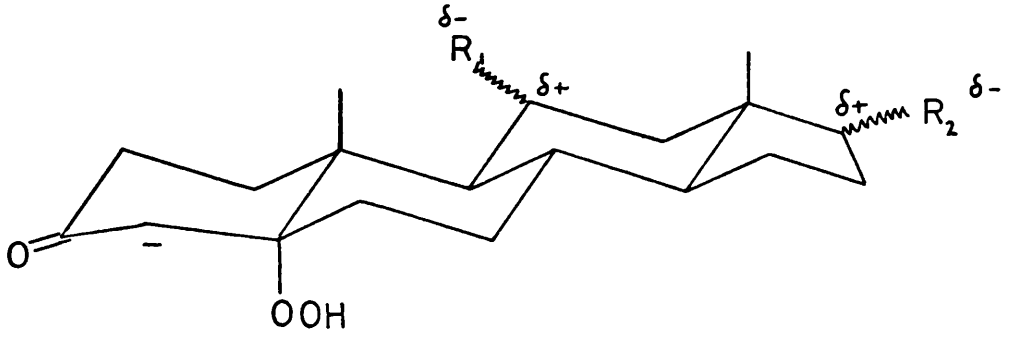


increase the proportion of α-epoxide formed.

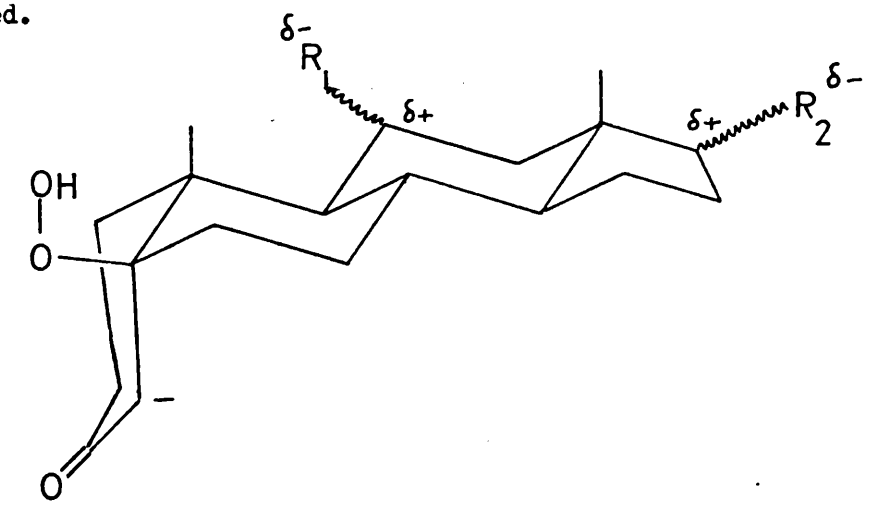
R_1	R_2	% α-epoxide
H	H	0
H	β-CHMe$(CH_2)_3$OH	11
H	α-OH	27
H	β-OH	31
α-OH	β-OH	0
β-OH	oxo	51
oxo	oxo	86

These results have been rationalised by Henbest in terms of dipole-dipole interactions. In the case of the hydroperoxyenolate

anion which leads to α-epoxide the interaction between the anion and the positive end of the remote dipole is through the steroid skeleton, a region of low dielectric constant which allows efficient interaction between the charges and hence stabilises the transition state leading to α-epoxides.



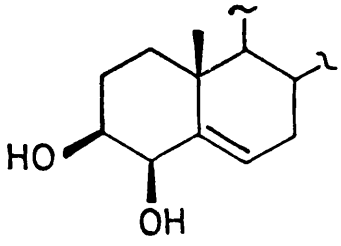
In the hydroperoxyenolate which leads to the β-epoxide such an interaction would take place through the solvent, a region of high dielectric constant and hence any stabilisation would be minimised or eliminated.

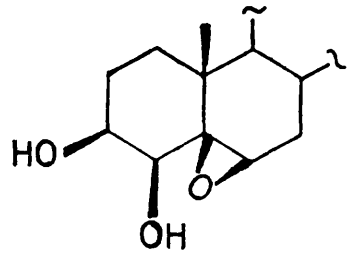


The inconsistences in this explanation have been acknowledged by its author and alternative interpretations have been made.[80]

The use of transition metal compounds as catalysts in epoxidations of olefinic alcohols with peroxy compounds often leads to high stereospecificity. In cases where the cis-epoxide has not

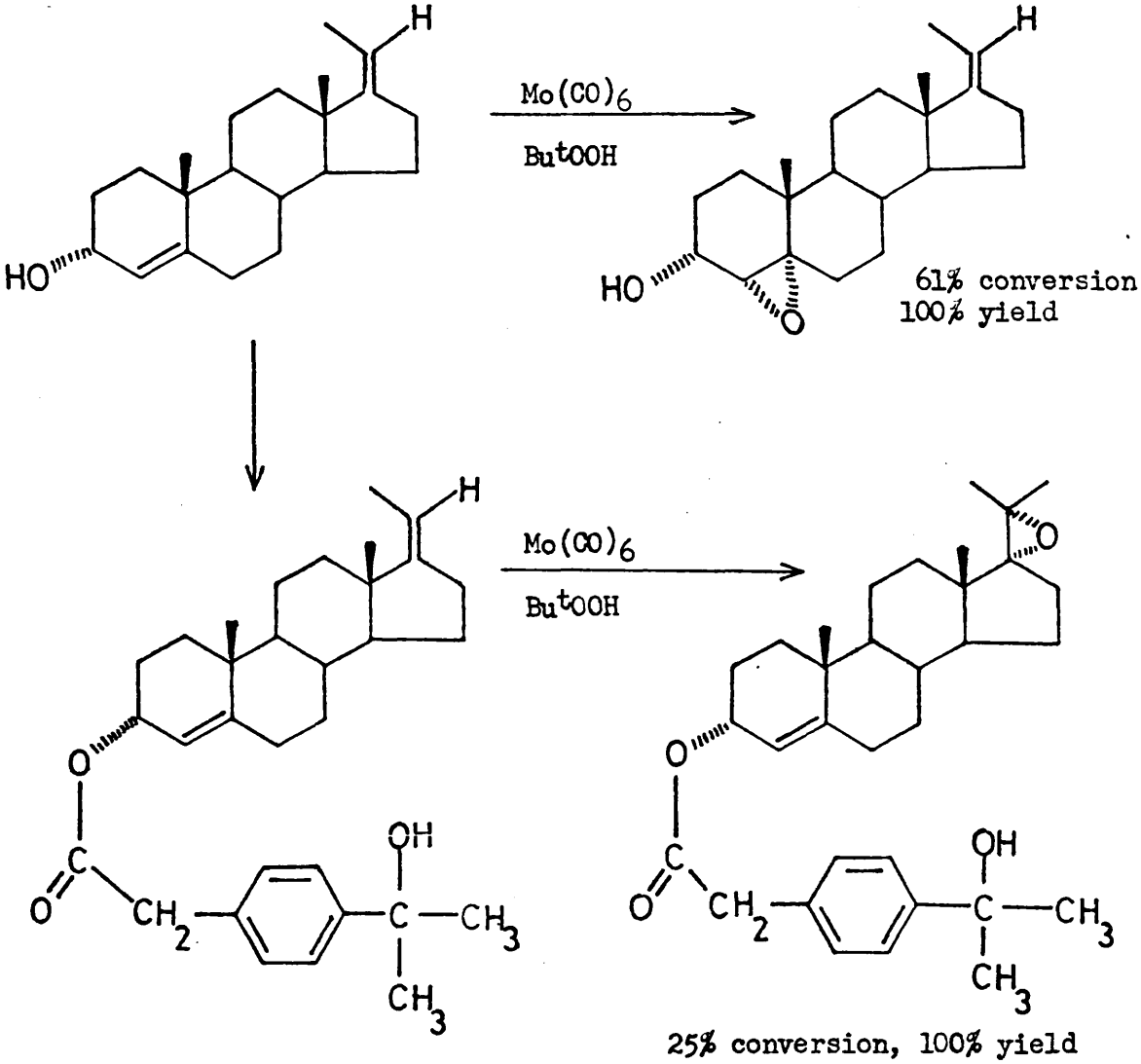
been the exclusive product, its yield has been improved by the use of these catalysts. For example, m-chloroperoxybenzoic acid epoxidation of 4β-hydroxycholesterol in methylene chloride gave approximately twice as much β-epoxide as α-epoxide.





When the catalyst was used, 95% of the product was β-epoxide.[81]

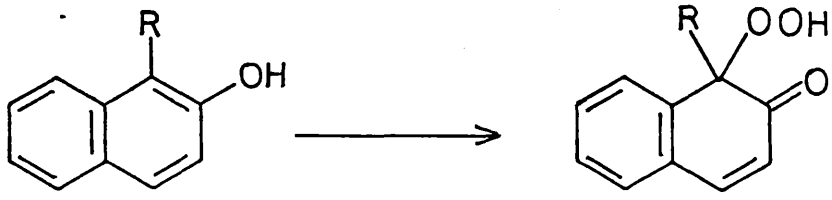
Catalysts, in conjunction with 'template spacers', can be used to epoxidise, stereospecifically, remote alkene functions in suitable molecules.[82]



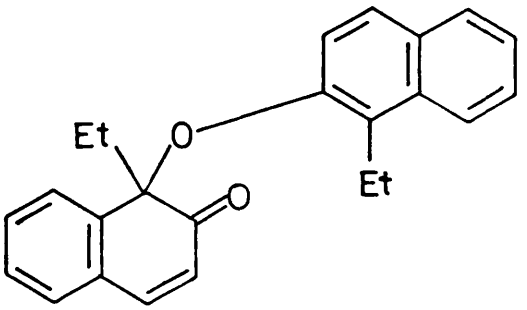
In this case, by forming a carefully chosen derivative of the original alcohol a hydroxyl group can be provided to participate, presumably by a mechanism such as discussed in the above section, in the stereospecific epoxidation of the remote double bond.

DISCUSSION

The present study of 1-aralkyl-2-naphthols (1) was stimulated by the observation that certain 1-alkyl-2-naphthols autoxidised to give, cleanly and in high yield, the corresponding hydroperoxyenone (2).



The original observation was made with 1-isopropyl-2-naphthol.[7] Compounds of this type (1) were, however, already known in the literature but frequently there had been no comment on their stability. Previously synthesised compounds were reinvestigated together with several new 1-alkyl-2-naphthols in order to investigate systematically the factors which influence autoxidation. The results of the study were that there was a good correlation between the rate of autoxidation for a particular 1-alkyl-2-naphthol and the degree of strain, due to the unfavourable peri-interaction. 1-t-Butyl- and 1-t-pentyl-2-naphthol autoxidise very rapidly, 1-isopropyl-, 1-cyclohexyl-, and 1-sec-butyl-2-naphthol autoxidise rapidly, all yielding the corresponding hydroperoxyenone, while 1-methyl-2-naphthol did not react with oxygen to any significant extent in eight days, even in the presence of potential initiators such as Co(acetylacetonate)$_3$. 1-Ethyl-2-naphthol gave a mixture of 1-ethyl-1-hydroperoxynaphthalen-2(1H)-one and the naphthoxy radical dimer.

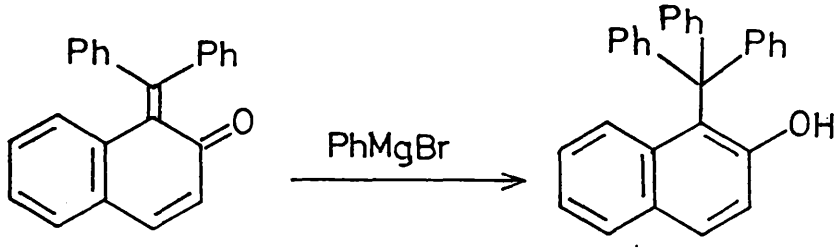


The closely related 1-benzyl-2-naphthol was reported[7] to be inert to oxygen over prolonged periods.

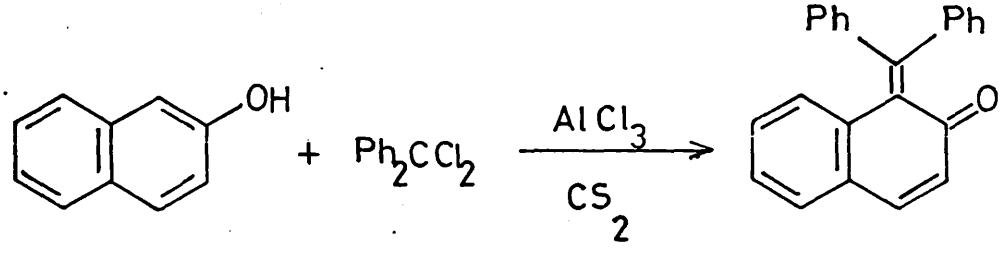
Preparation of 1-trityl-2-naphthol.

1-Trityl-2-naphthol (trityl = triphenylmethyl) was a compound which had previously been reported without any comment being made on its stability in air. This compound, structurally related to 1-t-butyl-2-naphthol, was expected to show a strong tendency towards autoxidation since there is evidence from the A values of cyclohexanes,[83] from conformations of tetrasubstituted ethanes,[84] and from the distortions of the 1,8-disubstituted naphthalenes[85] that the steric requirements of a phenyl group are greater than for a methyl group. It was recognised that, in 1-trityl-2-naphthol, the phenyl groups could adopt a propellor-like conformation similar to that found in tri- and tetra-aryl methanes where the ortho protons of each phenyl group lie opposite the face of the adjacent phenyl group.[86] Calculations of the energy of such molecules, particularly those with substituents in ortho positions, as in 1-trityl-2-naphthol, show that there is considerable strain. Attempts to construct a model of this substance with space-filling models support this view. It was hoped to gain some information about the effective size of the trityl group in this particular environment by measurement of the rate of autoxidation of

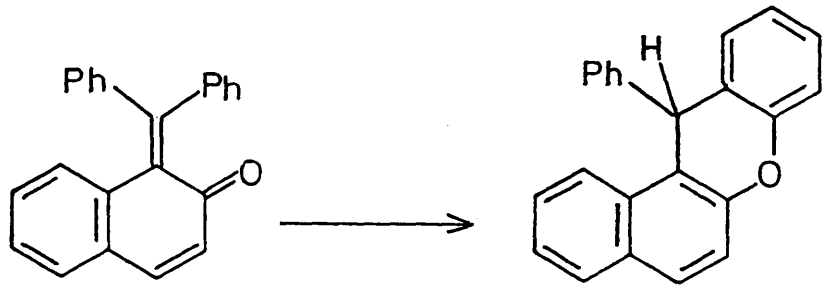
1-trityl-2-naphthol and comparison of that rate with those of the previously studied 1-alkyl-2-naphthols. The only reported route to 1-trityl-2-naphthol is the Grignard reaction of PhMgBr with o-naphthofuchsone[87]



and routes to this substance were therefore examined first. The fuchsone had been reported as the product of the reaction of dichlorodiphenylmethane with 2-naphthol in the presence of $AlCl_3$.[88] An attractively simple route to Ph_2CCl_2 was the reaction of benzene with carbon tetrachloride, again with $AlCl_3$. The authors reported good yields of Ph_2CCl_2 when an excess of carbon tetrachloride was used.[89] Repetition of their procedure gave a crude product containing benzophenone. Vacuum distillation of the crude product, after it had been heated with PCl_5 to convert the benzophenone to Ph_2CCl_2, gave the desired product but the yield was very low. Since the conversion of the benzophenone to Ph_2CCl_2 by PCl_5 had been effected relatively easily and in high yield, the original reaction was abandoned and benzophenone was used as a source of Ph_2CCl_2. With a stock of this compound the synthesis of o-napthofuchsone by the literature method was attempted.



The product obtained from this reaction was not the desired o-naphthofuchsone but a colourless isomer which showed a parent ion of mass 308 on mass spectral analysis and which gave combustion analysis results consistent with the required formula, $C_{23}H_{16}O$. This isomeric species had spectral characteristics which indicated that the corresponding xanthene had been formed, presumably by cyclisation of o-naphthofuchsone.

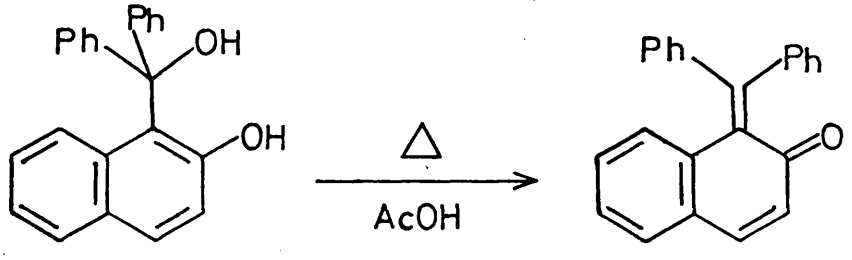


The NMR spectrum showed a multiplet at $\delta(CDCl_3)$ 7-8, 15H, and a singlet at δ 5.9, 1H. The UV spectrum, λ_{max} 255(4.36), 269(3.88), 280(3.81), 291(3.53), 317(3.11), and 336(3.16) nm, was similar to that of a 1-alkyl-2-naphthol and showed no enone band. The IR spectrum showed that, while there was no carbonyl group in the molecule, there was a signal due to C-O stretch at 1245 cm^{-1}. The formation of a xanthene is probably promoted by the presence of $AlCl_3$ which could enhance the electrophilicity of the carbonyl oxygen in the fuchsone and so favour cyclisation. The intended function of the $AlCl_3$ was to increase the reactivity of the Ph_2CCl_2 towards electrophilic aromatic substitution.

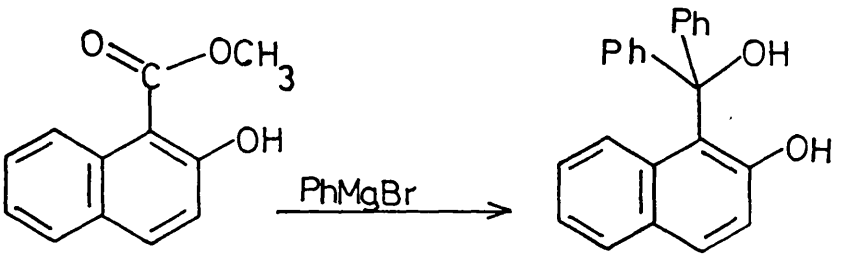
Another method of activating the system is available, one which would allow the omission of $AlCl_3$. o-Naphthofuchsone had been reported as the product of the reaction of Ph_2CCl_2 with an ethanolic solution of sodium naphthoxide.[90] The reaction was attempted and its progress monitored by T.L.C. This showed that there were three

components in the product mixture with R_f 0.8 (same as Ph_2CCl_2), 0.5, and 0.3 (same as 2-naphthol). There was no evidence for xanthene formation. The temperature of the system was increased in a stepwise manner in an attempt to decrease the quantity of 2-naphthol (presumably derived from unreacted naphthoxide by hydrolysis) and Ph_2CCl_2. There was no change in the T.L.C. It was thought possible that the Ph_2CCl_2 was reacting with the solvent to give the corresponding diethyl acetal and so the reaction was attempted in toluene. The naphthoxide was generated in dry methanol and was used as a crystalline slurry in toluene. The reaction was unsuccessful in that it produced a host of products (T.L.C. of the reaction mixture showed poorly separated spots from base line to solvent front). The reaction was repeated, taking particular care over the purity of the solvents but again the same type of mixture was obtained. Attempts to isolate single components from the mixture by column chromatography were unsuccessful.

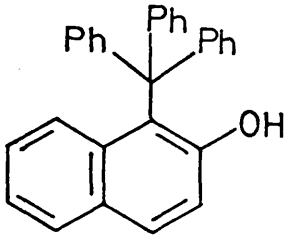
At this point, a completely different route to o-napthofuchsone was investigated. The preparation of the fuchsone had been reported by dehydration of diphenyl(2-hydroxy-1-naphthyl)methanol by warming in glacial acetic acid.[39]

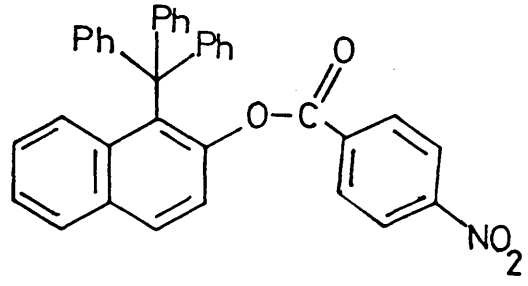


The carbinol was prepared from the methyl ester of 2-hydroxy-1-naphthoic acid by reaction with PhMgBr.



When these reactions were attempted, both proceeded smoothly, the Grignard in higher than 70% yield and the dehydration in higher than 90% yield. Grignard reaction with PhMgBr on the o-naphthofuchsone was carried out and, although addition was possible at three different positions, the product obtained was the desired 1-trityl-2-naphthol. The NMR spectrum consisted of a multiplet (δ 7-7.8, 21 H), and a singlet (δ 5.5, 1 H), which disappeared on addition of D_2O. The IR spectrum showed signals, at 805 cm^{-1}, indicating two adjacent aromatic protons and at 740 cm^{-1}, indicating four adjacent aromatic protons. The UV absorption was typical of a 1-alkyl-2-naphthol and although the spectrum was unaffected by the addition of a few drops of 6 M potassium hydroxide, a bathochromic shift was observed on addition of a pellet of KOH to both the sample and the reference cell. This behaviour is consistent with the product being a highly hindered phenol. Mass spectral analysis indicated that the molecular weight of the product was 386 and the product gave the correct combustion analysis results for 1-trityl-2-naphthol. A derivative, the p-nitrobenzoyl ester of the naphthol, was prepared. Mass spectral and combustion analysis results, IR, UV and NMR spectra were in agreement with the structure of the derivative.





However, the melting point of the isolated naphthol was not the same as the literature of 155°C. Even after several recrystallisations, the compound melted at a lower temperature and over a wider temperature range. The exact value of the melting point varied depending on how long the crystals remained on the melting point apparatus before the melting point was reached. (A typical melting point for crystals heated from room temperature was 98° - 125°C). It was concluded that the compound was either decomposing at these temperatures or was reacting with oxygen. The melting point of the crystals in a sealed capillary tube was 135-150°C and in a sealed tube under nitrogen, 154-156°C. The initially observed m.p. behaviour was, therefore, ascribed to reaction with oxygen. An attempt to increase the yield of 1-trityl-2-naphthol was made by the use of Cu(I)Cl, a reagent known to promote 1,4 addition in Grignard reactions.[91] However, no significant increase in the yield was obtained.

Autoxidation of 1-trityl-2-naphthol was attempted under the standard conditions used by Brady.[8] After forty hours the starting naphthol was recovered unchanged. (Total conversion of 1-t-butyl-2-naphthol to the corresponding hydroperoxyenone had required 0.5 h under the same conditions.) It was difficult to explain the stability of this compound to autoxidation. In order to establish if this stability were general for these 1-aralkyl-2-naphthols, 1-diphenylethyl- and 1-diphenylmethyl-2-naphthol were prepared from o-naphthofuchsone by Grignard addition of MeMgBr[92] and sodium

borohydride reduction, respectively. Neither of these two compounds showed any tendency towards autoxidation. Even allowing for the conformational possibilities available to these aromatic species it would have been remarkable if this alone accounted for such a dramatic change in the behaviour of, for example, 1-trityl-2-naphthol compared with 1-t-butyl-2-naphthol. The solution IR spectrum of the 1-trityl-2-naphthol revealed that the hydrogen of the hydroxyl group was completely intramolecularly bonded to one of the phenyl groups. The O-H stretching frequency was 3500 cm^{-1}, compared with 3610 cm^{-1} expected for a free phenol, and the OH signal was insensitive to dilution. Solution IR spectra were obtained for 1-diphenylethyl and 1-diphenylmethyl-2-naphthol together with those of the related 1-benzyl- and 1-phenyl-2-naphthol. These latter two compounds were prepared by direct alkylation of sodium napthoxide by benzyl bromide[7] and by iodination of 2-naphthol followed by photolysis of a benzene solution of the 1-iodo-2-naphthol.[93] The results obtained in the hydrogen bonding studies are tabulated below, where R is the substituent in the corresponding 1-aralkyl, 1-aryl, or 1-alkyl-2-naphthol.

R	O-H stretching frequency	
CPh_3	3500	cm^{-1}
$CMePh_2$	3505	
$CHPh_2$	3505	
CH_2Ph	3605 and 3540	
Ph	3550	
CH_3	3635	

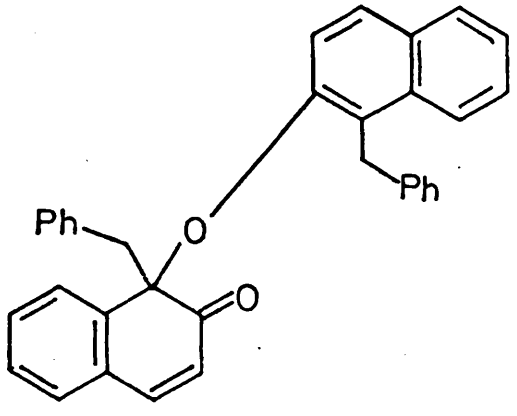
None of the compounds from this series of aryl and aralkylnaphthols autoxidise while their IR spectra show that in each case the phenolic OH group is hydrogen bonded to a phenyl group. In the case of the

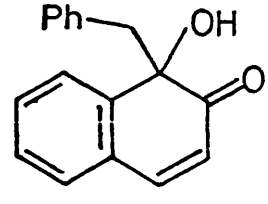
benzylnaphthol only about a third of the molecules show this H-bonding but in all the other cases there is no band for free OH. While the stability of some of these compounds may be due to the relatively small bulk of the substituent, for example, in the case of 1-phenyl-2-naphthol, it seems likely that in the more strained cases the H-bonding stabilises the phenol by preventing the hydrogen atom abstraction necessary to the autoxidation. A similar H-bonding effect between a phenolic OH and a phenyl group has been invoked in explanation of the fact that several o-(1-phenylethyl)phenols show reduced antioxidant ability relative to o-alkyl analogues.[94] It is, however, difficult to rationalise the stability of 1-benzyl-2-naphthol, the compound in which there is only a minor contribution from an intramolecularly H-bonded species, in terms of the small bulk of the benzyl group since the analogous 1-ethyl-2-naphthol does react with molecular oxygen, to give a mixture of hydroperoxyenone and O-C dimer, and arguing by comparison of a phenyl group with a methyl group the 1-benzyl-2-naphthol should be more strained than 1-ethyl-2-naphthol. A more detailed investigation of the susceptibility of 1-benzyl-2-naphthol to autoxidation was therefore undertaken.

Autoxidation of 1-benzyl-2-naphthol

A benzene solution of 1-benzyl-2-naphthol was stirred vigorously under an oxygen atmosphere for one week. T.L.C. of the reaction mixture showed three spots, one of which had the same R_f, 0.3, and the same characteristic colour development when treated with ceric ammonium sulphate solution as authentic 1-benzyl-2-naphthol. Preparative T.L.C. of the product yielded 432 mg of starting material, from an initial 501 mg, together with 10 mg (R_f 0.5), and 17 mg (R_f 0.2) of the two other components. Subsequent analytical T.L.C. showed that

the separation achieved by preparative T.L.C. was incomplete since the 17 mg portion still contained some 1-benzyl-2-naphthol. The relative size of the spots on the T.L.C. suggested and the integration of the NMR spectrum of this most polar portion, which is discussed later, showed that the mixture contained about one third 1-benzyl-2-naphthol. An attempt was made to accelerate the autoxidation of 1-benzyl-2-naphthol by employing cobalt(III) acetylacetonate as a catalyst. The reaction was repeated with a benzene solution of the naphthol to which a catalytic amount of $Co(acac)_3$ had been added, the solution being stirred vigorously under oxygen for one week as before. T.L.C. of the product showed three spots, R_f 0.5, 0.3, and 0.2. Preparative T.L.C. yielded 31 mg, 28 mg, and 44 mg respectively of these three components from an initial 106 mg of 1-benzyl-2-naphthol. Again the third portion was found to contain starting material, estimated at about one half of this sample of 44 mg. Autoxidation of 1-benzyl-2-naphthol had thus been shown to be very slow. It can be accelerated by $Co(acac)_3$. T.L.C. and spectral evidence, discussed below, shows that the same products are formed in approximately the same proportions whether the catalyst is present or not. The spectra of the two products suggested that they might be the hitherto unknown O-C dimer of 1-benzyl-2-naphthol and 1-benzyl-1-hydroxynaphthalen-2(1H)-one



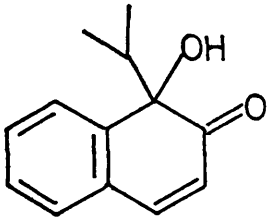


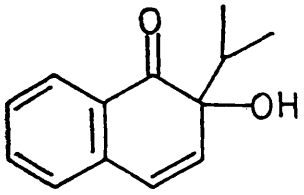
and such products had previously been obtained from autoxidations of analogous naphthols. Syntheses of these substances by unambiguous routes was therefore undertaken.

Treatment of an ethereal solution of 1-benzyl-2-naphthol with alkaline potassium ferricyanide gave the desired dimer in high yield. Mass spectral analysis showed that the product had the correct molecular weight, 466. The IR spectrum showed a strong absorption at 1675 cm^{-1}, indicating the presence of a carbonyl group, and a strong absorption at 1240 cm^{-1} and a medium absorption at 1075 cm^{-1} indicating the presence of a C-O-C aralkyl linkage. The UV spectrum resembled the superposition of a UV spectrum of a 1-alkyl-2-naphthol on a spectrum of a 1-alkyl-1-hydroxynaphthalen-2(1H)-one. The NMR spectrum showed two singlets (δ 3.3 (2H) and 4.75 (2H)) corresponding to two methylene groups in different chemical environments, a doublet (δ 6.15 (1H), J 10 Hz) and a doublet (δ 6.05 (1H), J 8 Hz) one of these being the α proton of the enone unit and the other being H_3 of the naphthalene unit. This high field absorption of H_3 had been previously observed in other O-C dimers from 1-alkyl-2-naphthols.[7]

The synthesis of 1-benzyl-1-hydroxynaphthalen-2(1H)-one was attempted by sodium periodate oxidation[43,44] of 1-benzyl-2-naphthol. After purification of the crude product by T.L.C., a colourless oil which did not crystallise was isolated. Analytical T.L.C. of this oil showed that it contained 1-benzyl-2-naphthol (estimated later at approximately 50%). The NMR spectrum showed a multiplet of aromatic protons (δ 6.6-7.8), an AB quartet (centred at δ 6.1, J 8 Hz) superimposed on a doublet (centred at δ 5.95, J 10 Hz), a singlet (δ 4.35) due to the methylene protons of the starting material, and a singlet (δ 3.0). The above pattern of superimposed doublet and quartet had been observed previously for the mixture of isomers resulting

from the ketol rearrangement of 1-hydroxy-1-isopropylnaphthalene-2(1H)-one to 2-hydroxy-2-isopropylnaphthalen-1(2H)-one





where the doublet was due to the α proton of the conjugated enone system and the quartet to the two olefinic protons of the isomer. The IR spectrum of the oil showed two types of hydroxyl group (3615 cm^{-1} and 3510 cm^{-1}), both insensitive to dilution, and a broad carbonyl signal (1685 cm^{-1}). Little information was gained from the UV spectrum, though the spectrum was the same as that of the isomeric mixture of isopropylhydroxyenones, since the oil was known to contain 1-benzyl-2-naphthol and this latter compound has a UV spectrum which is very similar to that of the mixture of ketols. Hydroxylation of the benzylnaphthol by periodate was therefore incomplete and also gave a mixture of ketols.

Another attempt was made in secure the desired hydroxynaphthalenone by initial acetoxylation followed by hydrolysis under mild conditions. The acetoxylation step proceeded smoothly and in high yield by treatment of 1-benzyl-2-naphthol with lead tetraacetate.[44c] NMR, UV, and IR spectra, mass spectral and combustion analysis all confirmed that the product was 1-acetoxy-1-benzylnaphthalen-2(1H)-one. Attempted hydrolysis of this compound in a mixture of aqueous sodium bicarbonate and ethanol for six hours at 25°C led to the recovery of unchanged starting material. Repetition of the hydrolysis at 40°C for two hours gave a product which was still mainly starting material but which already showed evidence, in the NMR spectrum, of both ketols. The mixture was heated at slightly higher temperatures until there was no starting

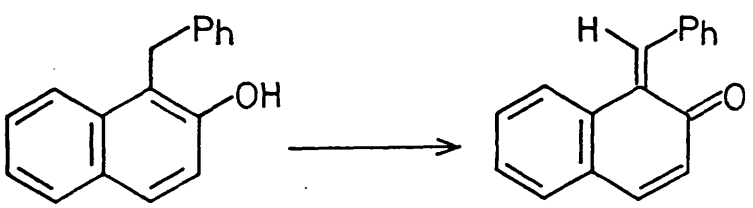
material left. After purification by preparative T.L.C. the main component had an NMR spectrum consistant with a mixture of ketols - aromatic multiplet (δ 6.8-8.2) with a low field proton signal due to the peri proton, H_8, in the 2-benzyl-2-hydroxynaphthalen-1(2H)-one, a doublet and quartet superimposed (δ 6-6.7), a broad singlet (δ 3.8) and a broad singlet (δ 3.5) both of which disappear on addition of D_2O, and a singlet (δ 3.0). The UV spectrum however showed no evidence of ketol rearrangement and was typical of a 1-alkyl-1-hydroxynaphthalenone. It was concluded that the product was a ketol rearranged mixture, the main component of which was the desired 1-benzyl-1-hydroxynaphthalen-2(1H)-one. The two synthetic routes to 1-benzyl-1-hydroxynaphthalen-2(1H)-one therefore both yielded a mixture of this ketol and its isomer. The ketol rearrangement seems to be fast. The two ketols have identical R_f's in all systems tried (or interconvert on the T.L.C. plate) and have NMR spectra which are distinguished only in the olefin region. The potentially magnetically non-equivalent methylene protons of both isomers have all got the same chemical shift so that the methylene region of the mixture shows as a narrow singlet.

The band of R_f 0.5 from the $Co(acac)_3$-catalysed autoxidation and the band of the same R_f from the uncatalysed autoxidation, both showed a single spot on TLC with the same R_f as the O-C dimer from the potassium ferricyanide oxidation. All three had the same colour development when treated with ceric ammonium sulphate solution. The NMR spectra of the three samples were the same. The material of R_f 0.3 from both reactions had the same R_f, the same colour development and the same NMR as authentic 1-benzyl-2-naphthol. The remaining fraction from both autoxidations and the product from the periodate oxidation each showed two spots on T.L.C. one of which had the same R_f and colour development as 1-benzyl-2-naphthol while the other spot had the same R_f

and colour development as the product from the hydrolysis of the 1-acetoxy-1-benzylnaphthalen-2(1H)-one. The NMR spectra of the product of the periodate oxidation and the fractions from the two autoxidations were the same, with the signal due to the benzylic methylene protons of 1-benzyl-2-naphthol varying in intensity in relation to the degree of contamination. Comparison of the integrations due to the methylene protons of 1-benzyl-2-naphthol and the magnetically equivalent protons of the ketols allowed the estimation of the ratio of these two components. In all other respects the spectra were the same as the NMR spectrum of the product from the hydrolysis of 1-acetoxy-1-benzylnaphthalen-2(1H)-one. It was concluded that the products of the autoxidation of 1-benzyl-2-naphthol were the corresponding O-C dimer and a mixture of 1-benzyl-1-hydroxynaphthalen-2(1H)-one and the isomer of this compound, 2-benzyl-2-hydroxynaphthalen-1(2H)-one, which is produced by ketol rearrangement. Catalysis by $Co(acac)_3$ leads to the formation of the same two products in about the same ratio and at a much greater rate.

Attempted dehydrogenation of 1-benzyl-2-naphthol with DDQ

Dehydrogenation of 1-benzyl-2-naphthol was seen as a possible route to an o-quinone methide, analogous to o-naphthofuchsone, but not reported in the literature.



Such a quinone methide would be synthetically useful as the starting material in the preparation of related 1-aralkyl-2-naphthols. Although such a compound would be less stable than o-naphthofuchsone, since it has

one less phenyl group to stabilise the system, the synthesis of this compound was attempted.

A methanolic solution of 1-benzyl-2-naphthol was treated with DDQ and the reaction mixture was stirred at room temperature for one hour. T.L.C. of the reaction mixture showed five spots. This complicated mixture yielded crystals on cooling. The material obtained in this way had the same R_f colour development when treated with ceric ammonium sulphate solution, IR, UV, and NMR spectra, and parent ion on mass spectral analysis as 1-benzyl-1-(1-benzyl-2-naphthoxy)naphthalen-2(1H)-one. Formation of phenoxy radical dimers from DDQ oxidation has been observed before.[33] The complicated mixture present in the mother liquors was not investigated further.

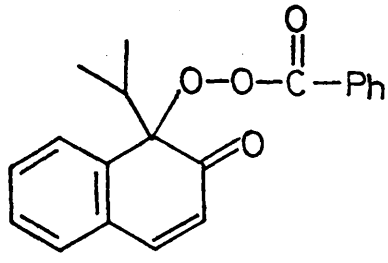
Thermolysis of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one

Two thermolysis experiments were of interest. The thermolysis of the title compound and the thermolysis of the perester derived from it and benzoic acid. This latter study was undertaken in connection with extensive investigations previously carried out into the kinetics of perester thermolysis. As stated in the introduction there are four main modes of perester decomposition with many peresters decomposing by homolysis with extrusion of CO_2.

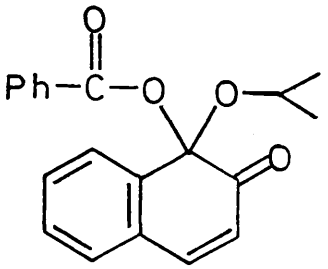
$$R\text{-}COO\text{-}OR' \longrightarrow R^{\bullet} + CO_2 + {}^{\bullet}OR$$

By kinetic studies of the rate of thermolysis of suitable peresters (either by monitoring the quantity of CO_2 formed at a given temperature but over different time intervals from identical samples in sealed evacuated tubes or by moniotring the diminution in the perester carbonyl signal of these same samples) information can be gained about the transition states of free-radical formation. The synthesis of a perester derived from 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one was attempted by adding a solution of benzoyl chloride in methylene

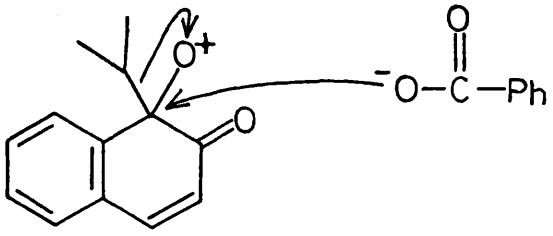
chloride to a solution of the hydroperoxynaphthalenone and pyridine in the same solvent. Equimolar quantities of the hydroperoxide, the acid chloride and the pyridine were used and although related perbenzoates were generally stable up to 130°C, as a precaution, the esterification was conducted at 0°C to reduce any decomposition. The mixture was stirred at 0°C for one hour and after work-up the product mixture was separated by column chromatography, the column being jacketed with crushed ice. The perester is generally obtained first from the chromatographic column since it is often the least polar material present. The crystalline product consistently obtained from attempted syntheses had an NMR spectrum consisting of a multiplet at δ 7-8.2 (10H), a doublet at δ 6.35, J 11 Hz (1H), a multiplet at δ 3.5 (1H) and two doublets at δ 1.38 and 1.1, J 7.0 Hz (6H). This low field absorption of the methine proton was not consistent with the desired perester



but suggests that the isopropyl group is attached to something more electronegative than C(1). The UV spectrum showed λ_{max} 285(3.92) nm and the IR spectrum showed absorptions at 1740 and 1710 cm^{-1}, and at 1090 cm^{-1}. Mass spectral analysis of the product showed that it had the same molecular weight, 322, as the desired product. On this evidence the product was assigned the structure



and is thought to be the product of a Criegee-type decomposition, i.e. heterolysis followed by alkyl shift and recombination.

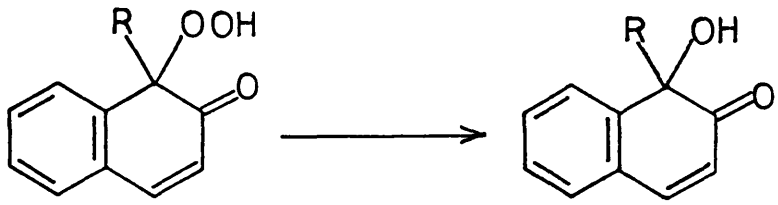


This crystalline compound was the only product obtained by column chromatography of a reaction mixture which, after work-up, had been shown, by T.L.C., to contain three components all with R_f's greater than any of the starting materials. The hydroperoxide was treated with pyridine in methylene chloride for four hours at $0^{o}C$ in the absence of benzoyl chloride. T.L.C. at the end of this period and the NMR spectrum of the product after work-up showed unchanged 1-hydroperoxy-1-isopropyl-naphthalen-2(1H)-one indicating that the hydroperoxide is stable to the reaction conditions and the work-up procedure and suggesting that all the products resulted from the rearrangement or decomposition of the perester. The several spots visible on the T.L.C. of the crude product mixture may have included perester but only the rearrangement product was obtained from a column of silica. An alternative route to the desired perester via the imidazolide resulted in the recovery of unchanged starting material although a sample of t-butylhydroperoxide was converted to the corresponding perester smoothly and in high yield by this method.

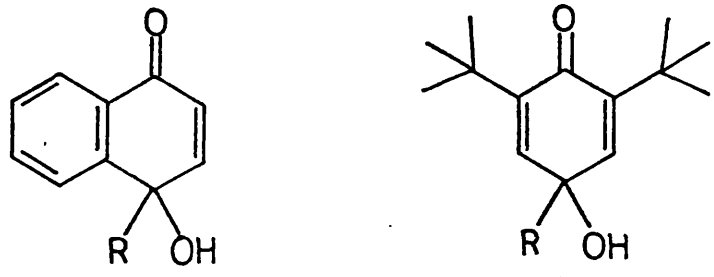
The observation that 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one melts with the evolution of gas led to the investigation of this process. In xylene solution, evolution of gas is observed above 128°C and can be explosive in concentrated solutions. The hydroperoxynaphthalene-one was thermolysed in ethylbenzene. The radical nature of the decomposition was indicated by identification by gas chromatography, of 2,3-diphenylbutane, resulting from the combination of radicals formed from the solvent during the thermolysis. One other component, which was not identified, was also observed by gas chromatography. T.L.C. of the brown oils left after thermolysis indicated the presence of other components which were not seen by the gas chromatographic technique but this complicated mixture was not further examined.

The epoxidation of chiral enones

As has been stated in the introduction, the relative importance of the factors determining the stereospecificity of an epoxidising system, for example, polar, conformational, and steric effects, is difficult to quantify in the rather complex systems studied previously. The stereochemical outcomes of these epoxidations were rationalised in terms of an interplay of these and other effects in order to account for the observed product ratios. It was necessary to find simpler molecules the structures of which could be varied extensively but also in a stepwise manner so that the importance of these effects could be clearly identified. The products obtained by the reduction of the 1-alkyl-1-hydroperoxynaphthalen-2(1H)-ones with dimethyl sulphide, the 1-alkyl-1-hydroxynaphthalen-2(1H)-ones were of interest in this connection.



The epoxidation of these chiral hydroxyenones could result in the formation of two epoxides, with the epoxide oxygen either cis or trans to the original hydroxyl group. Steric effects could be assessed by variation of the size of R and polar effects by conversion of the hydroxyl group to an ester or ether derivative. The effect of the relative position of the hydroxyl group and the double bond could be investigated by consideration of structurally related hydroxyenones, for example



Stereoelectronic effects and conformational mobility of the enones would be small in these systems.

It had already been shown that base-catalysed hydrogen peroxide epoxidation of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one gave a single epoxide in high yield, the trans stereochemistry of this product having been proven by base-catalysed rearrangement of the product.[95] Similarly, 1-hydroxy-1-methylnaphthalen-2(1H)-one was known to give a single epoxide. It had also be shown[96] that 1-acetoxy-1-isopropyl- and 1-methoxy-1-methylnaphthalen-2(1H)-one both gave only one epoxide and in the former case hydrolysis of the acetate yielded the previously

prepared 1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide. 1-Isopropyl-1-trimethylsiloxynaphthalen-2(1H)-one did not give a silylated epoxide but gave the 1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide presumably by initial hydrolysis followed by epoxidation. The trans stereochemical assignments for these compounds depended on the assumption that replacement of OH by OMe or isopropyl by methyl was unlikely to produce a total reversal of stereospecificity and on an examination of the signals due to the epoxide protons in the NMR spectra of the compounds. In each case, the signals due to the epoxide protons closely resembled the AM system found in the trans 1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide which had been unambiguously assigned. No more definite stereochemical assignment was possible. Neither ^{13}C NMR spectra nor the use of shift reagents[96] provided simple criteria. Support for the above trans assignments was therefore sought from synthesis of the corresponding cis epoxides. The epoxidation of these 1-alkyl-1-hydroxynaphthalen-2(1H)-ones was investigated using t-butyl hydroperoxide in the presence of catalytic amounts of $Mo(CO)_6$, and with peroxyacids - procedures both known to lead to high yields of cis epoxide with homoallylic alcohols. Initial investigation in this field had met with only limited success.[96,97] My work started with a reinvestigation of the epoxidation of 1-hydroxy-1-methylnaphthalen-2(1H)-one. Synthetic routes to the precursor of this compound, 1-methyl-2-naphthol were examined.

Preparation of 1-methyl-2-naphthol

The following two synthetic routes to 1-methyl-2-naphthol are recorded in the literature. One involves the reduction of 1-formyl-2-naphthol either by Wolff-Kishner reduction[98] or by reduction with sodium dihydro-bis(2-methoxyethoxy)aluminate (SDA),[99] the other involves hydrogenolysis of 1-morpholinomethyl-2-naphthol either by Raney-nickel

alloy[100] or by hydrogen in the presence of palladium supported on charcoal.[102] Both these methods were devised in order to produce 1-methyl-2-naphthol more satisfactorily than direct alkylation techniques.

Attempted SDA reduction of 1-formyl-2-naphthol

A xylene solution of 1-formyl-2-naphthol was treated with a benzene solution of SDA. The benzene was distilled off and the temperature was raised to 140°C. On addition of the SDA the pale yellow solution of 1-formyl-2-naphthol became opaque chalky yellow and was fluorescent translucent brown when the reaction was stopped. T.L.C. of the reaction mixture after one hour showed that the starting material, R_f 0.7, had been consumed and that three other components were present R_f 0.5, 0.3, 0.2. Authentic 1-methyl-2-naphthol had an R_f 0.5 and the same staining characteristics with ceric ammonium sulphate solution as the least polar component. The spot, R_f 0.3, had a distinctive pink colour under the same development conditions. This was interpreted as the observation of intermediate species in the reduction and the heating was continued. After two hours the T.L.C. pattern was similar but the spot R_f 0.2 was smaller. After three hours, the spot R_f 0.2 had almost disappeared and the spot, R_f 0.3, had increased. More SDA was added in an attempt to increase the amount of the component, R_f 0.5 but no further change was observed. SDA by itself was subjected to the work-up conditions in an attempt to explain the T.L.C. results. No spot was visible by T.L.C. of this control run. A crystalline material was eventually obtained from this reaction the melting point of which, 192-196°C with decomposition confirmed the T.L.C. evidence that it was different from 1-methyl-2-naphthol (lit.[99] m.p. 109-109.5°C). The UV spectrum of the compound was typical of a 1-alkyl-2-naphthol. As a mull in Nujol, the compound had an IR spectrum which showed a totally H-bonded O-H signal,

3415 cm^{-1}, no carbonyl signal, and signals at 810 cm^{-1} and at 740 cm^{-1} indicating two and four adjacent aromatic protons respectively. The compound was not soluble in carbon tetrachloride or chloroform but it did dissolve in d_6-acetone to give an NMR spectrum which showed a broad singlet, δ 9.0, which disappeared on addition of D_2O, a multiplet, δ 6.9-8.6, a sharp singlet, δ 4.95, and a broad singlet δ 3.2, which disappeared on addition of D_2O. Within the aromatic multiplet, a low field signal, δ 8.2-8.6, which integrated as one sixth the total aromatic signal, was typical of signals due to peri-protons observed in some 1-alkyl-2-naphthols. The method of preparation, the melting point and the spectral data given above suggest that the isolated product is 1-hydroxymethyl-2-naphthol (lit.[99] m.p. 192-193°C). Mass spectral analysis, however, shows no peak at 174 required for the hydroxymethylnaphthol but does show strong signals at 156 and 144 together with a very weak signal at 312. Integration of the NMR spectrum of the product consistantly showed the singlet, δ 4.95, to be one sixth the integral of the aromatic protons and not one third as required for the methylene protons of 1-hydroxymethyl-2-naphthol. Also the IR absorption, at 1050 cm^{-1}, ascribable to C-O stretching - O-H deformation (coupled) of a primary alcohol, although present, was uncharacteristically weak. Reduction of 1-formyl-2-naphthol in aqueous alkaline solution with sodium borohydride was carried out in order to obtain 1-hydroxymethyl-2-naphthol for comparison with the product from the SDA reduction. The reaction was followed by T.L.C. After the solution had been stirred at room temperature for 30 minutes there was no starting material, R_f 0.7, left. Of the three other spots, R_f 0.5, 0.3, and 0.2, the spot at 0.3 developed a pink colour when treated with ceric ammonium sulphate solution. Crystals were obtained from this reaction, the R_f, colour development, melting point, and NMR spectrum of which were the same as

those of the product from the SDA reduction. The integral of the NMR spectrum of the product from the sodium borohydride reduction showed the same ratio of one to six for the singlet, δ 4.95, to the aromatic multiplet, δ 6.9-8.6. A mixed melting point determination of these two crystalline reduction products shows no depression. These latter observations do not explain the initial inconsistencies but again suggest that the product from the SDA reduction was 1-hydroxymethyl-2-naphthol. The SDA reduction was repeated. T.L.C. of the reaction mixture showed the same product distribution as before. In my hands therefore the SDA reduction failed to give 1-methyl-2-naphthol cleanly. Another route via 1-morpholinomethyl-2-naphthol was investigated.

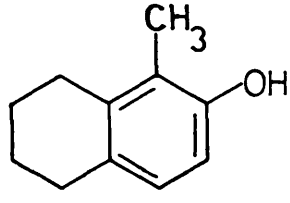
Preparation of 1-morpholinomethyl-2-naphthol

Repetition of a literature preparation[101a] led to the isolation of 1-morpholinomethyl-2-naphthol, smoothly and in high yield, from 2-naphthol, formalin, and morpholine.

Reduction of 1-morpholinomethyl-2-naphthol with Raney-nickel alloy

The hydrogenolysis was attempted on a larger scale (x 35) than was described in the literature.[100] The physical constraints of the larger scale reaction required that the addition take place over six hours as compared with half an hour in the literature example. T.L.C. of the crude product showed that there was still some starting material left. A crystalline compound, m.p. 113-114°C, was obtained. T.L.C. showed that this product was not 1-methyl-2-naphthol. The NMR spectrum showed a multiplet, δ 6.4-7.0, 2H, a broad singlet, δ 4.4, which disappeared on addition of D_2O, a multiplet, δ 2.4-2.9, 4H, a sharp singlet, 2.1, 3H, and a multiplet, δ 1.5-2.0, 4H. Mass spectral analysis indicated that the product had a molecular weight of 162. The UV spectrum of the compound, λ_{max} 280(3.14), was more akin to that of phenol than 1-methyl-2-

naphthol. The solution IR spectrum showed a free phenolic O-H, 3605 cm^{-1}, and absorptions due to aliphatic C-H stretching which were more intense relative to the aromatic absorptions than exhibited in a similar solution IR spectrum of 1-methyl-2-naphthol. A mull of the compound showed almost completely H-bonded O-H, and an absorption due to two adjacent aromatic protons, 805 cm^{-1}. The absorption associated with four adjacent aromatic protons was not observed. On this evidence it was concluded that the isolated product was the tetrahydro-analogue



of the desired product. This compound was already known and its literature preparation[103] involves the hydrogenation of 1-methyl-2-naphthol with Raney-nickel at 110°C and 100 atmospheres pressure of gaseous hydrogen. It was reported to melt at 113.5-114.5°C confirming our structure assignment. This reduction method was, therefore, not adequately developed for large scale runs.

Reduction of 1-morpholinomethyl-2-naphthol using Pd charcoal

A methanolic solution of 1-morpholinomethyl-2-naphthol to which a catalytic amount of 5% palladium-charcoal had been added was stirred vigorously overnight under an atmosphere of hydrogen gas. The product from this reaction was a dark brown oil which T.L.C. examination showed to be a complicated mixture. Crystals, which melted sharply at 80°C, were obtained from this oil. The NMR spectrum of these crystals showed a multiplet, δ 7.3-8.2 only. Mass spectral analysis showed that the compound had a molecular weight of 128. The UV spectrum of the compound was the same as that of naphthalene. The R_f of the compound was the same

as that of authentic naphthalene. Neither spot developed any colour when treated with ceric ammonium sulphate solution but both could be developed with iodine vapour. No depression in the melting point was observed when a mixed melting point determination was attempted with naphthalene. It was concluded that the product was naphthalene resulting, unexpectedly, from the over-reduction of 1-morpholinomethyl-2-naphthol. Subsequent reactions involving the Pd-charcoal catalyst were monitored closely by T.L.C. and were stopped, immediately, when all the starting material had been consumed. When this precaution was taken, 1-methyl-2-naphthol was obtained cleanly and in high yield.

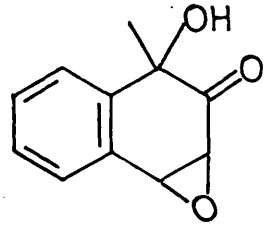
Preparation of 1-hydroxy-1-methylnaphthalen-2(1H)-one

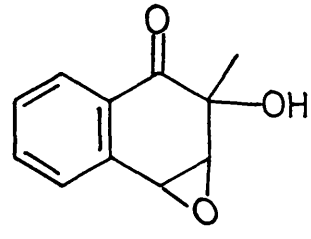
1-Hydroxy-1-methylnaphthalen-2(1H)-one was prepared, by repetition of literature methods, by treatment of 1-methyl-2-naphthol with chromium trioxide in glacial acetic acid[42] or with hydrogen peroxide in glacial acetic acid to which a small amount of concentrated sulphuric acid had been added.[49] The yields in these two reactions were approximately equal at about 50% but the peracetic acid oxidation was preferred because of the easier work-up. With the desired starting material attempts were made to prepare the cis 1-hydroxy-1-methylnaphthalen-2(1H)-one-3,4-epoxide for comparison with the compound isolated from the alkaline hydrogen peroxide epoxidation of 1-hydroxy-1-methylnaphthalen-2(1H)-one.

Attempted epoxidation of 1-hydroxy-1-methylnaphthalen-2(1H)-one

A benzene solution of 1-hydroxy-1-methylnaphthalen-2(1H)-one to which a catalytic amount of molybdenum hexacarbonyl had been added was treated with t-butyl hydroperoxide and refluxed for eight hours. The reaction mixture showed no discernable change by T.L.C. but the NMR spectrum of the product showed a doublet, δ 3.85, J 4Hz, and a doublet, δ 4.1, J 4Hz

indicating the presence of an epoxide. However, the NMR spectrum also showed evidence of ketol rearrangement with the doublet due to the α-proton of the enone system of the starting hydroxyenone superimposed on a quartet due to the olefinic protons in 2-hydroxy-2-methylnaphthalen-1(2H)-one and there were three sharp singlets, δ 1.3-1.6. Attempts to separate the components of this mixture by preparative T.L.C. were unsuccessful. Since this was so, it was not possible to determine whether this was the epoxide of the starting material or the epoxide of the ketol isomer.





The reaction was repeated at a lower temperature in an attempt to achieve epoxidation without ketol rearrangement this was unsuccessful.

It had already been shown[96] that epoxidation of 1-hydroxy-1-isopropylnapthalen-2(1H)-one with $Mo(CO)_6$ and t-butyl hydroperoxide led to the formation of 2-hydroxy-2-isopropylnaphthalen-1(2H)-one-3,4-epoxide. It was decided to investigate the relative susceptibilities of these two compounds, 1-hydroxy-1-methylnaphthalen-2(1H)-one and 1-hydroxy-1-isopropylnaphthalen-2(1H)-one, to ketol rearrangement under the influence of molybdenum hexacarbonyl. The 1-hydroxy-1-isopropyl-naphthalen-2(1H)-one can be prepared from the corresponding hydroperoxy species which is easily obtained by preparation of 1-isopropyl-2-naphthol.

Preparation of 1-isopropyl-2-naphthol

1-Isopropyl-2-naphthol was prepared by the previously reported[7] alkylation of sodium naphthoxide in toluene with 2-bromopropane. The

product obtained was the same in all respects as authentic material.

Preparation of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one

It had already been shown[7] that when oxygen was bubbled through a benzene solution of 1-isopropyl-2-naphthol, the naphthol was converted to the corresponding hydroperoxynaphthalenone. Repetition of this procedure led to the isolation of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one in high yield.

Preparation of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one

Of the several methods known to reduce a hydroperoxide to an alcohol treatment with dimethyl sulphide[23] has be shown to effect the transformation of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one to 1-hydroxy-1-isopropylnaphthalen-2(1H)-one cleanly and efficiently.[96] Repetition of this procedure gave the desired product in high yield.

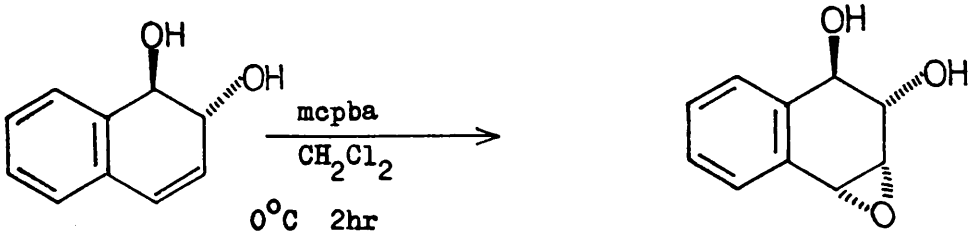
Treatment of 1-hydroxy-1-methyl- and 1-hydroxy-1-isopropylnaphthalen-2(1H)-one with molybdenum hexacarbonyl

Equimolar benzene solutions of 1-hydroxy-1-methylnaphthalen-2(1H)-one and 1-hydroxy-1-isopropylnaphthalen-2(1H)-one to which equivalent amounts of $Mo(CO)_6$ had been added were refluxed in the same oil bath. After three hours the NMR spectra of both these solutions were obtained. Ketol rearrangement was observed to have occurred in both cases. Careful integration of the region δ 6.7, in the 1-hydroxy-1-isopropylnaphthalen-2(1H)-one reaction, allowed the relative abundance of the two isomers to be estimated as approximately twice as much rearranged material as starting hydroxyenone. Integration of the aliphatic region in the NMR spectrum of the product obtained from the 1-hydroxy-1-methylnaphthalen-2(1H)-one which consisted of two sharp singlets indicated that there was four times as much starting material as ketolised product. After six hours refluxing this ratio was observed to be approximately three times

as much starting material as rearranged product. The relative susceptibility of these two compounds to ketol rearrangement is in accord with the expected relative migratory aptitude of the isopropyl group versus the methyl group. The fact that aryl migration was not observed is probably due to the stereoelectronic requirements of the rearrangement, the alkyl group at C(1) being closer to the preferred perpendicular disposition for attack on the carbon of the carbonyl group, than the bond between C(1) and C(9). Since 1-hydroxy-1-methylnaphthalen-2(1H)-one rearranges to 2-hydroxy-2-methylnaphthalen-1(2H)-one under the conditions of the epoxidation and since it would be expected that the product of ketol rearrangement, having a less electron deficient double bond, would epoxidise faster than the starting hydroxynaphthalenone it is probable that the epoxide, detected from the NMR spectrum of the product from the t-butyl hydroperoxide reaction with 1-hydroxy-1-methylnaphthalen-2(1H)-one but which could not be separated from starting material and ketol isomer, was not the desired product, 1-hydroxy-1-methylnaphthalen-2(1H)-one-3,4-epoxide but 2-hydroxy-2-methylnaphthalen-1(2H)-one-3,4-epoxide.

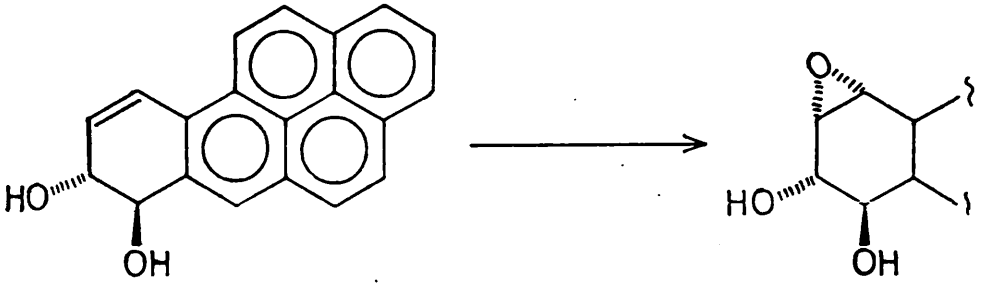
It had been shown[96] during attempts to effect cis-epoxidation of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one with m-chloroperoxybenzoic acid in dichloroethane at room temperature for eight days, with m-chloroperoxybenzoic acid in dichloroethane for 24 hours at 90°C in the presence of the radical scavenger 2,2'-thiobis(4-methyl-6-t-butylphenol), and with t-butyl hydroperoxide in the presence of $Mo(CO)_6$, that ketol rearrangement of the starting material followed by epoxidation was faster than epoxidation of the starting hydroxynaphthalenone since the only epoxide identified from these three reactions was cis-2-hydroxy-2-isopropylnaphthalen-1(2H)-one-3,4-epoxide. It seemed unlikely that further attempts to prepare cis-1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide by these methods would prove successful.

It was decided to convert the hydroxynaphthalenone to the corresponding diol. By this conversion, the nucleophilicity of the double bond and therefore the probability of forming an epoxide would be increased. Conversion of the diol-epoxide to the desired 1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide was envisaged either by the use of the chromium trioxide-pyridine complex[104] or in a "one-pot" conversion of the diol to the diol-epoxide, with m-chloroperoxybenzoic acid, followed by addition of a catalytic amount of 2,2,6,6-tetramethylpiperidine hydrochloride and lastly a second portion of m-chloroperoxybenzoic acid.[105] Clearly the generation of a second hydroxyl group complicates the system since both hydroxyl groups may influence the stereochemical outcome of the epoxidation, probably to different extents and sometimes in different senses. It might be predicted that the hydroxyl group of the allylic alcohol system would be dominant over the hydroxyl group of the homoallylic alcohol and there are examples where this seems to be so.[106,107]

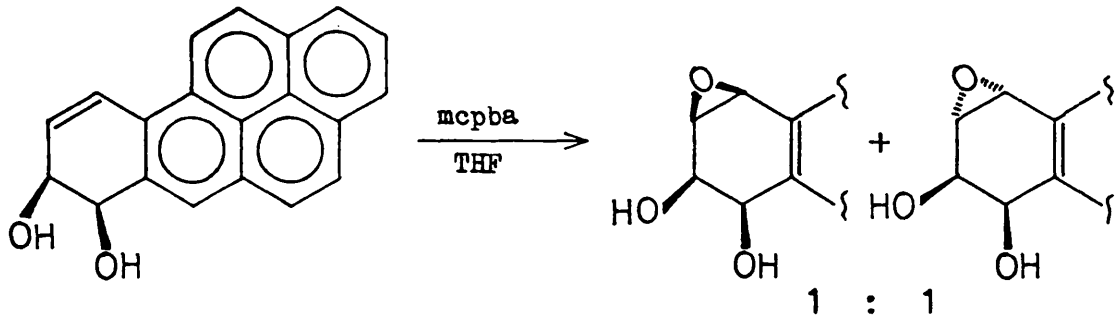


yield 60%: stereospecifically

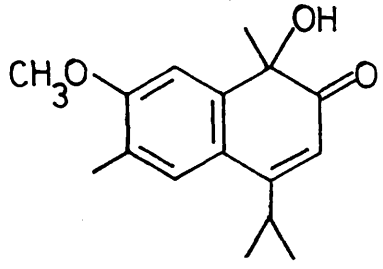
mcpba = m-chloroperoxybenzoic acid



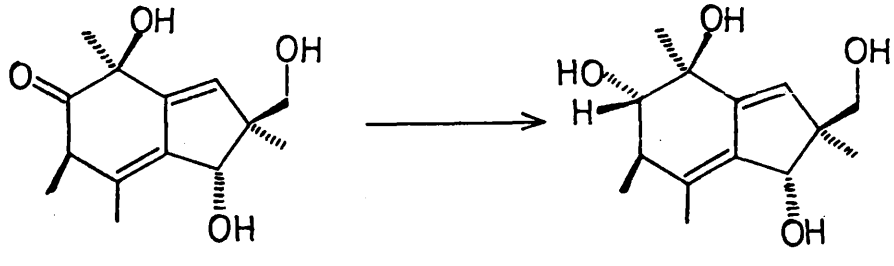
However the products obtained with other substrates are more difficult to rationalise, for example[107]



The stereochemistry of the reduction of the hydroxynaphthalenone was not predictable with certainty. A compound related to 1-hydroxy-1-isopropylnaphthalen-2(1H)-one,1,6-dimethyl-1-hydroxy-4-isopropyl-7-methoxynaphthalen-2(1H)-one



was reported to yield a single diol when treated with sodium borohydride.[108] No details of the stereospecificity of the reduction were given. Applying the rules, formulated to explain the stereochemistry of diols obtained by the reduction of acyclic α-hydroxyketones with sodium borohydride,[109] to 1-hydroxy-1-isopropylnaphthalen-2(1H)-one, a cyclic α-hydroxyketone, the predicted product would be the <u>trans</u>-diol. This was the stereochemistry of the product from the sodium borohydride reduction of, for example, isoilludin S giving dihydroisoilludin S.[110]



If the product from the reduction of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one with sodium borohydride were the trans-diol, then by analogy with the related examples given previously the most likely product expected from epoxidation with, for example, m-chloroperoxybenzoic acid followed by oxidation is trans-1-hydroxy-1-isopropylnaphthalen-2(1H)-one-3,4-epoxide. If the reduction led to the formation of the cis-diol the probability of ultimately isolating the desired cis-epoxide would be greater.

Reduction of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one with sodium borohydride

The reaction was carried out and a single diol was isolated in high yield. The solution IR spectrum of the product was examined for evidence of intramolecular hydrogen-bonding which was expected to be present in the cis-diol but not in the trans-diol. The IR spectrum showed a strong absorbance at 3592.5 cm^{-1} with a shoulder at 3630 cm^{-1}, both insensitive to dilution, and no carbonyl absorbance. If intramolecular hydrogen-bonding is present it is very weak. The UV spectrum showed λ_{max} 270 (3.54). The diol was sparingly soluble in $CDCl_3$ and showed a multiplet δ 6.8-7.7 (4H), a doublet of doublets δ 6.3 (1H) $J_{3,4}$ 10Hz $J_{2,3}$ 3Hz, a doublet of doublets δ 5.95 (1H) $J_{3,4}$ 10Hz $J_{2,4}$ 2Hz, a multiplet δ 4.9 (1H), a multiplet superimposed on a broad singlet, which later disappears on addition of D_2O, δ 2.0-2.8, and an apparent triplet δ 0.7-1.1 (6H), which appears as a quartet in the 90 MHz spectrum. In d_6-acetone the same signals are observed but the septet due to the methine proton of the isopropyl group is less obscured by the signal due to OH. In d_5-pyridine the spectrum is considerably different with a general downfield shift and the collapse of the three multiplets due to H(2), H(3), and H(4) to two sharp singlets. The spectrum shows a multiplet δ 7.8-8.2 (1H), a multiplet δ 7.0-7.5 (3H), a sharp singlet

δ 6.4, a broad singlet δ 6.3, a sharp singlet δ 5.5 (1H), a septet δ δ 3.0 (1H), and an apparent triplet δ 0.9-1.5 (6H). The singlet at δ 6.3 disappears on addition of D_2O and allows integration of the singlet at δ 6.4 as two protons. Mass spectral and combustion analysis confirmed the product was the diol. It was difficult to draw any definite conclusions about the stereochemistry of the product from the spectral information.

Attempted epoxidation of the diol with t-BuOOH and $VO(acac)_2$

A benzene solution of the diol was treated with t-butyl hydroperoxide in the presence of a catalytic amount of vanadyl acetylacetonate, $VO(acac)_2$, for 30 minutes under reflux. The NMR spectrum showed that there was no starting material left, that an epoxide had been produced but also that there was a mixture of ketol isomers present. It was not possible to say whether the diol had been converted to the hydroxynaphthalenone before or after epoxidation but the fact that there was no NMR absorption due to H(2) of the diol-epoxide indicated that the desired product had not been formed.

Attempted epoxidation of the diol with m-chloroperoxybenzoic acid

In diethyl ether prolonged treatment with peroxyacid at temperatures from 0°C to 40°C led to re-isolation of starting material. Similarly, diol was recovered from attempted cis-epoxidation with m-chloroperoxybenzoic acid at 0°C in methylene chloride. When this latter reaction was repeated at room temperature the NMR spectrum indicated that there was no starting material, that an epoxide was present, but again that ketol rearrangement had occurred. There was no evidence for the desired diol-epoxide. A successful epoxidation, from NMR spectral evidence, was carried out on cinnamyl alcohol with m-chloroperoxybenzoic acid at 0°C. This allylic alcohol was chosen as a model for the diol

and its behaviour showed that the reagents and reaction conditions were suitable for the epoxidation. The apparently facile oxidation of the diol to the mixture of hydroxynaphthalenones seems devoid of analogy or rationale. At this point attempts to prepare cis-1-hydroxy-1-isopropylnaphthalen-2(1H)-one were abandoned.

Epoxidation of 4-hydroxy-2,4,6-trialkylcyclohexa-2,5-dienones

It was decided to study three compounds, 4-hydroxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone, 2,6-di-t-butyl-4-hydroxyl-4-methylcyclohexa-2,5-dienone, and 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone in order to investigate, in this γ-hydroxyenone system, the influence of substituents on the stereochemistry of epoxidation. The epoxidation of these hydroxycyclohexadienones with t-butyl hydroperoxide and $Mo(CO)_6$ or with m-chloroperoxybenzoic acid to give cis-epoxides would also provide further information in connection with the assignment of the stereochemistry of the epoxides derived from the base-catalysed decomposition of the corresponding 4-hydroperoxy-2,4,6-trialkylcyclohexa-2,5-dienones (cf. pp. 23-24 of Introduction).

Preparation of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone

Treatment of an ethanolic solution of mesitol with technical cerium(IV) oxide and hydrogen peroxide followed by reduction of the initially formed hydroperoxide led to the isolation of the corresponding 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone in good yield.

Preparation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone

1) CeO_2/H_2O_2

Treatment of 2,6-di-t-butyl-4-methylphenol as detailed before led to isolation of the desired hydroxycyclohexadienone.

2) Base catalysed autoxidation

Oxygen was bubbled through an aqueous ethanolic solution of

2,6-di-t-butyl-4-methylphenol to which potassium hydroxide had been added. After two days no starting material could be detected by T.L.C. The product of this reaction was the same as that isolated in 1).

Attempted preparation of 2,4,6-tri-t-butyl-4-hydroxycyclohexa-2,5-dienone

Attempts to convert 2,4,6-tri-t-butylphenol to the corresponding hydroxycyclohexadienone with cerium(IV) oxide and hydrogen peroxide were unsuccessful. The reaction mixture was heated under reflux for 30 hours at which time T.L.C. showed mainly starting material together with one spot of higher R_f and one of lower R_f, both rather weak. Crystals, which were obtained from the crude reaction product, proved to be starting material.

Attempted epoxidation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone

1) with t-butyl hydroperoxide and $Mo(CO)_6$

When epoxidation was attempted with t-butyl hydroperoxide and $Mo(CO)_6$ a very complicated reaction mixture was obtained. The NMR spectrum showed some evidence for epoxide formation but the products of the reaction could not be separated by preparative T.L.C. The starting material was found to decompose when it was heated in benzene with a catalytic amount of $Mo(CO)_6$.

2) with H_2O_2 and base

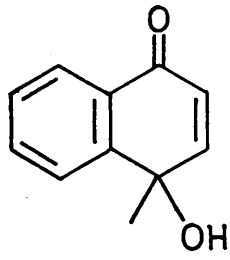
The hydroxydienone was treated with hydrogen peroxide and sodium carbonate, initially at 0°C for four hours, then at 25°C for 24 hours, and finally at 40°C for 24 hours. More peroxide was added each time the temperature was increased. No change could be detected by T.L.C. Some sodium hydroxide in aqueous ethanol was added to the reaction mixture. The NMR spectrum of the crude product after a further three

hours showed it to be starting material.

Epoxidation of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone

The cis-epoxidation of this hydroxycyclohexadienone with m-chloroperoxybenzoic acid had been previously reported.[111] Epoxidation therefore was attempted with hydrogen peroxide in aqueous ethanol with sodium carbonate in order to isolate the trans-epoxide. The temperature of the reaction was raised from $0^{o}C$ to $80^{o}C$ in a stepwise manner. Above $60^{o}C$ the reaction mixture started to turn brown and T.L.C. showed polar material at the base line. After the reaction mixture had been allowed to reflux for one hour, T.L.C. showed mainly starting material together with some highly polar material. The NMR spectrum of the reaction mixture confirmed that it was mostly starting material.

A system related to both those mentioned previously is the hydroxynaphthalenone derived from 4-methyl-1-naphthol.



It was hoped that this molecule would be stable to the epoxidation conditions.

Preparation of 4-methyl-1-naphthol[112]

The naphthol was prepared by sulphonation of 1-methylnaphthalene with concentrated sulphuric acid, conversion of the sulphonic acid, by addition of $BaCO_3$, to the barium salt which is sparingly soluble in water, allowing its separation from the insoluble barium sulphate derived from the excess sulphuric acid, conversion of the $Ba(SO_3Ar)_2$

to the sodium sulphonate, and, finally, production of the naphthol, in low yield overall, by heating with potassium hydroxide.

Preparation of 4-hydroxy-4-methylnaphthalen-1(4H)-one

Treatment of 4-methyl-1-naphthol with technical cerium(IV) oxide and H_2O_2 followed by addition of an excess of dimethyl sulphide yielded 4-hydroxy-4-methylnaphthalen-1(4H)-one. IR, UV and NMR spectra, mass spectral and combustion analysis were all consistent with the product being the desired hydroxynaphthalenone.

Epoxidation of 4-hydroxy-4-methylnaphthalen-1(4H)-one

1) with sodium carbonate and hydrogen peroxide

Treatment of the hydroxynaphthalenone with $NaCO_3/H_2O_2$ led to the formation of a single epoxide.

2) with m-chloroperoxybenzoic acid

When the hydroxynaphthalenone was treated with m-chloroperoxybenzoic acid for 7 hours at 0°C followed by 24 hours at 40°C, T.L.C. of the reaction mixture showed one spot with the same R_f as starting material. The NMR spectrum of the product, at this stage, showed that it was mainly starting material but the presence of a sharp singlet at δ 1.5 separate from the signal due to the methyl group of the hydroxy-naphthalenone together with the presence of a narrow quartet at δ 3.8 suggested that some epoxide had been produced. The reaction was continued for a further 28 hours at which time the signals due to starting material had disappeared and epoxide was observed to be the main product. Crystals were obtained from the crude reaction mixture which had the same melting point, T.L.C. behaviour and spectral characteristics as the epoxide from the base-catalysed hydrogen peroxide epoxidation. A mixed melting point determination of the two epoxides showed no depression. Examination of the mother liquors showed that

there were two other species present since there were three sharp singlets in the aliphatic region of the NMR spectrum. The presence of a quartet at δ 4.5 suggests that the epoxide of the opposite stereochemistry is formed in this peroxyacid epoxidation. By virtue of the known behaviour of peroxyacids in epoxidation it is probable that the epoxide isolated as the main product in this latter reaction is the cis-epoxide and that this is the epoxide formed stereospecifically in the base-catalysed hydrogen peroxide reaction.

Review of Epoxidation Procedures

t-Butyl hydroperoxide/$Mo(CO)_6$ or $VO(acac)_2$

Epoxidation of 1-hydroxy-1-methylnaphthalen-2(1H)-one and 4-hydroxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone with these systems was unsuccessful. It was already known that 1-hydroxy-1-isopropylnaphthalen-2(1H)-one gave cis-2-hydroxy-2-isopropylnaphthalen-1(2H)-one-3,4-epoxide when treated with t-butyl hydroperoxide and $Mo(CO)_6$. Although the $Mo(CO)_6$-promoted ketol rearrangement of 1-hydroxy-1-methylnaphthalen-2(1H)-one was shown to be slower than the rearrangement of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one under the same conditions, ketol rearrangement in the former compound still seems to be faster than formation of 1-hydroxy-1-methylnaphthalen-2(1H)-one-3,4-epoxide. Treatment of 4-hydroxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone with t-butyl hydroperoxide and $Mo(CO)_6$ led to a complex mixture. Although there was spectral evidence for epoxide formation, the components of the mixture could not be separated. The low nucleophilicity of the hydroxycyclohexadienone and the consequentially slow rate of epoxidation allows competition from other reactions catalysed by $Mo(CO)_6$, for example decomposition. t-Butyl hydroperoxide and vanadyl acetylacetonate unexpectedly re-oxidised the diol obtained by reduction of 1-hydroxy-1-

isopropylnaphthalen-2(1H)-one to the hydroxynaphthalenone which allowed ketol rearrangement to occur. Epoxidations with this system of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone and 4-hydroxy-4-methylnaphthalen-1(4H)-one were not tried. These observations are in accord with literature reports that this reagent system epoxidises electron rich alkenes. Even though they contain neighbouring hydroxyl groups, the enones studied here appear to be too weakly nucleophilic and processes other than epoxidation always intercede.

Peroxyacids

The epoxidation of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone by m-chloroperoxybenzoic acid is reported. 4-Hydroxy-4-methylnaphthalen-1(4H)-one was epoxidised with high stereoselectivity by m-chloroperoxybenzoic acid and, although there is no direct evidence, the epoxide is likely to be cis. It is known that this reagent did not epoxidise 1-hydroxy-1-isopropylnaphthalen-2(1H)-one because ketol rearrangement was faster. It was found that this also happens with 1-hydroxy-1-methylnaphthalen-2(1H)-one. This reagent caused oxidation of the allylic alcohol group of the dihydronaphthalenediol although such behaviour is not reported with any other allyl alcohol.

Alkaline hydrogen peroxide

Several 1-alkyl-1-hydroxynaphthalen-2(1H)-ones are reported to be oxidised by this system to single epoxides with high stereoselectivity and there is evidence that one of these has the hydroxyl group and the epoxide oxygen trans. Both the 4-hydroxycyclohexadienones studied by us were unaffected by this system perhaps because of congestion and perhaps because the α-alkyl groups make the 5-positions of the ring inadequately electrophilic. 4-Hydroxy-4-methylnaphthalen-1(4H)-one was however epoxidised successfully and stereoselectively to an epoxide

which is the same as that obtained by peroxyacid epoxidation and which may therefore be *cis*. The scope and selectivity of this system for the epoxidation of enones has therefore been explored a little further. The tentative conclusion that, while certain 1-hydroxynaphthalen-2(1H)-ones and this 4-hydroxynaphthalen-1(4H)-one are epoxidised with high stereoselectivity, the hydroxyepoxides may have opposite stereochemistries remains to be confirmed and explained.

EXPERIMENTAL

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

Infra-red (IR) spectra were recorded on either a Perkin Elmer 257 or 225 spectrophotometer.

Ultra-violet (UV) spectra were measured on a Pye Unicam S.P. 800 spectrometer as solutions, generally, in methanol. Extinction coefficients are quoted as log values and are placed in parenthesis.

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian T-60 (60 MHz) and a Perkin Elmer R 32 (90 MHz) in deuteriochloroform, unless otherwise stated, with tetramethylsilane (TMS) as internal standard.

Mass spectra (MS) were recorded on a G.E.C.-A.E.I. M.S. 12. High resolution mass measurements were made on an A.E.I. M.S. 902E.

Analytical gas chromatography was carried out on a Perkin Elmer F 11 instrument using a flame ionisation detector and a 15% SE 30 column.

Preparative thin layer chromatography (T.L.C.) was carried out using plates coated with 1 mm of Merck Kieselgel HF_{254}. Microslides were used for analytical thin layer chromatography and these were developed using 25% ethyl acetate-light petroleum, unless another solvent system is specifically stated, Light petroleum refers to the fraction b.p. 60-80°, unless otherwise stated.

Solutions were dried over anhydrous magnesium sulphate and solvents were removed on a rotary evaporator.

Preparation of dichlorodiphenylmethane[89]

1) Finely divided aluminium chloride (67.5 g) was suspended in carbon tetrachloride (150 ml). To this was added a mixture of carbon tetrachloride (90 ml) and benzene (90 ml) over a period of 45 min. By cooling and vigorously stirring the reaction mixture its temperature was kept below 30° as the addition was made. The mixture was allowed to stand overnight at room temperature and was then quenched by addition of ice. The carbon tetrachloride solution was separated from the acidic aqueous layer as quickly as possible, to avoid hydrolysis of the dichlorodiphenylmethane, washed with brine, dried and concentrated. The crude product, the IR spectrum of which showed an absorption at 1660 cm^{-1} due to benzophenone, was heated at 230° for 4 h with phosphorus pentachloride[113] (50 g) and then fractionally distilled. Fraction 1, distilling between 40 and 65° / 0.01 mm Hg, consisted of $POCl_3$ and PCl_5. Fraction 2, distilling between 103 and 105° / 0.01 mm Hg, consisted of dichlorodiphenylmethane as did fraction 3, distilling between 105-110° / 0.01 mm Hg. The product was a colourless liquid (28 g, 24%),

ν_{max} (liquid film) 3100-3000 (aromatic C-H stretch), 1485 and 1445 (skeletal C-C stretch) cm^{-1}. No signal due to C=O.

2) Dichlorodiphenylmethane was prepared more satisfactorily by treatment of benzophenone with phosphorus pentachloride as above.[113]

Attempted preparation of o-naphthofuchsone

1) A mixture of 2-naphthol (11 g), aluminium chloride (10.25 g), dichlorodiphenylmethane (15 g) and carbon disulphide (125 ml), protected from moisture by a drying tube filled with silica gel, was stirred overnight at room temperature.[88] The dark green suspension was refluxed for 1 h and then quenched by the addition of crushed ice. Steam distillation of the crude product gave dark brown plastic lumps

(9.25 g) which were treated with dilute alkali. The alkaline aqueous portion was separated, acidified and extracted with ether. The combined ethereal fractions were washed with brine and dried. Evaporation of the solvent gave a solid (2.75 g) which showed a single spot on T.L.C. with the same R_f and staining characteristics as authentic 2-naphthol. The remaining, alkali-insoluble, material was crystallised from glacial acetic acid yielding 12-phenyl-12H-benzo[a]xanthene (1.95 g), m.p. 170-172° (lit.[39] 172-3°),

λ_{max} (EtOH) 255(4.36), 269(3.88), 280(3.81), 291(3.53), 317(3.11) and 336(3.16) nm.

ν_{max} 1245 cm^{-1} (C-O stretch). No carbonyl.

δ 7.0-8.0, multiplet, 15H (aromatics), 5.9, singlet, 1H (Ar_3CH).

m/e 308 (M^+), 231 (M^+-77).

$C_{23}H_{16}O$ requires : C, 89.58; H, 5.23

found : C, 89.60; H, 5.40

T.L.C. of the mother liquors showed three spots, one with the same R_f as the xanthene and the same colour development, initially yellow but changing to orange on heating, with ceric ammonium sulphate solution. Preparative T.L.C. of 100 mg of the mother liquors yielded the xanthene (30 mg), benzophenone (53 mg) and 2-naphthol (12 mg).

2) To a solution of sodium (0.23 g) in ethanol (50 ml) was added a solution of 2-naphthol (1.42 g) in ethanol (50 ml) and then dichlorodiphenylmethane (1.18 g).[90] The solution turned brown and a crystalline precipitate was observed. The reaction mixture was heated to 40° for 30 min at which time T.L.C. showed three spots R_f 0.8, 0.5, and 0.3. Dichlorodiphenylmethane has an R_f 0.8 and 2-naphthol an R_f 0.3. The mixture was heated at 40° for a total of 2 h followed by 2 h at 60° and 2 h at 70°. No change was observed in the T.L.C. Independent investigation of the stability of the dichlorodiphenylmethane in ethanol showed that it reacted with the solvent. A modified version

of this reaction, substituting toluene for ethanol, was attempted.

3) To a solution of sodium (2.09 g) in anhydrous methanol was added 2-naphthol (13.0 g). The methanol was removed by evaporation and the crystalline sodium naphthoxide was treated with toluene (50 ml). The toluene was then evaporated and the process of addition and evaporation of toluene was repeated, in all, four times in order to ensure complete removal of methanol. The pale green crystals so obtained were separated from the surface of the flask and toluene (100 ml) was added. To this stirred slurry was added dichlorodiphenylmethane (10.8 g) and the mixture was left at room temperature for 1 h. Since the system was still basic after this interval, it was heated to 60° for 1 h. The organic phase was then found to be neutral. Ether was added to the system and the precipitated sodium chloride was separated by filtration. T.L.C. of the organic layer showed a poorly resolved streak extending almost to the top of the plate.

This reaction was repeated on a smaller scale with the same outcome. Attempts were made to purify the product from this second reaction by column chromatography without success.

Preparation of diphenyl(2-hydroxy-1-naphthyl)methanol[39]

To an ethereal solution of PhMgBr, prepared by addition of magnesium (1.44 g) to a solution of bromobenzene (9.42 g) in anhydrous ether (150 ml), was added a solution of the methyl ester of 2-hydroxy-1-naphthoic acid (2.02 g) in anhydrous ether (150 ml). All the components of the reaction mixture were rigorously dry and the reaction was conducted under an atmosphere of dry nitrogen. The solution of Grignard reagent changed from translucent grey to bottle green as the ester was added. After 13 h it had changed to a curdy lime-green. When the reaction mixture had been stirred at room temperature for 24 h a small aliquot was subjected to the work-up conditions and T.L.C. of

this sample indicated that starting material was still present. The reaction mixture was heated to 30° for 5 h after which no starting material could be detected. The reaction mixture was quenched by addition of a concentrated solution of ammonium chloride. The ethereal layer was separated and the aqueous fraction was extracted with ether (3 x 100 ml). The combined organic portions were washed with water and dried. Evaporation of solvent gave a solid (4.44 g) which smelled of bromobenzene. The crystalline mass was washed with petrol and then recrystallised from ethanol to which a few drops of ammonium hydroxide solution had been added to give diphenyl(2-hydroxy-1-naphthyl)methanol (2.57 g, 72%). These crystals turned red when heated above 120° and another crystalline species, m.p. 194-197°, was formed as the sample continued to be heated.

ν_{max} (Nujol) 3370 (H-bonded OH), 1600, 1580 (aromatic C=C), 1220 (C-O stretching, -O-H deformation of naphthol), 815 (2 adj. arom. H), 770 (4 adj. arom. H), 750 and 700 (5 adj. arom. H) cm^{-1}.

δ ($CDCl_3$) 6.8-7.8 (aromatics).

m/e 308 (M^+-18), 231 (M^+-95).

$C_{23}H_{18}O_2$ requires : C, 84.64; H, 5.56

found : C, 84.97; H, 5.60

Preparation of o-naphthofuchsone

Diphenyl(2-hydroxy-1-naphthyl)methanol (400 mg) in glacial acetic acid (2 ml) was refluxed for 5 min. On cooling o-naphthofuchsone was obtained as orange-red crystals (364 mg. 91%), m.p. 196-198° (lit.[39] m.p. 198°),

λ_{max} (MeOH) 268 (sh.), 280(3.80), 292(3.76), 337(3.59), 364(3.60) nm.

ν_{max} (Nujol) 1645 (C=O) cm^{-1}.

δ ($CDCl_3$) 6.8-7.6, multiplet, 15H (aromatics and β-proton of enone, 6.2, doublet, J 10Hz, 1H (α-proton of enone).

m/e 308 (M^+), 231 (M^+-77).

$C_{23}H_{16}O$ requires : C, 89.58; H, 5.23

found : C, 89.80; H, 5.40

Preparation of 1-trityl-2-naphthol[87,92]

To a stirred ethereal solution of PhMgBr, prepared by addition of magnesium (23.4 mg) to bromobenzene (15 3 mg) in anhydrous ether (20 ml) under nitrogen was added o-naphthofuchsone (100 mg) in ether (50 ml). The reaction mixture was stirred for 10 h at 30°C at which time no o-naphthofuchsone could be detected by T.L.C. The reaction mixture was treated with a concentrated solution of ammonium chloride. The ethereal layer was separated and the aqueous portion extracted with ether (3 x 50 ml). Evaporation of the solvent followed by recrystallisation from light petroleum gave 1-trityl-2-naphthol (63 mg. 50%).

λ_{max} (MeOH) 272(3.57), 284(3.61), 295(3.55), 335(3.38).

ν_{max} (KBr) 1610, 1590 (aromatic C=C), 1190 (C-O stretching, -O-H deformation of naphthol), 805 (2 adj. arom. H), 752 and 700 (5 adj. arom. protons), 749 (4 adj. arom. H) cm^{-1}.

ν_{max} (CCl_4) 3500 cm^{-1} (insensitive to dilution, intramolecularly H-bonded OH).

δ ($CDCl_3$) 7.0-7.8, multiplet, 21H (aromatic), 5.5, singlet, 1H (OH, exchanged by D_2O).

m/e 386 (M^+), 309 (M^+-77), 232 (M^+-155).

$C_{29}H_{22}O$ requires : C, 90.12; H, 5.74

found : C, 89.87; H, 6.02

The UV spectrum was unaffected by the addition of a few drops of either 6M aqueous potassium hydroxide or methanolic potassium hydroxide. A bathochromic shift was observed on addition of a

pellet of potassium hydroxide to both cells.

λ_{max} (MeOH) 278(sh.), 292(3.02), 305(sh.), 366(2.78).

m.p. 98-125° (on microscope slide)

135-150° (in a sealed tube)

154-155° (in a sealed tube under nitrogen) (lit.,[92] m.p. 155°).

Preparation of 1-trityl-2-naphthol in the presence of Cu(I)Cl

To a stirred ethereal solution of PhMgBr, prepared by addition of magnesium (312 mg) to bromobenzene (2.04 g) in anhydrous ether (150 ml), was added a catalytic amount of cuprous chloride (3.8 mg) and then o-naphthofuchsone (190 mg) in ether (100 ml). The reaction mixture was stirred under nitrogen for 10 h at 30° and was subjected to the work-up regime stated previously. A product was obtained (135 mg, 57%) identical in all respects with the 1-trityl-2-naphthol previously prepared.

Preparation of the p-nitrobenzoyl derivative of 1-trityl-2-naphthol[87]

To a solution of 1-trityl-2-naphthol (40 mg) in pyridine (2 ml) was added p-nitrobenzoyl chloride (47 mg). The reaction mixture was heated at 40° for 5 h after which time no starting material could be detected by T.L.C. The reaction mixture was poured on to iced water and the resulting solid was filtered, washed with sodium carbonate solution, and then with water. The solid crystalline product was dried in the vacuum pistol to give 1-trityl-2-naphthyl p-nitrobenzoate (50 mg, 90%) m.p. 211-213° (lit.,[87] m.p. 200°),

λ_{max} (MeOH) 265(4.48) nm,

ν_{max} (KBr) 1730 (C=O), 1523 and 1345 (aryl $-NO_2$ stretch), 805 (2 adj. arom. H), 750 (4 adj. arom. H), 745 and 705 (5 adj. arom. H) cm^{-1}.

δ (CS_2) 6.6-8.1, multiplet.

m/e 535 (M^+), 458 (M^+-77), 385 (M^+-150), 369 (M^+-166).

$C_{36}H_{25}NO_4$ requires : C, 80.73; H, 4.70; N, 2.62

found : C, 80.95; H, 4.78; N, 2.88

Preparation of 1-(1,1-diphenylethyl)-2-naphthol[92]

To a stirred solution of MeMgI, prepared by addition of magnesium (150 mg) to iodomethane (0.39 ml) in anhydrous ether (50 ml), under dry nitrogen was added o-naphthofuchsone (150 mg) in ether (100 ml). The orange colour was discharged almost immediately. The mixture was stirred for 14 h at room temperature, refluxed for 3 h, and then treated with cold dilute aqueous hydrochloric acid. The ethereal layer was separated and the aqueous layer extracted with ether (3 x 50 ml). The combined ethereal fractions were washed with 4% sodium carbonate solution, then with water, and dried. Evaporation of the solvent gave an almost colourless oil which showed one spot on analytical T.L.C. examination together with some polar material at the base line. Preparative T.L.C. of the reaction product showed one band, R_f 0.6, when eluted with 10% ethyl acetate/light petroleum (60-80°), and yielded 1-diphenylethyl-2-naphthol (87 mg, 55%) as a colourless oil. All attempts to induce crystallisation, as reported (lit.[92] m.p. 141°), failed.

λ_{max} (MeOH) 270(3.61), 280(3.65), 286(3.55), 325(sh.), 333(3.34) nm.

On addition of solid potassium hydroxide this changed to

$\lambda\lambda_{max}$ (MeOH) 280(3.45), 291(3.50), 301(sh.), 360(3.20) nm.

$\nu\nu_{max}$ (CCl_4) 3505 (H-bonded OH), 2980-2860 (C-H stretch) cm^{-1}.

δ ($CDCl_3$) 6.6-8.2, multiplet, 16H (aromatics), 4.8, singlet, 1H ((-OH, exchanged with D_2O), 2.45, singlet, 3H ($-CH_3$).

m/e 324 (M^+), 309 (M^+-15), 231 (M^+-93).

Preparation of 1-diphenylmethyl-2-naphthol

To a stirred solution of o-naphthofuchsone (280 mg) in ethanol (150 ml) at room temperature was added sodium borohydride (67 mg) in a mixture of ethanol (10 ml) and water (1 ml). The colour of the solution changed almost immediately from deep orange-red, to light cherry red, and finally after five minutes to yellow. T.L.C. of the reaction mixture showed one spot which had the same R_f as o-naphthofuchsone but a different colour when treated with ceric ammonium sulphate solution. Some of the solvent was evaporated and the solution was treated with water (100 ml) and ether (100 ml). The ethereal layer was separated and the aqueous layer extracted with ether (3 x 50 ml). The combined ethereal portions were washed with brine and dried. Evaporation of the solvent and recrystallisation from ethyl acetate-light petroleum gave 1-diphenylmethyl-2-naphthol (251 mg, 89 mg), m.p. 111-112.5°,

λ_{max} (MeOH), 271(3.74), 281(3.84), 292(3.78), 325(sh.), 336(3.58) nm.

ν_{max} (KBr), 3590 (H-bonded OH), 1615, 1595, 1515, and 1448 (arom. C=C), 1200 (C-O stretch coupled to -O-H deformation of naphthol), 815 (2 adj. arom. H) 745 and 708 (5 adj. arom. H), 735 (4 adj. arom. H) cm^{-1}.

δ ($CDCl_3$) 6.8-8.1 multiplet, 16H (aromatics), 6.4, singlet, 1H ($Ar_3C\underline{H}$), 4.55, singlet, 1H (OH, exchanged with D_2O).

m/e 310 (M^+), 231 (M^+-79), 167 (M^+-143).

$C_{23}H_{18}O$ requires : C, 89.00; H, 5.85

found : C, 88.71; H, 6.03

Preparation of 1-benzyl-2-naphthol[7,114]

To a methanolic solution of sodium methoxide, prepared by dissolving sodium (3.2 g) in dry methanol, was added 2-naphthol (20.04 g). When the 2-naphthol had dissolved, the solvent was evaporated, dry toluene (50 ml) was added and this, in turn, was evaporated. This process of addition and evaporation was repeated four times to remove all traces of

methanol. To the powdered sodium naphthoxide was added dry toluene (75 ml) and benzyl bromide (16.6 ml, 23.87 g). The stirred slurry was refluxed for 24 h. The reaction mixture was cooled and treated with water (150 ml). The toluene layer was separated and the aqueous layer was extracted with ether (3 x 100 ml). The combined organic portions were extracted with Claisen's alkali, prepared by dissolving potassium hydroxide (35 g) in water (25 ml), with cooling, followed by addition of methanol (100 ml), again with cooling. The alkaline extracts were back extracted with ether, acidified, extracted with ether and this ethereal solution washed with brine, dried and evaporated to give an orange solid (27.2 g). This crude product was vacuum distilled into three fractions. Fraction 1, distilling between 85-100°/0.01 mm Hg, consisted of 2-naphthol (1.2 g). Fraction 2, distilling between 100-118°/0.01 mm Hg, consisted of 2-naphthol and 1-benzyl-2-naphthol (1.7 g). Fraction 3, distilling between 118-158°/0.01 mm Hg, consisted of 1-benzyl-2-naphthol (21.2, 65%) which solidified on cooling. Recrystallisation from benzene gave white crystals, m.p. 110-111° (lit.,[114] 110-111°).

λ_{max} (MeOH) 259(sh.), 270.5(3.45), 280.5(3.55), 292(3.50), 325(3.22), 336(3.27) nm.

ν_{max} (CCl_4) 3605 and 3540 (free and H-bonded OH).

δ ($CDCl_3$) 6.9-8.1, multiplet, 11H (aromatics), 5.0, singlet, 1H (OH, exchanged with D_2O), 4.45, singlet, 2H ($-C\underline{H}_2-$).

Attempted autoxidation of 1-aralkyl-2-naphthols

Autoxidation of 1-trityl-, 1-diphenylethyl-, and 1-diphenylmethyl-2-naphthol was attempted by vigorously stirring 0.2M solutions of the naphthols, prepared by dissolving 1-trityl-2-naphthol (193 mg), 1-diphenylmethyl-2-naphthol (162 mg) and 1-diphenylmethyl-2-naphthol (155 mg) each in benzene (2.5 ml), under oxygen at 1 atmosphere pressure

in diffuse daylight. Solutions of these three naphthols were stirred under the stated conditions for 40 h. T.L.C. examinations and NMR spectra showed unchanged starting material in each case.

Autoxidation of 1-benzyl-2-naphthol

A solution of 1-benzyl-2-naphthol (501 mg) in benzene (11 ml) was stirred, vigorously, under oxygen for one week. Analytical T.L.C. of the solution showed mainly starting material, R_f 0.3, and other spot, R_f 0.2. Preparative T.L.C. showed three bands which gave 10, 432, and 17 mg of material, in order of increasing polarity. The main component was unchanged 1-benzyl-2-naphthol. The least polar component had the same NMR spectral characteristics as the O-C dimer produced by oxidation of 1-benzyl-2-naphthol with potassium ferricyanide,

δ ($CDCl_3$), 6.4-8.1, multiplet, 20H (aromatics and β-proton of enone), 6.2, doublet, J 10Hz, 1H, 6.1, doublet, J 9Hz (1H), 4.7, singlet, 2H ($Ar-CH_2-Ar$), 3.35, singlet, 2H ($Ar-CH_2-$).

and also the same R_f and colour development with ceric ammonium sulphate solution.

Analytical T.L.C. of the most polar band showed that it contained 1-benzyl-2-naphthol. This was confirmed by the NMR spectrum of the band which was the same as that of the main product of the sodium periodate oxidation of 1-benzyl-2-naphthol and, after the benzylic methylene signal due to 1-benzyl-2-naphthol, δ 4.45, had been subtracted, was also the same as the NMR spectrum of the mixture of ketol isomers obtained by the mild hydrolysis of 1-acetoxy-1-benzylnaphthalen-2(1H)-one. $\delta(CDCl_3)$ 6.6-7.8, multiplet (aromatics, 6.3 doublet, J 9Hz, and 6.1, doublet, J 9Hz (olefinic protons of 2-benzyl-2-hydroxynaphthalen-1(2H)-one), 5.95 doublet, J 10Hz (α-proton of enone system of 1-benzyl-1-hydroxy-naphthalen-2(1H)-one), 4.45, singlet ($-CH_2-$ of 1-benzyl-2-naphthol), 3.0 singlet ($-CH_2-$ from ketol isomers).

ν_{max} (CCl_4) 3605 and 3500 (free and intramolecularly H-bonded OH), 1685 (broad signal due to carbonyl groups) cm^{-1}.

Autoxidation of 1-benzyl-2-naphthol in the presence of $Co(acac)_3$

To a solution of 1-benzyl-2-naphthol (106 mg) in benzene (3 ml) was added cobalt acetylacetonate (23 mg) and the reaction mixture was stirred, vigorously, under oxygen for one week. Preparative T.L.C. of the product showed three bands which gave 31 mg, 28 mg, and 44 mg in increasing order of polarity. The most polar band had the same T.L.C. characteristics and NMR spectrum as 1-benzyl-1-(1-benzyl-2-naphthyloxy)naphthalen-2(1H)-one. The next, more polar band, was 1-benzyl-2-naphthol, on T.L.C. and NMR spectral evidence. The most polar band was found on analytical T.L.C. to contain 1-benzyl-2-naphthol and the NMR spectrum indicated that it also contained a mixture of ketol isomers.

Oxidation of 1-benzyl-2-naphthol with potassium ferricyanide

To a stirred solution of 1-benzyl-2-naphthol (145 mg) in ether (6 ml) was added a filtered saturated solution (1.5 ml) of potassium ferricyanide in 2M sodium hydroxide. After a few minutes crystals began to form. After the mixture had been stirred for 30 min the crude crystalline product was isolated by filtration. The crystals were washed with water, until the washings were colourless, and then with cold ether (2 x 5 ml). T.L.C. of the crystalline product showed one spot, R_f 0.6, different from starting material, R_f 0.32. Recrystallisation from ethyl acetate-light petroleum give 1-benzyl-1-(1-benzyl-2-napthyloxy)naphthalen-2(1H)-one (127 mg, 87%), m.p. 160-162°,

λ_{max} (MeOH) 273(3.75), 284(3.87), 296(3.90), 320(3.89)

ν_{max} (KBr) 1675 (C=O), 1240 and 1075 (aralkyl C-O-C stretch, anti-symmetric and symmetric) cm^{-1}.

δ ($CDCl_3$) 6.4-8.1, multiplet, 20H (aromatics and β-proton of enone), 6.1,

doublet, J 10Hz, and 6.0, doublet, J 9Hz, (α-proton of enone and H(3) of naphthalene ring, but individual assignment not possible), 4.7, singlet, 2H (Ar-CH_2-Ar), 3.35, singlet, 2H (Ar-CH_2-).

m/e 466 (M^+), 233 (M^+-233), 232 (M^+-234).

$C_{34}H_{26}O_2$ requires : C, 87.53; H, 5.62

found : C, 87.33; H, 5.87

Attempted preparation of 1-benzyl-1-hydroxynaphthalen-2(1H)-one

To a stirred solution of 1-benzyl-2-naphthol (234 mg) in aqueous acetate (water, 15 ml; acetone 10 ml) was added sodium periodate (428 mg) in water (2 ml). The progress of the reaction was monitored by T.L.C. After the solution had been stirred at room temperature for 4 h, T.L.C. showed mainly one spot with the same R_f as starting material but a distinctive maroon colour when treated with ceric ammonium sulphate compared with the grey/brown spot due to starting material. Preparative T.L.C. gave a colourless oil (175 mg) which would not crystallise. Analytical T.L.C. showed that the oil contained 1-benzyl-2-naphthol. This was confirmed by the NMR spectrum which also indicated that the oil contained a mixture of ketol isomers. The UV spectrum of the oil,

λ_{max} (CCl_4) 272, 282, 294, 317 nm

was consistent with the oil being a mixture of 1-benzyl-2-naphthol, 1-benzyl-1-hydroxynaphthalen-2(1H)-one and 2-benzyl-2-hydroxynaphthalen-2(1H)-one. The oil showed the same solution IR spectrum as the most polar band from preparative T.L.C. of the products from autoxidation of 1-benzyl-2-naphthol.

Preparation of 1-acetoxy-1-benzylnaphthalen-2(1H)-one

To a stirred solution of 1-benzyl-2-naphthol (234 mg) in a mixture of glacial acetic acid (10 ml) and acetic anhydride (2 ml) was added freshly crystallised lead tetra-acetate (670 mg). T.L.C. of the reaction

mixture after 30 min showed mainly one spot, R_f 0.5, different from starting material, R_f0.33. The reaction mixture was treated with ethylene glycol, followed by aqueous sodium bicarbonate. The aqueous layer was saturated with sodium chloride and extracted with ether (3 x 25 ml), the ethereal fractions were combined, washed with brine and dried and evaporation of solvent followed by crystallisation from methanol gave 1-acetoxy-1-benzylnaphthalen-2(1H)-one (260 mg, 89%), m.p. 99.5-101.5°,

λ_{max} (MeOH) 239(4.08), 312(3.88) nm.

ν_{max} (CCl_4) 1755 (ester C=O), 1680 (enone C=O)

δ ($CDCl_3$) 6.5-7.5, multiplet, 10H (aromatics and β-proton of enone), 6.05, doublet, J 10Hz, 1H (α-proton of enone), 3.2, singlet, 2H ($-CH_2-$), 2.1, singlet, 3H (-Me)

m/e 292 (M^+), 249 (M^+-43)

$C_{19}H_{16}O_3$ requires : C, 78.06; H, 5.52

found : C, 78.2 ; H, 5.73

Attempted preparation of 1-benzyl-1-hydroxynaphthalen-2(1H)-one

To a stirred solution of 1-acetoxy-1-benzylnaphthalen-2(1H)-one (114 mg) in ethanol (5 ml) was added sodium carbonate (212 mg) in water (2 ml). After the reaction mixture had been stirred at 25° for 6 h it was extracted with ether, the ethereal fractions combined, dried, and the solvent evaporated. The NMR spectrum of this material indicated that it was unchanged starting material. This was dissolved once more in ethanol and treated with sodium carbonate, as before, for 2 h at 40°, after which the NMR spectrum showed mainly starting material but also evidence for ketol rearrangement. The mixture was heated at 50° for 2 h.

The NMR spectrum of the product obtained showed that it was a mixture of ketol isomers and that no starting material remained. Although integration of the signals in the NMR spectrum suggested that ketol rearrangement had occurred to a significant extent, the UV spectrum

λ_{max} (MeOH) 314 nm

was typical of a 1-alkyl-1-hydroxynaphthalen-2(1H)-one.

Attempted preparation of 1-phenylmethylenenaphthalen-2(1H)-one

To a stirred solution of 1-benzyl-2-naphthol (234 mg) in methanol (2.5 ml) was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (223 mg). The mixture was stirred under nitrogen for 1 h and T.L.C. examination of the reaction mixture showed five main spots poorly resolved from one another and also a lot of polar material at the base line. The reaction mixture was cooled and a precipitate formed. Recrystallisation of this material from chloroform-light petroleum gave 1-benzyl-1-(1-benzyl-2-naphthoxy)naphthalen-2(1H)-one (51 mg, 22%), m.p. 160-162°. The UV, IR, and NMR spectra of the product were the same as those of the O-C dimer made by ferricyanide oxidation of the naphthol and no depression was observed when a mixed melting point determination was done.

m/e 466 (M^+).

SDA reduction of 1-formyl-2-naphthol[99]

To a stirred solution of 1-formyl-2-naphthol (25.8 g) in dry xylene (300 ml) at 0° under nitrogen was added sodium dihydrobis(2-methoxyethoxy)-aluminate (SDA) (100 ml of a 70% benzene solution). Another portion of xylene was added (180 ml) and the benzene was distilled off. The temperature of the reaction mixture was raised to 140° and held there for 3 h. T.L.C. examination after 1 h showed three spots, R_f 0.5 (same as authentic 1-methyl-2-naphthol), 0.3, and 0.2. The spot, R_f 0.2, diminished with continued heating but spot, R_f 0.3, which developed a characteristic pink colour on treatment with ceric ammonium sulphate solution, increased in size relative to the spot, R_f 0.5. More SDA (50 ml) was added and the mixture was refluxed for 2 h without any effect. The mixture was cooled to 0°, diluted with ether (400 ml) and decomposed with a 20% solution of sulphuric acid, again, with cooling. The organic layer was separated and

the aqueous layer extracted with ether (3 x 100 ml). The combined ethereal fractions were washed with brine and dried and the solvent was evaporated to give crystals and a red/brown oil. Subsequent recrystallisation gave, on the evidence its spectral characteristics and by comparison with the product obtained from the reduction of 1-formyl-2-napthol with sodium borohydride, 1-hydroxymethyl-2-naphthol (22.2 g, 85%) m.p. 192-196° with decomposition (lit.[99] m.p. 192-193°), λ_{max} (MeOH) 269(sh.), 280.5(3.70), 291.5(3.65), 324(sh.), 336(3.53) nm ν_{max} (Nujol) 3330 (H-bonded OH) cm^{-1}. No carbonyl.
δ (d_6-acetone) 9.0, broad singlet (OH, exchanged with D_2O), 8.2-8.6, multiplet (aromatic), 6.9-7.9, multiplet, (aromatics), 4.95, singlet ($-CH_2-$), 3.2, broad singlet (OH, exchanged with D_2O)
m/e 156 (M^+-18).

The integration of the NMR spectrum showed a ratio of 1:5 for the aromatic protons, consistant with six aromatic protons with one of them a peri-proton, but the integral of the benzylic methylene is only half the value it should be by comparison.

This reduction with SDA was repeated with the same outcome.

Reduction of 1-formyl-2-naphthol with sodium borohydride

To a stirred solution of 1-formyl-2-naphthol (172 mg) in aqueous sodium hydroxide (25 ml) was added sodium borohydride (80 mg) in water. The progress of the reaction was monitored by T.L.C. and after 30 min there were three spots, R_f 0.5, 0.3, and 0.2. The spot, R_f 0.5, developed a pink colour with ceric ammonium sulphate solution. The reaction mixture was acidified, extracted with ether (4 x 50 ml), the combined ethereal fractions were washed with brine and dried, and evaporation of the solvent gave 1-hydroxymethyl-2-naphthol (159 mg, 91%), m.p. 192-195°, with decomposition. The NMR spectrum of this compound and the inconsistant integral were the same as those of the product from the SDA reduction and a mixed melting point determination of the two showed

no depression.

Preparation of 1-morpholinomethyl-2-naphthol[101a]

To a stirred solution of 2-naphthol (28.9 g) in 95% ethanol (300 ml) at room temperature was added firstly, morpholine (18 ml) and then formalin (16 ml). After 3 h the reaction mixture was cooled and the product crystallised. Recrystallisation gave 1-morpholinomethyl-2-naphthol (44.2 g, 90%), m.p. 114.5-115.5° (lit.[101a] m.p. 114.5-115°) from ethanol,

δ ($CDCl_3$) 10.5-11.3, broad singlet, 1H (OH exchanged with D_2O), 6.9-8.0, multiplet, 6H (aromatics), 4.1, singlet, 2H (benzylic methylene), 3.8, multiplet, 4H (protons α to O in morpholine ring), 2.65, multiplet, 4H (protons β to O in morpholine ring).

Hydrogenolysis of 1-morpholinomethyl-2-naphthol with Raney-Ni alloy

To a stirred solution of 1-morpholinomethyl-2-naphthol (34.27 g) in 10% aqueous potassium hydroxide (350 ml) heated to reflux was added Raney-nickel alloy (172 g) in small portions. The Raney-Ni alloy was added over 6 h. The reaction mixture was filtered, hot, through a celite pad. Care was taken to keep the celite pad wet, since the nickel residue is pyrogenic, and the residue was washed with water. The metal was destroyed by careful treatment with dilute nitric acid. T.L.C. of the product showed four spots, R_f 0.6, 0.5, 0.3, and 0.15. Authentic 1-methyl-2-naphthol had an R_f 0.5 and 1-morpholinomethyl-2-naphthol an R_f 0.3. However, the colour of authentic 1-methyl-2-naphthol on treatment with ceric ammonium sulphate solution was not matched by anything in the reaction mixture. The filtrate was acidified with dilute hydrochloric acid and the aqueous layer extracted with ether (4 x 150 ml). The combined ether fractions were washed with brine and dried, and the solvent evaporated to give a crystalline product, R_f 0.6. Recrystallisation of the crude product from ethyl acetate-light petroleum

gave 5,6,7,8-tetrahydro-1-methyl-2-naphthol (14.8 g, 64%), m.p. 113-114° (lit.[103] m.p. 113.5-114.5°),

λ_{max} (MeOH) 280(3.14), 287(sh.) nm

ν_{max} (Nujol) 3250 (H-bonded OH), 805 (2 adj. arom. H) cm^{-1}.

No signal due to 4 adj. arom. H.

ν_{max} (CCl_4) 3605 (free OH), 2980-2820 cm^{-1} (aliphatic C-H stretch, more intense, relative to the aromatic C-H stretch, than the corresponding signal in authentic 1-methyl-2-naphthol).

δ ($CDCl_3$) 6.4-7.0, multiplet, 2H (aromatic), 4.4, singlet, 1H (OH, exchanged with D_2O), 2.4-2.9, multiplet, 4H (protons α to aromatic ring), 2.1, singlet, 3H (-Me), 1.5-2.0, multiplet, 4H (protons β to aromatic ring).

m/e 162 (M^+)

The only literature preparation of this phenol involves reduction of 1-methyl-2-naphthol in ethanol with gaseous hydrogen and Raney-nickel catalyst at 110° and 100 atmospheres pressure.[103]

Preparation of 1-methyl-2-naphthol by Pd-charcoal reduction of 1-morpholinomethyl-2-naphthol

To a solution of 1-morpholinomethyl-2-naphthol (22.3 g) in methanol (3 l) was added 5% palladium-charcoal (1.77 g) and the mixture was stirred vigorously under hydrogen. After 6 h, T.L.C. showed only one spot with the same R_f as authentic 1-methyl-2-naphthol, 0.5. The catalyst was removed by filtration, and evaporation of the solvent led to crystallisation. The crystalline product was washed with water to remove morpholine and recrystallisation from methanol-water gave 1-methyl-2-naphthol (12.3 g, 84%), m.p. 110-112° (lit.[99] 109-109.5°),

δ ($CDCl_3$) 6.8-8.0, multiplet, 6H (aromatics), 5.4, singlet, 1H (OH, exchanged with D_2O), 2.5, singlet, 3H (-Me).

Over-reduction in this reaction can be avoided by monitoring the progress

of the reduction by T.L.C. and by removing the catalyst by filtration when no starting material can be detected.

Over-reduction of 1-morpholinomethyl-2-naphthol with Pd-charcoal catalyst

To a solution of 1-morpholinomethyl-2-naphthol (4.88 g) in methanol (500 ml) was added 5% palladium-charcoal (400 mg) and the mixture was stirred vigorously under hydrogen. T.L.C. examination of the mixture after 3 h showed that the hydrogenolysis was complete. The reaction vessel was isolated from the hydrogen resevoir but was left unstirred overnight under the remaining hydrogen. Evaporation of the solvent gave crystals in a brown oil. The crude product was recrystallised first from methanol and then from light petroleum to give naphthalene (0.9 g, 35%)
m.p. 79-80° (lit., 80.2°),
λ_{max} (MeOH) 247(sh.), 257(sh.), 266(3.66), 275(3.70), 283(3.54), 285.5(3.54) nm
δ ($CDCl_3$) 7.3-8.2, multiplet (aromatics)
m/e 128 (M^+)

Preparation of 1-hydroxy-1-methylnaphthalen-2(1H)-one

1) Chromium trioxide/acetic acid oxidation[42]

To a stirred solution of 1-methyl-2-naphthol (2 g) in glacial acetic acid (75 ml) was added chromium trioxide (2 g) in glacial acetic acid (70 ml), slowly and with cooling. The solution, at this point dark blue, was stirred at room temperature for 36 h, by which time it was dark green. Most of the acetic acid was evaporated at reduced pressure and water (150 ml) was added. The aqueous layer was extracted with ether (3 x 50 ml), the combined ethereal fractions were washed first with aqueous sodium bicarbonate solution, then with brine and dried. Evaporation of the solvent gave a brown oil. A few drops of ethyl

acetate were added to the crude product which yielded crystals on cooling. Recrystallisation from chloroform-light petroleum gave 1-hydroxy-1-methylnaphthalen-2(1H)-one (1.11 g, 50%) m.p. 86-88° (lit.[43] m.p. 88-89°),

δ ($CDCl_3$) 7.0-7.7, multiplet, 5H (aromatics and β-proton of enone), 6.1, doublet, J 10Hz, 1H (α-proton of enone), 4.3-5.0, broad singlet, 1H (OH, exchanged with D_2O), 1.5, singlet, 3H (-Me).

2) Peracetic acid oxidation[49]

To a stirred solution of 1-methyl-2-naphthol (4 g) in glacial acetic acid (80 ml) was added a solution containing glacial acetic acid (40 ml), hydrogen peroxide (28%, 40 ml) and concentrated sulphuric acid (0.8 ml). The reaction mixture was stirred for 4 h at room temperature and then poured on to water (200 ml). The aqueous layer was saturated with sodium chloride, extracted with ether (4 x 100 ml), the combined ethereal extracts were neutralised with sodium bicarbonate solution and extracted with aqueous sodium hydroxide (5%; 4 x 50 ml). Re-acidification of the aqueous alkaline extract, extraction of the acidic aqueous layer with ether and evaporation of solvent gave 1-methyl-2-naphthol (0.6 g). The ethereal fraction left after aqueous alkaline extraction was washed with brine and dried and the solvent evaporated to give crystals in an oily matrix. Recrystallisation from chloroform-light petroleum gave 1-hydroxy-1-methylnaphthalen-2(1H)-one (2.39 g, 54%), m.p. 86-88°. The NMR spectrum of the product was the same as that of the product from the chromic acid oxidation and a mixed melting point determination showed no depression.

m/e 174 (M^+), 158 (M^+-16).

Attempted preparation of cis-1-hydroxy-1-methylnaphthalen-2(1H)-one-3,4-epoxide

To a stirred solution of 1-hydroxy-1-methylnaphthalen-2(1H)-one (157 mg)

in benzene (5 ml) was added t-butyl hydroperoxide (108 mg) and molybdenum hexacarbonyl (35 mg). The reaction mixture was refluxed for 8 h, the progress of the reaction being monitored by T.L.C. After this time, one spot with the same R_f as starting material was observed. The NMR spectrum of the product in $CDCl_3$ showed a doublet, δ 3.85, J 4Hz and a doublet, δ 4.1, J 4Hz, suggesting the presence of an epoxide. However, the NMR spectrum also showed evidence for ketol rearrangement, an AB quartet, δ 6.45, J 10Hz, and δ 6.2, J 10Hz, superimposed on a doublet δ 6.15, J 10Hz. There were also three sharp singlets, δ 1.3-1.6, indicating that the product was a mixture of at least three components. Attempts to separate these components by preparative T.L.C. were unsuccessful. The reaction was repeated with the same molar ratio of reactants but with the mixture heated to 60°. The same type of product mixture was obtained.

Preparation of 1-isopropyl-2-naphthol[7]

To a solution of sodium methoxide in methanol, prepared by adding sodium (5.01 g) to anhydrous methanol (145 ml), was added 2-naphthol (31.42 g). When the 2-naphthol had been digested, the methanol was evaporated and redistilled, sodium-dried toluene (50 ml) was added. This, in turn, was evaporated under reduced pressure. This process of addition and evaporation of toluene was repeated four times. The sodium naphthoxide was powdered and toluene (150 ml) was added followed by 2-bromopropane (20 ml). The reaction mixture was refluxed under nitrogen for 30 h. Further portions of the halide (20 ml) were added at four-hourly intervals, the total volume added was 100 ml. The reaction mixture was cooled and water (150 ml) was added. The aqueous layer was extracted with toluene (3 x 50 ml) and the combined organic portions were washed with brine and dried, and the solvent evaporated to give a red oil (40.7 g). The aqueous layer was acidified, extracted with ether,

the combined ethereal fractions washed with brine and dried, and the solvent evaporated to give a dark brown oil (0.4 g), which was shown, by T.L.C., to be mainly 2-naphthol. The red oil from the toluene layer was fractionally distilled. Fraction 1, distilling between 85-98°/0.01 mm Hg (6.97 g) consisted of a mixture of 2-naphthol and 1-isopropyl-2-naphthol. Fraction 2, distilling between 99-102°/0.01 mm Hg (8.04 g) and fraction 3, distilling between 102-105°/0.01 mm Hg (20.75 g) were 1-isopropyl-2-naphthol. All three fractions solidified on standing. Crystallisation of fraction 2 and 3 from benzene gave 1-isopropyl-2-naphthol (26.7 g, 66%) m.p. 72-74° (lit.[7] m.p. 72-74°) δ ($CDCl_3$) 6.5-8.1, multiplet, 6H (aromatics), 4.75, broad singlet, 1H (OH, exchanged with D_2O), 3.85, septet, J 7 Hz, 1H (-C<u>H</u>Me_2), 1.45, doublet, J 7Hz, 6H (-CH(CH_3)$_2$).

A similar reaction was carried out to prepare 1-isopropyl-2-naphthol but the sodium naphthoxide was generated by addition of sodium hydride to a solution of 2-naphthol. In all other respects the reaction conditions were the same. 1-Isopropyl-2-naphthol was obtained in 62% yield.

When magnesium naphthoxide, generated by the addition of CH_3CH_2MgBr in ether at room temperature to a solution of 2-naphthol in toluene, was used in place of the sodium salt, unchanged starting material was identified as the main component of the reaction mixture.

<u>Autoxidation of 1-isopropyl-2-naphthol</u>[7]

A solution of 1-isopropyl-2-naphthol (7.3 g) in benzene (200 ml) was stirred vigorously under oxygen at room temperature in diffuse sunlight for 24 h. Evaporation of solvent led to crystallisation of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one (5.9 g, 69%), 135-137° (lit.[7] m.p. 135-137°), δ ($CDCl_3$) 7.2-7.8, multiplet, 5H (aromatics and β-proton of enone), 6.15, doublet, J 10Hz, 1H (α-proton of enone), 2.1, septet, 1H

($-C\underline{H}Me_2$), 0.85 and 0.8, two doublets each with J 7Hz, total 6H, ($-CH(C\underline{H}_3)_2$).

Attempted esterification of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one

To a stirred solution of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one (1.09 g) in methylene chloride (20 ml) at 0° was added pyridine (0.5 ml). A solution of benzoyl chloride (1.05 g) in methylene chloride (10 ml) was added to the reaction mixture, slowly and with cooling, and the solution was stirred at 0° for 1 h. The reaction mixture was washed with water (25 ml), with 0.5M sulphuric acid (2 x 25 ml), with saturated sodium bicarbonate solution (3 x 25 ml) and lastly with water (2 x 25 ml). The components of the methylene chloride solution were separated by column chromatography using a column packed with alumina and surrounded with a jacket of crushed ice. Elution of the column with methylene chloride and evaporation of the solvent from the eluate gave a crystalline product. Recrystallisation of this gave 1-benzoyloxy-1-isopropoxynaphthalen-2(1H)-one (0.195 g, 11%), m.p. 185-187°,

λ_{max} (EtOH) 285 (3.90) nm

ν_{max} (KBr) 1740 and 1710 cm^{-1}

δ ($CDCl_3$) 7.0-8.2, multiplet, 10H (aromatics and β-proton of enone), 6.35, doublet, J 11Hz, 1H (α-proton of enone), 3.50, septet, 1H ($-C\underline{H}Me_2$), 1.35, doublet, J 7Hz, 3H (-Me), 1.1, doublet, J 7Hz, 3H (-Me).

δ ($CDCl_3$) 7.0-8.2,

m/e 322 (M^+). 279 (M^+-43)

M^+ required for $C_{20}H_{18}O_4$: 322.1205

found : 322.1202

Attempts to prepare the desired peroxyester by reaction of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one with the imidazolide formed by reaction of benzoyl chloride with imidazole in methylene chloride were unsuccessful.

Thermolysis of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one

A solution of 1-hydroperoxy-1-isopropylnaphthalen-2(1H)-one (230 mg) in ethylbenzene (5 ml) was heated until the hydroperoxide decomposed (above 128°). G.C. analysis showed that 2,3-diphenylbutane was formed, by comparison with an authentic sample, indicating a radical pathway for the decomposition.

Preparation of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one[96]

1-Hydroperoxy-1-isopropylnaphthalen-2(1H)-one (3 g) in ethanol (150 ml) was treated with dimethyl sulphide[23] (6 ml). The reaction mixture was stirred for a few minutes then poured into water (250 ml) and cooled. The crystalline product obtained was filtered off, washed with iced water and dried overnight in the vacuum pistol to give 1-hydroxy-1-isopropylnaphthalen-2(1H)-one (2.47, 89%) m.p. 85-88° (lit.[7] m.p. 88-89°).

Treatment of 1-hydroxy-1-methyl and 1-hydroxy-1-isopropylnaphthalen-2(1H)-one with molybdenum hexacarbonyl

Two solutions, one of 1-hydroxy-1-methylnaphthalen-2(1H)-one (130 mg) and molybdenum hexacarbonyl (26 mg) in benzene (4 ml) and the other of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one (150 mg) and molybdenum hexacarbonyl (27 mg) in benzene (4 ml) were refluxed in the same oil bath. After 3 h, the NMR spectra of these two systems both showed ketol rearrangement. In the case of the 1-hydroxy-1-methylnaphthalen-2(1H)-one system integration of the two sharp singlets in the aliphatic region allowed the estimation of the relative contribution of each isomer at four times as much starting material as ketol isomer. The aliphatic region in the case of the 1-hydroxy-1-isopropylnaphthalen-2(1H)-one system was too complicated to allow accurate integration but by careful integration of the region, δ 6-7, containing the superimposed

doublet and quartet, it was found that there was twice as much rearranged material as starting material. After a further 3 h refluxing the 1-hydroxy-1-methylnaphthalen-2(1H)-one system showed approximately three times as much starting material as rearranged product.

Reduction of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one

To a solution of 1-hydroxy-1-isopropylnaphthalen-2(1H)-one (208 mg) in ethanol (10 ml) was added a solution of sodium borohydride (190 mg) in a mixture of ethanol (40 ml) and water (4 ml) at 0°. The reaction mixture was stirred for five minutes at which time T.L.C. examination showed that there was little starting material left. The mixture was left for a further ten minutes and then treated with water (50 ml) and ether (50 ml). The organic layer was separated and the aqueous portion washed with ether (4 x 20 ml). The combined organic fractions were dried and the solvent evaporated to give the diol (185 mg, 90%). The melting point of the crystals obtained by recrystallisation of the crude reaction product from ethyl acetate-light petroleum was 116-119°. Recrystallisation produced crystals which partly melted at 120° but without widespread liquid formation and were converted to either another crystalline modification or another crystalline compound which then melted at 135-138°. On cooling the sample, crystals reformed. These were found to melt at 140-143°. The fact that the melting point went up with the repetition of the melting point determination suggests that the diol is being converted cleanly to some other compound with a higher melting point and that the amount of this compound in the sample increases as the diol is heated. The unheated crystals had the following properties,

λ_{max} (MeOH) 270(3.54) nm

ν_{max} (CCl_4) 3592.5 with a shoulder at 3630 cm^{-1}

δ ($CDCl_3$) 6.8-7.7, a multiplet, 4H (aromatics), 6.3, doublet of doublets, $J_{3,4}$ 10Hz, $J_{2,3}$ 3Hz, 1H (-CH=C<u>H</u>-CHOH-), 5.95, doublet of doublets, $J_{3,4}$ 10Hz, $J_{2,4}$ 2Hz, 1H (-C<u>H</u>=CH-CHOH-), 4.9, multiplet, 1H (-C<u>H</u>OH-), 2.0-2.8, a multiplet ($Me_2C\underline{H}$-) superimposed on a broad singlet (2 x -OH, both exchanged by D_2O), 0.7-1.1, an apparent triplet in the 60MHz spectrum, a double doublet in the 90MHz spectrum, J 7Hz, 6H (-CH($C\underline{H}_3$)$_2$).

δ (d_6-acetone) same as above except 2.8-4.2, broad doublet, 2H (2 x -OH, both exchanged by D_2O), 2.45, septet, J 7Hz, 1H (-C<u>H</u>Me_2).

δ (d_5-pyridine) 7.8-8.2, multiplet, 1H, and 7.0-7.5, multiplet, 3H (aromatics), 6.4, singlet, 2H (-C<u>H</u>=C<u>H</u>-), 6.3, broad singlet, 2H (2 x OH, both exchanged by D_2O), 5.5, singlet, 1H (-C<u>H</u>(OH)-), 3.0, septet, J 7Hz, 1H (-C<u>H</u>Me_2), 0.9-1.5, an apparent triplet, J 7Hz, 6H (-CH($C\underline{H}_3$)$_2$).

m/e 204 (M^+), 161 (M^+-43)

$C_{13}H_{16}O_2$ requires : C, 76.44; H, 7.90

found : C, 76.65; H, 7.83

<u>Attempted epoxidation of the diol with t-BuOOH and VO(acac)$_2$</u>

To a solution of the diol (50.5 mg) and vanadyl acetylacetonate (2.3 mg) in benzene (10 ml) was added t-butyl hydroperoxide (53 mg). t-Butyl hydroperoxide was obtained by extracting Koch-Light pract. (70% + 30% di-t-butyl peroxide) with 15% aqueous potassium hydroxide solution and precipitating the hydroperoxide from the separated aqueous layer by addition of an excess of solid ammonium chloride. The reaction mixture was refluxed for 30 min at which time T.L.C. examination showed three components, none of which were starting material. The NMR spectrum of the crude reaction mixture,

δ ($CDCl_3$) 6.9-8.0, multiplet, 6.3, quartet, J 10Hz, 6.05, doublet, J 10Hz, 4.1, doublet, J 4Hz, 3.95, J 4Hz, 3.0-3.7, broad singlet, 1.7-2.4, multiplet, 0.8-1.7, multiplet,

confirms that there is no starting material, by the disappearance of the signals due to the two olefinic protons, at δ 6.3 and 5.95, and the signal due to the proton attached C(2), at δ 4.9. The fact that this latter signal is not present in the reaction mixture indicated that none of the desired diol epoxide has been formed. Epoxide is, however, present in the mixture. In view of the evidence for ketol rearrangement it is probable that the epoxide is 2-hydroxy-2-isopropyl-naphthalen-1(2H)-one-3,4-epoxide. No further attempts to identify the products of this reaction were made.

Attempted epoxidation of the diol with m-chloroperoxybenzoic acid

1) To a stirred solution of the diol (128 mg) in ether (20 ml) under nitrogen at 0° was added, dropwise, a solution of m-chloroperoxybenzoic acid (178 mg) in ether. T.L.C. of the reaction mixture after 15 h at 0° and after 12 h at room temperature showed mainly starting material. More m-chloroperoxybenzoic acid (80 mg) was added. T.L.C. after a further 12 h at room temperature and, after addition of more peroxyacid (77 mg), after 3 h at 40°, still showed mainly starting material. This was confirmed by the NMR spectrum of the reaction mixture on work-up (treat the crude reaction mixture with 10% sodium sulphite solution until a test with starch-iodide paper is negative, wash the organic layer with sodium bicarbonate solution, then with brine and dry, and evaporate solvent).

2) To a stirred solution of m-chloroperoxyacetic acid (165 mg) in methylene chloride (3 ml) under nitrogen at 0° was added the diol (150 mg) in methylene chloride (7 ml). After 3 h, T.L.C. showed mainly starting material and more peroxyacid (190 mg) was added. After a total of 10 h the NMR spectrum of the reaction product showed that it was starting material.

3) To a stirred solution of m-chloroperoxybenzoic acid (277 mg) in

methylene chloride (5 ml) under nitrogen at room temperature was added the diol (129 mg) in methylene chloride (10 ml). The progress of the reaction was monitored by T.L.C. and after 3 h there was no starting material. There was one less polar component together with some polar material at the base line. After the work-up, the NMR spectrum of the crude product showed that there was no diol or diol-epoxide but that it did contain a mixture of ketol isomers.

Epoxidation of cinnamyl alcohol with m-chloroperoxybenzoic acid

To a stirred solution of cinnamyl alcohol (1.07 g) in methylene chloride (30 ml) at 0° was added m-chloroperoxybenzoic acid (2.22 g). The reaction showed no starting material on T.L.C. examination after 3 h. The NMR spectrum of the cinnamyl alcohol had shown

δ 7.0-7.4, multiplet, 5H (aromatics), 6.0-6.8, multiplet, 2H (-CH=CH-), 4.2, doublet, 2H (=CH-CH_2-), 4.0, broad singlet, 1H (-OH, exchanged by D_2O).

The NMR spectrum of the product showed no olefinic protons, δ 6.0-6.8 but did show a complex multiplet, δ 3.5-4.5, composed of signals due to the epoxide protons, methylene protons and the hydroxyl group. There was no sign of oxidation of the alcohol.

Preparation of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone

Mesitol (2.04 g) in ethanol (150 ml) was treated with technical cerium(IV) oxide (6.01 g) and hydrogen peroxide (28%; 300 ml) and the mixture stirred at reflux for 2 h. T.L.C. of the reaction mixture showed one spot which was not starting material. The mixture was cooled and filtered. Water (1 l) was added to the ethanolic solution which was then extracted with ether (4 x 100 ml). The combined organic fractions were treated with dimethyl sulphide (2 ml). The excess of this volatile compound was easily removed by evaporation. The organic portion was washed with water, to remove dimethyl sulphoxide and dried.

Evaporation of the solvent gave the hydroxycyclohexadienone (1.6 g, 70%) m.p. 45-46° (lit.[115] m.p. 45.5-46°),

δ ($CDCl_3$) 6.7, singlet, 2H (β-protons of dienone) 4.3, singlet, 1H (-OH, exchanged by D_2O), 1.8, singlet, 6H (α-methyl groups), 1.4, singlet, 3H (γ-methyl group).

m/e 152 (M^+), 137(M^+-15), 136(M^+-16), 121(M^+-31).

Preparation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone

1) 2,6-Di-t-butyl-4-methylphenol (668 mg) in ethanol (60 ml) was treated with technical cerium(IV) oxide (1.23 g) and hydrogen peroxide (28%; 30 ml) and the mixture was heated to reflux. T.L.C. examination of the reaction mixture after 45 min showed starting material, R_f 0.85, and one other spot, R_f 0.65. After 90 min only the latter spot was observed. The mixture was cooled and filtered. Water (300 ml) was added to the filtrate which was then extracted with ether (3 x 75 ml). The combined organic fractions were treated with dimethyl sulphide (1 ml), washed with water, and dried. Evaporation of the solvent gave the hydroxycyclohexadienone (502 mg, 70%), m.p. 112-113° (lit.[23] m.p. 112-113°).

δ ($CDCl_3$) 6.6, singlet, 2H (β-protons of dienone), 1.35, singlet, 3H (γ-methyl group), 1.2, singlet, 18H (α-t-butyl groups).

2) Potassium hydroxide (200 mg) in water (0.5 ml) was added to 2,6-di-t-butyl-4-methylphenol (450 mg) in ethanol (5 ml).[15] The solution was stirred vigorously under oxygen and the reaction was monitored by T.L.C. After two days no starting material could be detected. There was a spot with the same R_f, 0.65, as the product from the cerium oxide oxidation but there was a streak of more polar material from the base-line. The solution was poured on to water (70 ml) which was then extracted with ether (3 x 50 ml). The combined ethereal portions were treated with dimethyl sulphide (1 ml), washed

with water, and dried. Evaporation of the solvent gave a brown oil from which the hydroxycyclohexadienone was obtained (223 mg, 46%), m.p. 112-113° and NMR spectrum as given for the product from the singlet oxygen oxidation.

Attempted preparation of 4-hydroxy-2,4,6-tri-t-butylcyclohexa-2,5-dienone

2,4,6-Tri-t-butylphenol (1.32 g) in ethanol (100 ml) was treated with cerium(IV) oxide (2.01 g) and hydrogen peroxide (28%; 50 ml) and the mixture stirred at reflux. After 30 h, T.L.C. of the reaction mixture showed two spots, one with the same R_f as the starting material, 0.8, and another very weak spot at R_f 0.6. The mixture was cooled and filtered. Water (600 ml) was added and the filtrate was extracted with ether (3 x 75 ml). The combined organic fractions were treated with dimethyl sulphide, washed with water, and dried. Evaporation of the solvent gave unchanged starting material.

Attempted epoxidation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone with t-butyl hydroperoxide and $Mo(CO)_6$

To a stirred solution of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (169 mg) in benzene (5 ml) under nitrogen was added molybdenum hexacarbonyl (16.5 mg) and t-butyl hydroperoxide (152 mg) and the reaction mixture was heated to reflux. The progress of the reaction was monitored by T.L.C. and heating was continued for 10 h until no more starting material, R_f 0.55, could be detected. Four other spots R_f 0.8, 0.65, 0.4, and 0.35 were observed. The NMR spectrum of the crude product suggested that epoxide had been formed, δ ($CDCl_3$) 4.15, doublet, J 7Hz, 3.95, doublet, J 7Hz, but examination of the olefinic and aliphatic regions of the spectrum, both of which showed complex multiplets, indicated that the crude product was made up of

several components. Attempts to isolate and characterise the epoxide by preparative T.L.C. were unsuccessful. The thermal stability of a solution of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone in benzene in the presence of molybdenum hexacarbonyl was investigated. 2,6-Di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (109 mg) in benzene (3.2 ml) to which molybdenum hexacarbonyl (10.6 mg) had been added was heated to reflux. The reaction mixture was examined, hourly, by T.L.C. and after 3 h no starting material, R_f 0.55, could be detected but three other spots R_f 0.8, 0.65, and 0.45 were observed. No attempts were made to identify the products of the thermolysis.

Attempted epoxidation of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone with alkaline hydrogen peroxide.

To a stirred solution of 2,6-di-t-butyl-4-hydroxy-4-methylcyclohexa-2,5-dienone (240 mg) in ethanol (10 ml) under nitrogen was added anhydrous sodium carbonate (100 mg) in water (1.5 ml) and hydrogen peroxide (28%. 2 ml). The reaction mixture was examined at intervals by T.L.C. No change was observed after 4 h at 0° nor after 24 h at 25°. More hydrogen peroxide (28%, 2 ml) was added and the mixture was stirred for 24 h at 40°. Since there was still no change, sodium hydroxide (50 mg) in aqueous ethanol and hydrogen peroxide (28%, 2 ml) were added. T.L.C. showed no change after 3 h and the reaction mixture was extracted with ether, the combined ethereal extracts were washed with brine and dried and the solvent evaporated to give unchanged starting material (230 mg), on the evidence of identical NMR spectra.

Attempted epoxidation of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone with alkaline hydrogen peroxide

A stirred solution of 4-hydroxy-2,4,6-trimethylcyclohexa-2,5-dienone

(99 mg) in ethanol (10 ml) was treated with anhydrous sodium carbonate (100 mg) in water (1.5 ml) and hydrogen peroxide (28%, 1 ml) added. The progress of the reaction was monitored by T.L.C. The reaction mixture was stirred for 1 h at each of the following temperatures, 0°, 20°, 40°, 60° and 80°. The solution started to turn brown above 60° but T.L.C. showed mainly starting material with some very polar material at the base line. The reaction mixture was worked-up as in the previous reaction and led to the isolation of unchanged starting material.

Preparation of 4-methyl-1-naphthol[112]

1-Methylnaphthalene (140 g) was treated with concentrated sulphuric acid (140 ml) and the reaction mixture was stirred, initially with cooling and then at room temperature, for 6 h. The reaction mixture was dissolved in water and the unreacted hydrocarbon was separated. The aqueous solution was heated and neutralised by addition of barium carbonate (400 g). Insoluble barium sulphate was removed by filtration and extracted repeatedly with boiling water. On cooling, the initial filtrate and the combined aqueous extracts, gave crystals of the barium salt of the sulphonic acid, (96 g, 33%). This salt (96g) in boiling water (3 l) was treated with sodium sulphate (23.5 g) and boiled for 1 h. The barium sulphate produced was removed by filtration and the filtrate was evaporated to give the corresponding sodium sulphonate (71.3 g, 87%). This was added to potassium hydroxide (350 g) in water (70 ml) which had been heated in a stainless steel beaker until it had become homogeneous and liquid. The reaction mixture was swirled and warmed. There was a very slight effervescence initially and a black oily mass formed on top of the potassium hydroxide after a few minutes. The mixture was cooled, treated with water (2 l), acidified with dilute sulphuric acid, extracted with ether the ethereal fractions combined, washed with brine and dried, and the

solvent evaporated to give a dark brown viscous oil (37.45 g). T.L.C. examination of the crude product showed it to be mainly one component, R_f 0.7 (30% ethylacetate-light petroleum), together with several other more polar species. Fractional vacuum distillation of the oil led to the isolation of three fractions over the boiling point range 115-128°. Unfortunately the stability of the vacuum achieved by the pump was not good and it varied from 0.6 mm Hg initially to 1.1 mm Hg. Combination of these fractions and crystallisation gave 4-methyl-1-naphthol (15 g, 10%), m.p. 84-86° (lit.[112] m.p. 86-87°).
δ ($CDCl_3$) 8.05-8.4, multiplet, 1H, 7.7-8.0, multiplet, 1H, 7.3-7.7, multiplet, 2H (aromatic), 7.0, doublet, J 7Hz, 1H (aromatic), 6.55, doublet, 7Hz, 1H (aromatic), 5.5, singlet, 1H (OH, exchanged with D_2O), 2.5, singlet, 3H, (-Me).

Preparation of 4-hydroxy-4-methylnaphthalen-1(4H)-one

4-Methyl-1-naphthol (2 g) in ethanol (100 ml) was treated with technical cerium(IV) oxide (5.06) and hydrogen peroxide (28%; 62.5 ml) and the mixture heated to reflux. T.L.C. examination showed that no starting material, R_f 0.8, remained and the reaction mixture showed a single spot, R_f 0.55. After the reaction mixture had cooled, cerium(IV) oxide was removed by filtration and the volume of the filtrate reduced by evaporation before addition of water (500 ml) and extraction of the aqueous layer with a mixture (1:1) of ether and light petroleum (5 x 100 ml). The combined organic fractions were treated with dimethyl sulphide (2 ml), washed with water, and dried. Evaporation of the solvent gave 4-hydroxy-4-methylnaphthalen-1(4H)-one (2 g, 90%), m.p. 100-102°.
λ_{max} (EtOH) 229(3.45), 246(3.9), 269(3.82) nm
ν_{max} (CCl_4) 3600 and 3470 (free and intermolecularly H-bonded OH), 1675 (C=O) cm^{-1}.

δ ($CDCl_3$) 7.05-8.0, multiplet, 4H (aromatic), 6.85, doublet, J 10Hz, 1H (β-proton of enone), 6.1, doublet, J 10Hz, 1H (α-proton of enone), 2.95, singlet, 1H (OH, exchanged with D_2O), 1.8, singlet, 3H (-Me).

m/e 174 (M^+), 159 (M^+-15).

$C_{11}H_{10}O_2$ requires : C, 75.84; H, 5.79

found : C, 75.62; H, 5.95

Epoxidation of 4-hydroxy-4-methylnaphthalen-1(4H)-one with alkaline hydrogen peroxide

To a stirred solution of 4-hydroxy-4-methylnaphthalen-1(4H)-one (208 mg) in ethanol (10 ml) was added sodium carbonate (105 mg) in water (1.5 ml) and hydrogen peroxide (28%; 2 ml). T.L.C. examination of the reaction mixture after 30 min showed one spot, R_f 0.5, which developed a different colour from starting material when treated with ceric ammonium sulphate solution. The reaction mixture was extracted with ether (3 x 30 ml), the combined ethereal extracts were washed with brine, and the solvent evaporated to give 4-hydroxy-4-methylnaphthalen-1(4H)-one-2,3-epoxide (148 mg, 60%), m.p. 165-167°,

λ_{max} (EtOH) 253(4.01), 290(3.16) nm

ν_{max} (CCl_4) 3585 (free OH), 1698 (C=O) cm^{-1}

δ ($CDCl_3$) 7.2-8.0, multiplet, 4H (aromatics), 3.8, narrow multiplet, 2H (epoxide protons), 2.7, singlet, 1H (OH, exchanged with D_2O), 1.5, singlet, 3H (-Me).

m/e 190 (M^+), 175 (M^+-15).

$C_{11}H_{10}O_3$ requires : C, 69.46; H, 5.30

found : C, 69.20; H, 5.35

The NMR spectrum of the mother liquors did not show any evidence for the formation of the epoxide of the opposite stereochemistry.

Epoxidation of 4-hydroxy-4-methylnaphthalen-1(4H)-one with m-chloroperoxybenzoic acid

To a stirred solution of 4-hydroxy-4-methylnaphthalen-1(4H)-one (92 mg) in methylene chloride at 0° was added m-chloroperoxybenzoic acid (130 mg). The progress of the reaction was monitored by T.L.C. There was no change after 7 h at 0° or after 24 h at 40° by T.L.C. but the NMR spectrum of the reaction mixture suggested that epoxide was being formed (δ 3.8, narrow multiplet). Another portion of m-chloroperoxybenzoic acid (330 mg) was added to the reaction mixture and the system was refluxed for 28 h. The reaction mixture was treated with 10% sodium sulphite solution, until a test with starch-iodide paper was negative, the organic layer was washed with sodium bicarbonate solution, then with brine and dried and the solvent was evaporated to give 4-hydroxy-4-methylnaphthalen-1(4H)-one-2,3-epoxide (48 mg, 48%) m.p. 165-167°,

ν_{max} (CCl_4) 3585 (free OH), 1698 (C=O) cm^{-1}

δ ($CDCl_3$) 7.2-8.0, multiplet, 4H (aromatic), 3.8, narrow multiplet, 2H (epoxide protons), 2.5, broad singlet, 1H (OH, exchanged with D_2O), 1.5, singlet, 3H (-Me).

m/e 190 (M^+), 175 (M^+-15)

$C_{11}H_{10}O_3$ requires : C, 69.46; H, 5.30

found : C, 69.25; H, 5.48

The NMR spectrum of the combined mother liquors from the recrystallisations of the product from this reaction suggests that there are two other components present since there are three sharp singlets in the aliphatic region, δ 1.5, 1.65, and 1.85. The presence of a narrow multiplet, δ 4.5, suggests that the epoxide of the opposite stereochemistry was also present. NMR analysis of the crude reaction mixture suggests that the isolated epoxide and the second, unisolated,

epoxide are present in the ratio of 3:1. Attempts to separate the components present in the mother liquors by preparative T.L.C. were unsuccessful.

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