A Thesis
entitled
THE ACIDITY OF "HYDROCARBON ACIDS"
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DOCTOR OF PHILOSOPHY
by
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The work described in this thesis is my own, except where otherwise stated, and has not been used in support of an application of any other degree.

It was carried out at the Australian National University (1969-1972), during the tenure of a research scholarship from the Australian National University.

\[ \text{Signature}\]

**SUMMARY**

Part II describes the effect of structure on acidity of hydrocarbons. This includes comparison of the rates of isomerisation of various olefinic hydrocarbons and the study of the mechanism of reductive cleavage of allylic alcohols and esters.

Part III describes the action of base on various cyclohexadienes which involves disproportionations, dehydrogenations and isomerisations. The work is essentially concerned with understanding factors which may alter the nature of products in metal-ammonia or metal-amine reductions. The factors mentioned may lead to unwanted secondary reaction products or may be responsible for inefficiency in reduction. These effects are interpreted in terms of the thermodynamic stabilities or kinetic acidities of the various hydrocarbons.

Part IV describes some carbanionoid reactions of the aromatic system involving "benzyne" intermediates. The effects of substituents on the polar addition of nucleophiles
to 2,3- and 3,4-dehydroanisoles have been studied. Such additions may be controlled by the distribution of electron density in the "benzyne" (kinetically controlled) or may be controlled by the stability of the resulting adduct (thermodynamic).
EXPERIMENTAL SECTION

The following points are relevant to all experimental work described.

M.p. were determined on a Kofler block and are uncorrected. Infrared spectra were taken as a film unless otherwise stated on a Perkin-Elmer 257 spectrophotometer and ultraviolet spectra were measured for ethanol solutions unless otherwise stated, on a Unicam SP800 spectrophotometer. N.m.r. spectra were recorded on a Varian HA-100 spectrometer using deuterochloroform as solvent, and chemical shifts are quoted as $\delta$ (parts per million) downfield from tetramethylsilane as internal standard. Mass spectra were recorded on an A.E.I. MS-902 instrument.

Analytical and preparative g.l.c. were examined on a Varian Aerograph 202-1C instrument, using stainless steel columns (length 6', internal diameter 0.25") with helium as the carrier gas.

The usual work-up procedure involved washing organic extracts with water, then after being shaken with brine, and dried over anhydrous magnesium sulphate, they were concentrated in vacuo.

Liquid ammonia was distilled from sodium before use directly into the reaction vessel.
CHAPTER 1

ACIDITIES OF "HYDROCARBON ACIDS"

This Thesis is concerned with carbanions produced in several ways, by either proton removal, or as intermediates in reduction reactions. It is therefore necessary to consider some of the basic aspects of the subject.

Some organic compounds are known which function as acids in the classical sense, in that a proton is removed from a C-H bond, the resultant conjugate base being known as a carbanion.

\[ \text{C} - \text{H} \iff \text{C}^- + \text{H}^+ \]

Since reactions are known in which protons are abstracted from saturated hydrocarbons and since most organic compounds contain C-H bonds, most organic compounds are potential carbon acids. It follows then that organic compounds can be classified according to their acid strengths, which in turn is related to the base strength of their conjugate bases and, therefore, to the stability of carbanions.

The acid strength of the carbon acids have both thermodynamic and kinetic aspects. Thermodynamic acidity deals with the position of equilibria between acids and their conjugate bases whereas kinetic acidity pertains to the rate at which acids donate protons to bases. Acid-base theory was largely developed in terms of oxygen acids and bases. The rates of proton transfer were so fast that they have only been measured in the 1950's and 1960's with
modern instruments. Thus the concept of kinetic acidity has applied most frequently to carbon acids since the usually relative rates at which they donate protons to bases can be easily measured.

Fundamental to a description of carbanions is a ranking of these anions with respect to their stability. The thermodynamic acidity is related to the equilibrium constant of a reaction such as

$$\text{RH} + \text{R'M} \xrightleftharpoons[K]{\text{K}} \text{RM} + \text{R'H} \quad (M = \text{metal ion})$$  \hspace{1cm} (1)

and the pKa of carbon acids provide a convenient device for measuring carbanion stability. Equilibrium constants for the reaction generally formulated by the equation above have been measured\(^1,^2\) (in ether or cyclohexylamine solvent) and the relative pKa's of a series of carbon acids calculated using the equation (5) based on the definition of pKa.

$$\text{R'M} \xrightarrow[K]{\text{K'}} \text{R'}^- + \text{M}^+$$  \hspace{1cm} (2)

$$\text{RM} \xleftarrow[K]{\text{K}} \text{R}^- + \text{M}^+$$  \hspace{1cm} (3)

$$\text{pKa-pka'} = -\log \frac{[\text{R}^-]}{[\text{RH}]} + \log \frac{[\text{R'}^-]}{[\text{R'H}]}$$  \hspace{1cm} (4)

$$\text{pka-pK'a} = -\log \frac{[\text{RM}]}{[\text{RH}]} + \log \frac{[\text{R'M}]}{[\text{R'H}]}$$  \hspace{1cm} (5)

Equation (1) formulates the equilibrium involved in the metalation reaction and equations (2) and (3) the dissociation constants for the two carbon salts. This led to pKa estimates that reached to cumene (α-position) with a pKa of 37.

The tendency to form carbanions is, not surprisingly, but little marked with aliphatic hydrocarbons for the C-H bond is a fairly strong one and there is normally no
structural feature that either promotes acidity in the hydrogen atom or that leads to significant stabilisation of the carbanion with respect to the original undissociated molecule. For this reason the pKa of the less acidic hydrocarbons was not accessible by the above procedure. The relative acidities of the weaker hydrocarbon acids involved measurements\textsuperscript{3, 4} of the equilibrium constants of equations (6) and (7).

\[
\text{RLi} + \text{R'I} \xrightleftharpoons[K]{K} \text{RI} + \text{R'Li} \quad \text{(6)}
\]

\[
\text{R-Mg}^- + \text{R'-Hg}^- \xrightleftharpoons[K]{K} \text{R'-Mg}^- + \text{R-Hg}^- \quad \text{(7)}
\]

If the carbon-iodine bonds of equation (6) and the carbon-mercury bonds of equation (7) are taken as models for the carbon-hydrogen bonds of the carbon acids, then the acidity scale can be extended to include even such poor acids as cyclohexane. Thus almost all types of organic compound can be ranked as carbon acids.

**Kinetically controlled acid dissociation:** The relative acid strengths discussed so far were obtained when equilibrium had been established between each acid and its conjugate base, that is, when the acidity was thermodynamically controlled. In some synthetic applications for example bromination of ketones, the initial acid dissociation \((k_1, \text{Eq. 8})\) is rate determining and irreversible because the subsequent reaction of the carbanion \((k_2)\) is faster.

\[
\text{X-H} + \text{Base} \xrightleftharpoons[k_1]{k_{-1}} \text{B.H}^+ + \text{X}^- \xrightarrow[k_2]{\text{products}}
\]

Therefore it must be stressed that the position of an acid
on the thermodynamic scale may not coincide with its position as determined by the relative ease of proton abstraction (kinetically controlled scale). Pearson and Dillon\(^5\) have correlated the strengths of many acids on the two scales. Diethyl malonate ionises \((k_1)\) at about one thousand times the speed of nitro-ethane \((k_1)\) in water yet it is a far weaker acid on the thermodynamic scale \((K_a)\):

\[
\text{EtO}_2\text{C-CH}_2\text{-COOEt} \rightleftharpoons \frac{k_1}{k_1} (\text{EtOOCC})_2\text{CH}^- + \text{H}_3\text{O}^+
\]

\[
\text{CH}_3\text{-CH}_2\text{-NO}_2 \rightleftharpoons \frac{k_1}{k_1} \text{CH}_3\text{-CH}-\text{NO}_2^- + \text{H}_3\text{O}^+
\]

\[
\frac{k_1}{k_{-1}} = K_a = \frac{k_1}{k_{-1}}
\]

Diethyl malonate \(2.5 \times 10^{-5}\) \(5 \times 10^8\) \(5.0 \times 10^{-14}\)

Nitroethane \(3.7 \times 10^{-8}\) \(1.5 \times 10\) \(2.5 \times 10^{-9}\)

Kinetic acidity is usually measured by following base-catalysed hydrogen deuterium exchange between a carbon acid and an oxygen or nitrogen acid of the medium. These rates are generally much easier to measure than the dissociation constants of the carbon acids. The rates of exchange of very non-acidic compounds such as cyclohexane and cyclohexylamine (catalysed by cesium cyclohexylamide), have been measured.\(^6\)

**Relationship between thermodynamic and kinetic acidities**

The relationship between thermodynamic and kinetic acidity is given by the equation\(^7\):

\[
\log k_A = \alpha_A \log K_A + \log G_A
\]

\((k_A = \text{rate constant}, K_A = \text{dissociation constant}, \alpha_A \text{ and } G_A \text{ are constants})\)
This relationship is obeyed for oxygen acids only where there is similarity of structure. Therefore, among carbon acids, where there is much greater diversification of structure, the relationship is only partially successful. The best values for $\alpha_A$ have ranged between 0.4 and 0.6, therefore a change of one pKa unit corresponds to about 2 powers of 10 change in rate constant for proton removal.

Thermodynamic and kinetic acidities often run parallel - the more exothermic the reaction the faster it is, given the correct type of transition state. This makes it possible to base some qualitative arguments about acidities (kinetic) by considering the stabilities (energy levels of the anions) (see chapter II and chapter III).

**Substituent Effects:** The data for the acidity scale of carbon acids in water show that the following groups can be arranged in the following order with respect to their ability to acidify carbon hydrogen bond:

$$\text{NO}_2 > \text{CO} > \text{SO}_2 > \text{COOH} > \text{COOR} > \text{CN} \sim \text{CONH}_2 > X > H > R$$

Such an effect is found to operate in base-catalysed cleavage of some ethers and is discussed further later (See IV.2). The order above is different from that obtained for the ability of the same substituent to acidify the $\text{O-H}$ bond:

$$\text{SO}_2 > \text{NO}_2 > \text{COOH} \simeq \text{CN} > \text{CO} > X$$

The effect on carbon acidity of accumulating several of the same acidifying substituents on the same carbon atom are not additive. The departure appears greatest for the most strongly acidifying substituent, the nitro group.
The inability of all atoms to occupy the same plane in the anion (for steric reasons) appears responsible. Through the base-catalysed hydrogen-deuterium exchange in potassium amide-ammonia base-solvent system, Shatenshtein and co-workers\textsuperscript{8} have accumulated many relevant points concerning the kinetic acidity of weak hydrocarbon acids. Saturated hydrocarbons can behave as proton donors and the degree of substitution at carbon by other carbon affects the acidity of the attached hydrogens. The following order of acidity is obtained:

\[ H_2 > CH_4 > CH_3CH_3 > (CH_2)_6 > (CH_3)_3CH \text{ (methine hydrogen)} \]

and this is the order predicted on the basis of electron-releasing capacity of C-C bond as compared with C-H bond. Carbanion stability, which correlates with carbon acidity seems to decrease as hydrogen attached to the carbanion is successively substituted with alkyl groups.

Allylic hydrogens are shown\textsuperscript{9} to be exchangeable much more readily than vinylic hydrogens. With allylic and benzylic "acids" the acidity is related to the difference in \( \pi \) delocalisation between the acid and the anion. This difference is large and acidity is high compared with saturated hydrocarbons where it is virtually non-existent. Vinylic hydrogens, however are exchangeable by multiple allylic rearrangement.

\[
\begin{align*}
CH=CH-CH_3 & + KND_2 \rightarrow (CH_2=CH-CH_2 \rightleftharpoons CH_2-CH=CH_2) \\
CH_2=CH-CH_2D & \rightarrow (CH_2=CH-CHD \rightleftharpoons CH_2-CH=CHD) \\
(CH_2=CH-CHD_2 & + CH_2D-CH=CHD) \rightarrow \text{ etc.}
\end{align*}
\]
Substitution of the vinyl hydrogens of propene with methyl groups decreases the rate of exchange of the allylic hydrogens the decrease being greater, the greater the number of methyl groups.

It was found that naphthalene exchanges 10 times faster at the α-position and 4 times faster at the β-position than benzene. Further, it was found that methyl groups on a benzene ring depress the rate of exchange of the ring. Electron-releasing effect and steric inhibition of the derived carbanion are probably responsible for the trends. The relative rates of hydrogen isotopic exchange of arylalkanes show that the following compounds can be arranged in order of the acidity at the α-position:

\[ C_6H_5CH_3 > C_6H_5CH_2CH_3 > C_6H_5CH(CH_3)_2 \]

This is expected on the basis of electron-releasing character of a methyl group.

**Medium Effects:** Because of the large solvation energies involved in ionisation of a carbon acid, both thermodynamic and kinetic acidities vary markedly with solvent type. For example, Cram and others found that the rates of racemisation of 2-methyl-3-phenylpropionitrile reflect the rates of carbanion formation. With potassium methoxide as base, the rate in 1.5% methanol-98% dimethylsulphoxide is 10⁷ times the rate in pure methanol. The greatly enhanced activity of the methoxide anion in dimethylsulphoxide compared to methanol reflects that the anion is hydrogen-bonded in the latter solvent. When a methoxide anion is turned into a methanol molecule by proton abstraction from the 2-position.
of 2-methyl-3-phenylpropionitrile, the hydrogen bond must be partially broken, a process that raises the energy of the transition state. The activity of the hydroxide anion was found to approach that of triphenylmethyl anion at low concentrations of water in dimethylsulphoxide\textsuperscript{14}. A carbon acidity scale in dimethylsulphoxide\textsuperscript{15} based on the water system showed that the pKa's of the carbon acids were lower than in the non-polar solvents (ether\textsuperscript{1}, cyclohexylamine\textsuperscript{2}). These differences in pKa are probably associated with differences in the states of the anions. In the non-polar solvents the anions are undoubtedly ion-paired, whereas in dimethylsulphoxide, the ion pairs are probably at least partially dissociated.

**Reactivities of mesomeric carbanions**

(a) **Isomerisation by proton transfer:**

The prototropic rearrangement of a double bond has been carried out with a number of strong basic reagents including KNH\textsubscript{2} in NH\textsubscript{3}\textsuperscript{16,17}, LiNHCH\textsubscript{2}CH\textsubscript{2}NH\textsubscript{2}\textsuperscript{18}, organosodium\textsuperscript{19} and bases in dimethylsulphoxide\textsuperscript{20}.

\[
\begin{align*}
\text{C} &= \text{C} - \text{C} + \text{B}^\ominus \overset{\text{H}}{\longrightarrow} \text{C} &= \text{C} - \equiv \text{C} + \text{HB} \overset{\text{H}}{\longrightarrow} \text{C} &= \text{C} = \text{C} + \text{B}^\ominus \\
\text{C} &= \text{C} - \equiv \text{C} + \text{B}^\ominus \overset{\text{H}}{\longrightarrow} \text{C} &= \text{C} = \equiv \text{C} + \text{HB} \overset{\text{H}}{\longrightarrow} \text{C} &= \text{C} = \text{C} + \text{B}^\ominus
\end{align*}
\]

Such rearrangements are frequently wholly or partially intramolecular\textsuperscript{21,22}.

A suggested mechanism\textsuperscript{23} for the intramolecular route in mono-olefins involves a transition state such as
In extended anions (e.g. from polyenes), there is little intramolecularity\textsuperscript{23}. The higher the dielectric constant (e.g. DMSO) the more a free ionic mechanism is involved.

When isomerisations occur to give two isomers, the kinetically controlled one is predominantly that with H \textit{cis}, e.g.\textsuperscript{24}

This gradually converts into the thermodynamic mixture of \textit{cis} and \textit{trans}. But-1-ene gives initially \textit{trans}:\textit{cis} but-2-ene (1:47) compared with the equilibrium ratio of (4:1). One explanation given is the more favourable dipole interactions in the anion leading to the \textit{cis} isomer\textsuperscript{25}.

The rate of isomerisation\textsuperscript{26} of olefins in DMSO-BuO is

\[
\begin{align*}
\text{CH}_2=\text{CH} & > \text{Ph} > \text{H} > \text{Me} > \text{Et} > \text{C}_3\text{H}_7 > \text{iC}_3\text{H}_7 > \text{t.Bu}.
\end{align*}
\]

Straight chain groups are in order of inductive effects but in branched chain, steric inhibition of anion solvation is probably important.

The transition state is largely carbanionic and attached substituents approach a planar configuration, maximising electron delocalisation. Angle strain in some cyclic systems partially inhibits such delocalisation\textsuperscript{27}.

Eventual equilibrium mixtures\textsuperscript{24} are close to thermodynamically calculated ones and more highly substituted double bonds predominate e.g. 2-methyl-pent-2-ene (80%).
2-methyl-pent-1-ene (10%), 4-methyl-pent-1-ene (1%).

Conjugative effects are more important, e.g. propenyl-benzene (10^{-3-4}) over allylbenzene but ring systems may produce other effects due to conformations, reducing differences^{28}.

More discussion on the isomerization of a double bond is reserved for a later section of this thesis (II.1).

(b) Protonation of allylic anions: Hughes and Ingold^{29} stated that the kinetic protonation of a mesomeric anion tends to give the thermodynamically least stable and most acidic isomer. The cyclohexadiene system has been examined^{30}. The 1,3-predominates over the 1,4- in base-catalysed equilibrium (2.2:1) (t-amyl oxide). Using D labelled solvent the interconversion (at low conversions) gives a D incorporation of 8:1 either way. The least stable isomer is produced 8 times as fast as the stable isomer in protonation of the carbanion.

\[ \frac{k_2}{k_1} = 8 \quad \text{and} \quad \frac{k_1}{k_2} = \approx 0.05 \]

In the case of \( \text{PhCHMeCH}=\text{CH}_2 \rightarrow \text{PhCMe}=\text{CHMe} \), however^{31}, protonation to Me is 20 x reprotonation in the benzylic position. Ionisation of the starting material is 10-100 x that of the conjugated product. The least stable isomer loses a proton very rapidly, but the anion is most rapidly protonated to give the stable isomer in this case (t.BuOH). Such cases can be related to the
energy profile of the reaction, involving the levels of stable and unstable isomers, and the anion, and the highest of the activation energy for the protonation deprotonation reactions. The simple Ingold rule therefore does not always apply. (See chapter II and III for further discussion.)

c (c) Alkylation of allylic carbanions: In 1947 Birch clearly distinguished between the results of reversible and irreversible additions of protons to mesomeric anions pointing out that, with the former, "the product is the thermodynamically stable isomer, but this is not necessary or even usually true for non-reversible reactions" (see above).

Alkylation does not always behave like protonation and would not be expected to because of differing natures of the transition states. (See III.2). Unlike protonations C-alkylations are virtually always irreversible and therefore kinetically controlled. Comparisons must be made therefore with kinetically controlled products of protonation. In some cases the positions are the same, e.g. the addition of proton or methyl group to the salt derived from 2,5-dihydroanisole was found to take place in the 2-position, ortho to the methoxy group. However in others, the positions may be different (see chapter III). O-alkylation is frequently reversible unlike C-alkylation.

Relative stability of Olefins

The factors governing the relative thermodynamic stabilities of olefins particularly dihydrobenzenes and hexahydronaphthalenes is worth mentioning in view of the
results of experiments described later (III.1).

A well recognised factor affecting alkene stability is the degree of substitution by alkyl groups; although there is considerable disagreement as to the cause of the effect, its magnitude is known to be about 2-4 kcal/mole.\textsuperscript{35} An equilibrium mixture of the hexahydronaphthalenes (1)-(4) below was found\textsuperscript{30} to contain (1) 53.7%; (2) 25.2%; (3) 14.1% and (4) 6%.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{hexahydronaphthalenes.png}
\end{figure}

Taking statistical factors into account it was found that (2) and (3) were favoured in isomerisations by factors of 2 over (1) and (4). The percentages showed that other hexahydronaphthalenes were less stable than (1) by 1.31 (2); 1.85 (3); 1.93 (4) kcal/mole.

It was found that transoid dienes are more stable than cisoid ones with the same degree of alkyl substitution by about 2-4 kcal/mole.\textsuperscript{30} Diene (1) is more stable than (3) by 1.84 kcal/mole and more stable than (5) by at least 3.6 kcal/mole. The compound (2) is more stable than (6) by at least 2.9 kcal/mole. There are cases in which transoid dienes have been shown to be more stable (qualitatively) than cisoid dienes with more alkyl substituents. e.g. (7) is more stable\textsuperscript{36} than (8) and (9) is more stable\textsuperscript{37} than (10).

It was found that 1,4-cyclohexadienes (4) and (11) were essentially of the same stability as the corresponding
The diene (12) was found to be only 0.07 kcal/mole more stable than (11) at 95°. In acyclic systems and cyclooctadienes, the conjugated isomer was found more stable than the unconjugated isomer by several kcal/mole. This was explained as being due to delocalisation and/or hybridisation. A stabilising feature of about 2 kcal/mole present in 1,4-cyclohexadienes and absent in other 1,4-dienes is responsible for these trends. The stabilisation in 1,4-cyclohexadiene is probably due to interaction between the double bonds in what has been suggested as the most stable conformation, the π electrons of the double bonds are quite close on one side of the ring. A similar effect has been suggested in cycloheptatrienes.

**Hydrogenolysis of allylic and benzylic alcohols and esters**

It was early pointed out that ready hydrogenolysis of allylic alcohols could only be achieved if the intermediate mesomeric anion contains a CH₂ or CHAr at one or other end (not necessarily at the point where the OH was sited), and that this could be correlated with the
"acidity" of the conjugate hydrocarbon acid.

The reductive cleavage was interpreted as involving a mesomeric anion intermediate and from the studies of effects of substitution on the rate of reductive fission, the formation of the transition state was considered to favour addition of 2 electrons.

\[ C\equiv C - C\equiv O H \xrightarrow{2e} \left( \begin{array}{c}
\text{C} \\
\text{C}
\end{array} \right) + \text{OH} \xrightarrow{H^+} \left( \begin{array}{c}
\text{C} \\
\text{C}
\end{array} \right) \]

As will be pointed out later (II.3), a one electron addition transition state is probably more reasonable.

\[ C\equiv C - C\equiv O H \xrightarrow{1e_{\text{slow}}} \left( \begin{array}{c}
\text{C} \\
\text{C}
\end{array} \right) + \text{OH} \xrightarrow{1e_{\text{fast}}} \left( \begin{array}{c}
\text{C} \\
\text{C}
\end{array} \right) \]

By conversion of the OH above into a group which gives a more stable anion, e.g. OAc, reduction is greatly facilitated and in all cases hydrogenolysis occurs. The ester group probably provides an easier entry for the electron (see chapter II, section 3).

In these reductive cleavages of allylic compounds, two products were usually obtained, one with a double bond in the original position the stereochemistry of which was unchanged. The new double bond was reported to be found in both cis and trans configurations, the latter predominating. Further examinations into the stereochemistry of such products have been made in chapter II of the thesis.

Reduction of benzyl alcohol and methoxy-benzyl alcohols showed that p-methoxybenzyl alcohol underwent minimal hydrogenolysis while ortho-OMe had no effect in inhibiting hydrogenolysis. Further investigations
into the effects of these substituents are also included in the later sections of the thesis (chapter II, section 3).

Reduction of conjugated double bonds

The reduction of carbon-carbon unsaturated systems is possible when the multiple bonds are conjugated, because the charges are stabilised by resonance. Isoprene \( \text{CH}_2=\text{CMe} \cdot \text{CH}=\text{CH}_2 \) is reduced by sodium in ammonia through the dianion \( \text{CH}_2-\overset{\text{C}}{\text{Me}}-\overset{\text{CH}}{\text{CH}}-\overset{\text{CH}_2}{} \). High resonance energy as in the benzene ring may make reduction difficult. Fused benzene rings are more easily reducible not only because the resonance energy for a given ring is lower but because the charge can be distributed over the whole molecule. Conjugation with aromatic systems has a stabilising effect e.g. \( \text{PhCH}=\overset{\text{CH}}{\text{Ph}} \rightarrow \overset{\text{Ph}}{\text{CH}}=\overset{\text{CH}}{\text{Ph}} \rightarrow \text{PhCH}_2 \cdot \text{CH}_2 \cdot \text{Ph} \).

The effects of substitution on the reduction of an unsaturated system are somewhat more complicated than the fission reactions already considered because the two carbon atoms remain attached to each other. Even with the addition of one electron to give an anion radical, it is clear that the essential step is the addition of a negative charge, so the ease of reduction should be affected in the same way. Groups which tend to charge the conjugated system negatively such as alkyl groups, lower the ease of reduction; the methoxy groups in a benzene ring can exercise either activating or deactivating influence according to its position: 1-methoxy-naphthalene reduces in the unoccupied ring, 2-methoxy-
naphthalene in the occupied ring. The effects of the methoxy group in an aromatic ring conjugated with a double bond has been examined further in a later discussion (chapter II).

**Metal-ammonia reduction of cyclic compounds**

The subject of the reactivities of aromatic radical anions and of cyclohexadienyl anions particularly with protons, are fundamental for understanding the products of metal-ammonia reduction of aromatic compounds. This can be seen from the sequence of reactions:

![Diagram of chemical reactions involving metal-ammonia reduction of cyclic compounds](image)

Alkylation of anion radicals or dianions can also be carried out if these are sufficiently stable to be produced in solution rather than as labile intermediates (see chapter III, section 2). It is necessary to carry them out as separate processes because of competitive reduction of alkylating agents (e.g. methylation of naphthalene\(^49\)).

The subject of alkylations of such mesomeric anions is therefore an important one in understanding such processes.

Acid-base reactions, leading to mesomeric carbanions can also be used to help elucidate reduction reactions which generate anions (the same ones) but in a different way.
The reductive process above can be carried out past the dihydro stage (e.g. using lithium in ethylamine⁵⁰). The mechanism of production of tetrahydrocompounds in such reactions can be further understood by studying the effect of a strong base such as amide anion on cyclohexadienes. It was earlier deduced¹⁶ that cyclohexa-1,3-diene disproportionates into benzene and cyclohexene by the action of potassamide anions in liquid ammonia.

Therefore the study of factors operating in cases where strongly basic anions are formed as the result of a reduction process, particularly of aromatic nuclei is of considerable theoretical and experimental importance since this will lead to a better understanding of the formation of secondary products (products with differing degree of reduction to the primary products).

Benzyne. Structure and reaction

The formation of benzyynes by the action of a base such as potassium tert-butoxide in dimethylsulphoxide is a reaction initiated by anion formation due to proton abstraction:

\[
\text{Br} + \text{B}^+ \rightarrow \text{Br} + \text{B}^+ \rightarrow (\text{benzyne})
\]

The structure of benzyne is discussed in a later section of the thesis (IV.1).

The dehydroaromatic bond in benzyne is probably easy to polarize and it is therefore to be expected that as soon as a charged particle or dipole approaches
dehydrobenzene, a partial ionic structure is thereby induced:

\[ \begin{align*}
\text{dehydrobenzene} & \\
\text{with positive charge} & \quad \text{with negative charge}
\end{align*} \]

The effect of substitution on this dipolar form is of interest and is therefore examined in the present work.

The addition of nucleophiles to the unsubstituted benzyne can only lead to one product.

\[ \begin{align*}
\text{nucleophile} & \quad \text{benzyne} & \quad \text{product}
\end{align*} \]

When substituents are present, two isomers are obtained usually with gross differences in ratio. The inductive effect of the substituents has been found to be important in explaining the ratio of isomers obtained.

The amide anion for example, in liquid ammonia adds to 1-methoxy-2,3-dehydrobenzene giving predominantly a meta addition product.

\[ \begin{align*}
\text{amide anion} & \quad \text{1-methoxy-2,3-dehydrobenzene} & \quad \text{meta addition product}
\end{align*} \]

The inductive effect of the methoxy group helps to stabilise the negative charge in the ortho-position of the adduct. In 1-methoxy-3,4-dehydrobenzene where inductive effect is probably considerably reduced both meta- and para-substituted products were obtained in
equal amounts$^{51,52}$.

The interpretation of some other results has been found to be impossible on the ground of inductive effects alone, e.g. the ratio of para- to meta-substituted nitrobenzene obtained$^{53}$ in the addition of various nucleophiles to 4-nitrobenzyne was much smaller than that expected on the basis of inductive effects alone. It was therefore interpreted that a substituent such as NO$_2$ attracts electrons strongly by its mesomeric effect and thus confers a partial positive charge to the aromatic $\pi$ orbital in the para position. Hence it leads to an isomer ratio smaller than that expected on the basis of inductive effects alone.

The study of the effects of substituents on benzyne reactions is therefore of importance in understanding the nature of the reaction products. The results of such study are discussed later (chapter IV, section 1).
CHAPTER II

The Effect of Structure on Hydrocarbon Acidity

Two aspects involving anion formation have now been examined. These are (1) effects of structure on new examples of bond isomerisation through carbanions, and (2) effects of structure on the hydrogenolysis of allylic esters and alcohols in connection with (a) rates, and (b) the nature and stereochemistry of the products.

The first is an extension of literature work in the area, the second is an attempt to see whether the rate determining stage could involve one electron addition, although the products are clearly obtained from the protonation of mesomeric anions and also to see what is the stereochemistry of the "new" double bond in the protonation of the mesomeric anion formed by reduction.

In order to see how close the mechanisms of reduction and isomerisation are, it would have been desirable to compare similar cases, but this is difficult experimentally.

Reductions give regiospecific allylic systems, e.g.

\[ \begin{align*}
R_1C \overset{\text{trans}}{\rightleftharpoons} C \overset{\text{cis and trans}}{\rightleftharpoons} R_2 \\text{OH}
\end{align*} \]

whereas isomerisation can give a mixture because there are two sets of allylic H which can be involved.
It was felt therefore that the experimental problems of separation and identification of the three products, and transfer of the results back to the ratios of the two possible anions, and further to the ratios of stereoisomers in each, was an impossible task with the equipment at our disposal. If there is any steric isomerisation of the original double bond, the task becomes more impossible still. The initial attempt was therefore to look at a situation, particularly with the reductions, which is a simpler case.

II.1 Further Examinations of Bond Isomerisations

Bond isomerisations of olefinic compounds have received much attention during the last few years both in their theoretical and practical aspects. The knowledge of the conditions under which isomerisation of olefin occurs
is valuable for the conversion of olefins to their isomers and is also an important consideration when olefins are not readily available by other means.

The correlation between carbanion stability and hydrocarbon acidity has been pointed out. It was concluded, partly on the basis of cleavages of allylic alcohols and esters, that allylic anions are more readily produced the higher the degree of arylation and the lower the degree of alkylation of either end; the most acidic hydrocarbon acids are those which carry a terminal =CH₂ and can produce similar anions.

This conclusion was tested using the ability of solutions of potassamide in ammonia to cause migration of the double bond through proton removal and it was concluded in general that anion stability is decreased (due to inductive and solvation factors) by alkylation and increased by arylation, leading to the conclusion that acidities are affected in the same manner. Later workers using for example deuterium-exchange techniques confirmed this view of the results of substitution.

The original method using potassium amide in liquid ammonia has been largely superseded as a practical method by potassium-tert-butoxide in dimethylsulphoxide. This reagent generates initially largely the α,β-2-ene from a 1-ene, and accordingly the original observation of the conversion of oct-1-ene into oct-2-ene has been re-examined to determine the configuration of the product (a procedure not possible when the original work was done) and also to see whether there is any evidence in this solvent (NH₃) which is protonic, that the same factors operate as in the non-protonic
dimethylsulphoxide.

**Effects of extra unsaturation.** Effects of structure other than the substitution of the ends of the potential anion could be important. The initial work\(^1\) showed that 2,5-dimethylhexa-1,5-diene (8a) could be converted into 2,5-dimethylhexa-2,4-diene (9a), at a rate which quantitatively appeared to be much greater than the conversion of \(\text{octene}^7\) into \(\text{octene}\). In order to examine the matter further, hexa-1,5-diene is examined under conditions comparable to those used with oct-1-ene, and also 4-phenylbut-1-ene.

In the results presented below, the relevant fact is the rate of disappearance of the starting material compared with hept-1-ene under similar conditions.

**RESULTS**

*Action of potassium amide solution in ammonia on olefinic hydrocarbons*

<table>
<thead>
<tr>
<th>HYDROCARBON</th>
<th>REACTION TIME (hr)</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hept-1-ene</td>
<td>2</td>
<td>Hept-1-ene 81%; <em>trans</em>-Hept-2-ene 11%; <em>cis</em>-Hept-2-ene 8%.</td>
</tr>
<tr>
<td>Hept-1-ene</td>
<td>4</td>
<td>Hept-1-ene 48%; <em>trans</em>-Hept-2-ene 29%; <em>cis</em>-Hept-2-ene 23%.</td>
</tr>
<tr>
<td>Hept-1-ene</td>
<td>6</td>
<td>Hept-1-ene 45%; <em>trans</em>-Hept-2-ene 38%; <em>cis</em>-Hept-2-ene 18%.</td>
</tr>
<tr>
<td><em>cis</em>-Hept-2-ene</td>
<td>16</td>
<td><em>trans</em>-Hept-2-ene 100%.</td>
</tr>
<tr>
<td>4-Phenylbut-1-ene</td>
<td>2</td>
<td>4-Phenylbut-1-ene 55%; 1-Phenylbut-2-ene 34%; 1-Phenylbut-1-ene 8%.</td>
</tr>
<tr>
<td>HYDROCARBON</td>
<td>REACTION TIME (hr)</td>
<td>PRODUCTS</td>
</tr>
<tr>
<td>---------------------</td>
<td>-------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>4-Phenylbut-1-ene</td>
<td>4</td>
<td>4-Phenylbut-1-ene 52%; 1-Phenylbut-2-ene 40%; 1-Phenylbut-1-ene 8%.</td>
</tr>
<tr>
<td>4-Phenylbut-1-ene</td>
<td>6</td>
<td>4-Phenylbut-1-ene 52%; 1-Phenylbut-2-ene 40%; 1-Phenylbut-1-ene 8%.</td>
</tr>
<tr>
<td>Hexa-1,5-diene</td>
<td>2</td>
<td>Hexa-1,5-diene 23%; Hexa-2,4-diene 77%.</td>
</tr>
<tr>
<td>Hexa-1,5-diene</td>
<td>4</td>
<td>Hexa-1,5-diene 14%; Hexa-2,4-diene 86%.</td>
</tr>
<tr>
<td>Hexa-1,5-diene</td>
<td>6</td>
<td>Hexa-1,5-diene 5%; Hexa-2,4-diene 95%.</td>
</tr>
<tr>
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<td>2</td>
<td>2,5-Dimethylhexa-1,5-diene 39%; 2,5-Dimethylhexa-2,4-diene 61%.</td>
</tr>
<tr>
<td>2,5-Dimethylhexa-1,5-diene</td>
<td>4</td>
<td>2,5-Dimethylhexa-1,5-diene 30%; 2,5-Dimethylhexa-2,4-diene 70%.</td>
</tr>
<tr>
<td>2,5-Dimethylhexa-1,5-diene</td>
<td>6</td>
<td>2,5-Dimethylhexa-2,4-diene 100%.</td>
</tr>
</tbody>
</table>

In all experiments one mole equivalent quantity of hydrocarbon was acted upon by 4 mole equivalent amount of base. The reaction product was taken up in ether washed with water, dried and analysed immediately on the g.l.c. or by u.v.

The cis and trans-2-heptene formed were identified by g.l.c. (50°, 20% Ucon) by comparison with authentic specimen. Cis- and trans-2-heptene were obtained commercially (Fluka A.G.) and cis-2-heptene has t_R 7 min and trans-2-heptene t_R 5 min. 1-Heptene has t_R 6 min.
The isomerisation of 4-phenyl-1-butene in liquid ammonia was accompanied by formation of polymeric material which increased with the length of the reaction time. This is probably derived from 4-phenyl-1-butene by addition of a carbanion to a conjugated double bond. Enough conjugated olefin could be present from equilibrium protonation of the mesomeric anion.

\[
\begin{align*}
\text{Ph-CH} = \text{CHR} & \quad \rightarrow \quad \text{Ph-CH} \_2 - \text{CHR} \\
\text{CHCH} = \text{CH-} & \quad \downarrow \quad \text{CH-CH} = \text{CH-} \\
\text{Ph} & \quad \downarrow \quad \text{Ph}
\end{align*}
\]

The 1-phenyl-2-butene (5) was identified by g.l.c. using authentic specimen synthesised by hydrogenation of 1-phenyl-2-butyne. The last compound was obtained by the method of Johnson et al\textsuperscript{56} through the reaction

\[
\begin{align*}
\text{CH}_3\text{C}=\text{CH} & \quad \xrightarrow{\text{C}_2\text{H}_5\text{MgBr}} \quad \text{CH}_3\text{C}=\text{CMgBr} \\
& \quad \downarrow \quad \text{C}_6\text{H}_5\text{CH}_2\text{Br} \\
& \quad \text{CH}_3\text{C}=\text{CCH}_2\text{C}_6\text{H}_5
\end{align*}
\]

(1-phenyl-2-butyne)

1-Phenyl-1-butene (7) was also identified by g.l.c. by comparing with authentic specimen obtained by isomerisation of 4-phenyl-1-butene through the action of potassium tert-butoxide in dimethylsulphoxide. This reaction was first obtained here and 1-phenyl-1-butene was produced in 90% yield by this method; \( \lambda_{\text{max}} \) 251 nm, \( \epsilon \) 17,000, \( \delta \) (CDCl\textsubscript{3}) 1.12 (t, 3H, Me), 2.25 (m, 2H, methylenic), 6.3 (m, 2H, olefinic), 7.28 (m, 5H, aromatic). 4-Phenyl-1-butene (4) has \( t_R \) 3 min, 1-phenyl-2-butene (5) has \( t_R \) 3.7 min, and
1-phenyl-1-butene has $t_R$ 4.8 min (150°, 10% A.P.L.).

The products from the isomerisation of 1,5-hexadiene and 2,5-dimethylhexa-1,5-diene were analysed by u.v. spectra. After isomerisation in liquid ammonia for 6 hours, hexa-1,5-diene gave a product which was essentially hexa-2,4-diene, $\lambda_{\text{max}}$ 217 nm, $\varepsilon$ 19,950 (pure hexa-2,4-diene, $\lambda_{\text{max}}$ 217 nm, $\varepsilon$ 21,000). 57 2,5-Dimethylhexa-1,5-diene after 6 hours gave only 2,5-dimethylhexa-2,4-diene in 90% yield, $\lambda_{\text{max}}$ 251 nm, $\varepsilon$ 23,000 (pure 2,5-dimethylhexa-2,4-diene has $\lambda_{\text{max}}$ 251 nm, $\varepsilon$ 23,000). 57

The percentages quoted represent the proportion of each compound present in the reaction product as found by g.l.c. or u.v. and do not represent yields.

The results show that the hexadienes (8a) and (8b) disappear at a much faster rate than 1-heptene (1). Cis-2-heptene is quantitatively converted into its thermodynamically more stable isomer (trans-2-heptene) in 16 hours. The results further show contradiction to the results of similar isomerisations carried out in DMSO. The results here show a predominance of the trans-isomer as against the cis-isomer formed in the DMSO reactions. The significance of these results is discussed in detail below.
The reaction is due to the free energy of delocalization which is involved in the noncovalent nature of the union before it is being formed.

From base-catalyzed deuterium exchange reactions, it has been shown that such reactions are largely intramolecular. Any mechanism involving the formation of base-catalyzed charge with alkoide attack and isomerization is reproduced below.
DISCUSSION

Mechanisms: In the base-catalysed isomerisation of olefins, a reasonable mechanism involves the formation of transition state such as:

The acidity is due to the free energy of delocalisation which is involved in the mesomeric nature of the anion as it is being formed.

From base-catalysed deuterium exchange reactions, it has been shown that such reactions are largely intramolecular. The mechanism of base-catalysed exchange with alkoxide anions and isomerisation is reproduced below.
Base as an ion pair (in non-dissociating solvents) or as a free anion (in dissociating solvents) abstracts a proton from the benzyl carbon atom to form in one transition state a carbanion hydrogen-bonded to the same hydroxyl group at both the benzyl and methylene carbon. When a metal cation is present, exchange occurs at the front face of the carbanion, collapse of which to starting material gives material of retained configuration. Exchange involves rotation of the metal cation, and its ligands within the ion pair and collapse to the starting material both processes occurring faster than ion pair dissociation. In the dissociating solvents, the asymmetrically solvated anion exchanges with solvent to form an isotopically labelled inverted exchanged starting material. 3-Phenyl-but-1-ene above
isomerised with 50-60\% intramolecularity. Higher intramolecularity was noted\textsuperscript{25} for 1-pentene and it was pointed out that the difference in pKa between olefin and proton donor as well as the concentration of proton pool could affect the amount of intramolecularity observed.

Many factors could affect the rate of prototropic shifts. A linear free energy relationship was found between the bromination (base-catalysed) of cyclic and acyclic ketones and the base-catalysed isomerisation of the corresponding olefins\textsuperscript{26} (figure 1). This free energy relationship strongly suggested similar transition states and rate-determining steps for the two reactions. It was concluded that the anionic isomerisation was controlled by the rate at which the \( \alpha \)-hydrogen was removed by base. Factors that stabilise the transition state relative to the ground state or that destabilise the ground state relative to the transition state will facilitate proton removal. The energy of the transition state will be at a minimum when there is maximum opportunity for bond formation between the \( \text{Sp}^3 \)-\( \sigma \) orbital made available by the leaving hydrogen and the \( \pi \)-orbital of the \( \text{ex} \) double bond. Any factors that lead to ease of \( \pi \)-\( \pi \) overlap in the transition state should increase reaction rates. The reaction profile was as shown below.
Maximisation of P-π overlap also explained the more rapid isomerisation of the methylenecyclobutane compared to methylenecyclopentane and cyclohexane.

The extent of C-H bond cleavage in the transition state was determined via deuterium labelling experiments using perdeuterio-1-pentene in the system potassium-tert-butoxide-dimethylsulphoxide. It was shown that the C-H bond was largely broken in the transition state and that carbon-hydrogen bond cleavage was rate-determining. The intramolecular proton rearrangement suggested that although bond cleavage of C-H bond was nearly complete in the transition state, the protonated base was not free to exchange.

In the isomerisations above (Table 1), 2,5-dimethyl-1-hexadiene (8a) disappears at a rate about 2 times faster than 1-heptene. This could not be due to the presence of the methyl groups in the diene (8a) since 1,5-hexadiene (8b)
is also found to disappear at about the same rate as the 2,5-dimethylhexa-1,5-diene. Solubility is ruled out as a factor here since all the olefins are soluble at the concentrations used. An explanation then seems to lie in the second unsaturated centre. As mentioned above, the rate determining step is the abstraction of α-H to give the anion (3a) in the case of 1-heptene and the anion (10a) in the case of the diene (8a).

Therefore the formation of the anion (10a) is probably rate-determining since the acidity of the diene (9a) should be high in view of the charge distribution in the anion (12). These isomerisations proceed via metal salts, which in some cases are present in high concentration. The critical stage
with 1,5-dienes is obviously the first bond shift since the acidity is greatly increased in the 2,5-dienes by increased resonance in the ion. The question why an unconjugated double bond increases the rate of formation of an anion such as (10a) is not readily apparent. This could involve stabilisation of the anion by electron acceptance by the double bond.

This is not a particularly favourable process but possibly could render some assistance. It has been found that no isomerisation takes place unless the first potential anion has a CH₂ or a CHPh group in the system. Furthermore, the reduction of 1,5-dienes with calcium hexammoniate or sodium in ammonia must be preceded by isomerisation to conjugated dienes, and is not observed unless the same conditions are fulfilled.¹⁶,⁵⁹

Base-catalysed equilibration of simple olefins resulted in mixtures in which the isomer most highly substituted predominated. Eventual equilibrium mixtures²⁴ are close to thermodynamically calculated ones, e.g. 2-methylpent-2-ene (80%), 2-methylpent-1-ene (10%), 4-methylpent-1-ene (1%). More highly substituted double bonds predominate, each alkyl additional increases stability by a factor of 5-10. In general, successive substitution of alkyl groups (not highly branched) for hydrogens of ethylene tends to give more stable structures than their less substituted isomers. This generalisation
grows out of the electron-releasing effects of the alkyl groups, and the electron-withdrawing effect of the vinyl groups. With tert-butyl and like groups, steric effects are superimposed, and this generalisation can break down particularly with cis isomers.

Conjugative effects on equilibria of aryl and vinyl groups are more important than the alkyl group effects above, e.g. propenylbenzene dominate over allylbenzene by a factor of about $10^{5-4}$ at equilibrium. The isomerisation of 4-phenyl-1-butene (Table 1) probably goes through the path

$$\text{PhCH}_2\text{CH}_2\text{CH} = \text{CH}_2 \rightarrow \text{PhCH}_2\text{-CH} - \text{CH}_2$$

(4)

$$\text{PhCH}_2\text{CH} = \text{CHCH}_2 \text{CH}_3 \leftarrow \text{PhCH}_2\text{-CH} - \text{CH} - \text{CHCH}_2 \text{CH}_3$$

(7)

$$\text{PhCH} = \text{CHCH}_2 \text{CH}_3 \leftarrow \text{PhCH}_2\text{-CH} - \text{CHCH}_2 \text{CH}_3$$

(6)

The formation of the anion (3b) is likely rate-determining since the acidity of the hydrocarbon (7) is high due to the charge distribution in (6). The initial rate of formation of the anion (3b) is faster than that of (3a) but as in the case of the 1,5-dienes above, the reason for this is not readily apparent. The formation of the anion (3b) is probably favoured by electron acceptance by the ring.
The polymeric material obtained is probably derived from the attack of a carbanion on a conjugated compound such as (7). This point has already been noted. The situation is complicated by the fact that the anion (6) is probably stable in liquid ammonia and is kinetically protonated on work-up to give a mixture of the 1-phenylbut-2- and -1-enes. The quantitative conversion of the 4-ene (4) to the 1-ene (7) by potassium-tert-butoxide action in DMSO showed the role due to the conjugative effect of the aryl group in compound (7). However, since there is no significant difference in the rates of isomerisation of both 1-heptene and 4-phenyl-1-butene, the phenyl group in the 4-position is likely exerting very little influence on the rate of removal of the allylic proton.

Ratio of cis- to trans-isomers. Experimental evidence$^{60}$ has shown that allylic anions are fairly stable with regard to geometrical configuration, although slow inversion of geometry can occur. Enantiomeric anions are very unstable, and by comparing rates of racemisation with D exchange$^{61}$ carbanions are found to racemise if they live long enough in a symmetrical environment.

In the kinetically and thermodynamically controlled ratio of cis-trans isomers produced in isomerisation of 1-alkenes to 2-alkenes, evidence has accumulated that isomers tend to predominate in kinetically controlled processes in which two hydrogens are cis to one another. For instance, although trans-2-butene predominates over cis-2-butene in an equilibrium mixture by a factor of about 4, base-catalysed isomerisation of 1-butene to the
2-butenes gives a mixture in which the cis dominates over the trans by a factor of about 47. This was explained on the basis that the cis-allylic anion is more stable than the trans because of the more favourable pole-dipole interactions in the cis isomer. Steric effects oppose this pole-dipole effect, become dominant with more hindered systems, and trans isomers result.

\[
\begin{array}{c}
\text{(cis-butenylanion)} \\
\text{(trans-butenylanion)}
\end{array}
\]

In those cases where kinetic control leads to the less stable isomer, Price and Snyder pointed to a possible explanation which assumes a ground state conformational control of products. It is assumed that that conformation is favoured in the starting material which places \( \beta \)-hydrogen cis to the double bond, and thus allows the \( \pi \)-electrons of the double bond to interact with two of the hydrogens of the \( \beta \)-carbon. The proposed steric course of pentene rearrangement is given below.
If it is assumed that conformation A is favoured over B by a factor as small as 2 kcal/mole, due perhaps in part to favourable interaction between two of the methyl group hydrogens and the π-electrons of the double bond, then rate constants $K_A$ and $K_B$ can be nearly equal yet there will be a great preference for cis-2-butene in the initial isomerate. The cis to trans interconversion of carbanions would presumably be slow due to double bond character at
the 2,3-bond, which would restrict rotation there.

The results (Table 1) indicate that the conformation B is probably more favoured in liquid ammonia and hence the predominance of the trans-2-heptene in the products. There is another explanation which may be that the cis-2-alkene formed is interconverting into the trans-isomer. This is supported by the fact that cis-2-heptene in the results above (Table 1) is quantitatively converted to the trans-isomer in sixteen hours.

It should be further pointed out that for many years, Hughes and Ingold\textsuperscript{29} suggested that the kinetic protonation of a mesomeric anion should give the more acidic and less thermodynamically stable isomer. Such a generalisation however is found not to apply in all cases and Cram has formulated three basic activation energy-reaction coordinate profiles for formation and collapse of allylic and related anions.

![Activation energy-reaction coordinate profiles for formation and collapse of allylic and related anions.](image)
The first profile (a) embodies the Hughes-Ingold rule, of which abundant examples are available. In the second (b), the unstable isomer is still the more acidic as suggested by Hughes and Ingold but the allylic anion collapses to the thermodynamically more stable isomer. The third profile (c) shows a complete contradiction to the Hughes-Ingold rule.

Because of the large solvation energies involved in transforming a covalent carbon-hydrogen bond into a carbanion, one might expect that the rates of carbanion generation and capture are highly dependent on the character of the solvent. Therefore activation energy-reaction coordinate profiles might vary for similar processes as one goes from one solvent to the other and this might at least be partially responsible for the observed differences in the ratio \( \text{cis} \) to \( \text{trans} \) isomers for base-catalysed isomerisations in dimethylsulphoxide and liquid ammonia.
II.2 Kinetically controlled protonations of ArC\_\_\_\_C\_\_\_\_CMe\_\_\_

KNH\_\_\_\_NH\_\_\_\_ seems to give high concentrations of salt with PhCHC=C or PhC=C-CH, presumably the same ion PhC\_\_\_\_C\_\_\_\_C for both.

Previous work\textsuperscript{44} had involved reduction of PhCH=C:Me\_\_\_\_OH, presumably via this ion to hydrocarbon; it was decided to examine the effects of substitution in the Ph on the nature of kinetically formed hydrocarbon. Since not all hydrocarbon may be there as salt, the ratio of base used is important. This ratio is also examined.

In an anion of the type

\begin{equation}
\text{(14)}
\end{equation}

kinetic protonation at C\_\_\_\_ is likely to be encouraged by the inductive effects of the Ph and that at C\_\_\_\_\_\_ reduced due to electron-donating effects of the methyl group. The effect of substituents in the Ph would be to affect the ratio of protonations occurring at C\_\_\_\_ or C\_\_\_\_\_. It was found\textsuperscript{47} that o-methoxy and m-methoxy do not inhibit hydrogenolysis but that p-methoxy has an inhibitory effect. Examination therefore of the effects of the methoxy groups present in the Ph on the kinetic protonation of the anion above should reveal more clearly the role being played by these substituents in these type of reactions.

It is also of interest to see what if any influence the structure of the proton-donor has in such kinetic proton-
The proton donors examined include the bulky tert-butanol and the non-sterically hindered ammonium cation.

The detailed results are given below.

Table II

<table>
<thead>
<tr>
<th>OLEFINS</th>
<th>OLEFIN CONCENTRATION M.MOLES</th>
<th>KNH₂ M.MOLES</th>
<th>PROTON DONOR</th>
<th>PRODUCTS</th>
<th>RATIO OF 13/15</th>
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<tr>
<td>(13a)</td>
<td>6.8</td>
<td>6.8</td>
<td>tert-butanol</td>
<td>47</td>
<td>53</td>
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<tr>
<td>(13a)</td>
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<td>6.8</td>
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<td>62</td>
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<td>(13a)</td>
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<tr>
<td>(13a)</td>
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<td>NH₄Cl</td>
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<td>(13a)</td>
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<td>(13a)</td>
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<tr>
<td>(13b)</td>
<td>6.8</td>
<td>6.8</td>
<td>tert-butanol</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>(13b)</td>
<td>6.8</td>
<td>6.8</td>
<td>NH₄Cl</td>
<td>70</td>
<td>30</td>
</tr>
<tr>
<td>(13b)</td>
<td>6.8</td>
<td>13.6</td>
<td>tert-butanol</td>
<td>35</td>
<td>65</td>
</tr>
<tr>
<td>(13b)</td>
<td>6.8</td>
<td>13.6</td>
<td>NH₄Cl</td>
<td>24</td>
<td>76</td>
</tr>
<tr>
<td>(13b)</td>
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<td>27.2</td>
<td>tert-butanol</td>
<td>trace</td>
<td>100</td>
</tr>
<tr>
<td>(13b)</td>
<td>6.8</td>
<td>27.2</td>
<td>NH₄Cl</td>
<td>16</td>
<td>84</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>6.8</td>
<td>tert-butanol</td>
<td>100</td>
<td>trace</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>6.8</td>
<td>NH₄Cl</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>13.2</td>
<td>tert-butanol</td>
<td>78</td>
<td>22</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>13.2</td>
<td>NH₄Cl</td>
<td>100</td>
<td>trace</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>27.2</td>
<td>tert-butanol</td>
<td>68</td>
<td>32</td>
</tr>
<tr>
<td>(13c)</td>
<td>6.8</td>
<td>27.2</td>
<td>NH₄Cl</td>
<td>70</td>
<td>30</td>
</tr>
</tbody>
</table>

TABLE II

Action of potassamide solution in liquid ammonia on olefins.
The results were monitored in a gas-liquid chromatograph (5% Carbowax, 120°) and the products (15) were all identified by n.m.r. Other conditions as stated under Table 1 (II.1) also apply here.

\[
\begin{align*}
  (13) & \quad (a) \quad R = R' = H \\
        & \quad (b) \quad R = \text{OMe}, \quad R' = H \\
        & \quad (c) \quad R = \text{H}, \quad R' = \text{OMe}
\end{align*}
\]

The starting olefin (13) was reacted with potassamide solution in liquid ammonia and in each case the potassium salt was formed immediately as indicated by the appearance of the red colour of the solution. After 10 minutes, the reaction mixture was quenched with tert-butanol or ammonium chloride. The product was taken up in ether and examined as under Table 1.

1-(p-Methoxyphenyl)-3-methyl-but-1-ene (13c) was recovered unchanged when equivalent amounts of the olefin and potassamide were used.

The results clearly show that the methoxy group when in the p-position of the Ph inhibits the addition of protons at the position C1 of the anion (14) while the o-methoxy group shows no inhibitory effect.

The results further show that with a low concentration of base acting on say (13a), kinetic protonation of (14a), gives a ratio of (13a)/(15a) of about 0.9. With a larger amount of base (about 4M) acting on (13a) kinetic protonation leads exclusively to (15a).
It appears from the results above that the nature of the proton donor is probably not important. The importance of these results is reserved for the discussion below.

DISCUSSION

It has been suggested that in protonation by irreversible addition, the $H^+$ adds predominantly to the charge in its most stable position, in the case of mesomeric allylic ions to the least alkylated or most arylated end of the system. This suggestion amounts to the same as the Hughes-Ingold rule above (II.1). As shown in the energy-reaction coordinate profiles above and as further pointed out later (see III), these simple views do not always hold and the structure of the anion is largely the controlling factor for reactions of low activation energy.

A very good case to consider is the interconversions of cyclohexa-1,3- and -1,4-dienes. The first experimental work concerned the following equilibria and reactions.

\[
\begin{align*}
&\text{(16)} \quad \text{or (18)} \quad \text{or (18)} \\
&\begin{array}{c}
\text{OMe} \\
\text{NH}_2
\end{array}
\end{align*}
\]

A small proportion of $\text{KNH}_2$ in $\text{NH}_3$ established the thermodynamic equilibrium between (16) and (18) (about 1:3), the anion (17) merely acting as a turntable. With a larger (> 1 m) proportion of $\text{KNH}_2$ acting on either (16)
or (18), the salt (17) was mainly present. Kinetic protonation of (17) by ROH or H₂O gave principally (16).

The equilibria and reactions above can be related to the reactions involved in the kinetic protonation of

\[
\begin{align*}
\text{ArC} & \xrightarrow{\text{H}^+} \text{ArCH}^+ \text{Me}_2
\end{align*}
\]

In liquid ammonia in presence of small amounts of base (see Table II), the following equilibrium is probably set up.

\[
\begin{align*}
\text{(13)} & \xrightleftharpoons{\text{NH}_3} \text{(14)} \\
\text{(a)} & \quad R = R' = H \\
\text{(b)} & \quad R = \text{OMe}, \quad R' = H \\
\text{(c)} & \quad R = H, \quad R' = \text{OMe}
\end{align*}
\]

However, when excess amount of KNH₂ (about 4M) is used on (13a or b), only the anion (14a or b) is present and kinetic protonation by tert-butanol or NH₄⁺ gives almost exclusively (15a or b) which is the less thermodynamically stable isomer. Salt formation is therefore a method of converting the thermodynamically more stable isomer (13) into the less stable isomer (15), using kinetic control in final protonation.

The results (Table II) clearly indicate a dual role for the methoxy substituent in the Ph. The o-methoxy appears to play a neutral role since kinetic protonation of (13a) or (13b) gives similar results.
The p-methoxy however shows a clearly inhibiting role towards addition of proton at C₁ of the anion (14c). In these kinetic protonations, addition of H⁺ probably occurs at the position of readiest charge location and the effect of the p-methoxy then was to destabilise the charge at C₁, through its mesomeric effect.

\[
\begin{align*}
\text{MeO}^- & \quad \text{CH} = \text{CHR} \\
\end{align*}
\]

an extreme of which will be the conjugation of 1-double bond with the ring

\[
\begin{align*}
\text{MeO}^+ & \quad \text{CH} \quad \Theta \quad \text{CHR} \quad \text{(sort of extended conjugation)}
\end{align*}
\]

The results observed here may be used to explain some of the frequently observed differences between o- and p-methoxy groups. For instance, benzyl alcohol is reducible initially to toluene, but p-methoxybenzyl alcohols undergo minimal hydrogenolysis under appropriate conditions and the ring is reduced instead. For benzyl alcohol the ease of fission is o-OMe > m-OMe > p-OMe. The action of benzyl alcohol was probably to prevent concentration of charge on the benzylic carbon thereby accumulating it on oxygen which prevents hydrogenolysis since it was pointed out that if a negative charge is placed by salt formation on the oxygen of allyl or benzyl alcohol, the fission is prevented.
Nature of proton donors. From the steric point of view, it seems that in donating a proton to anion such as (14a), the tert-butanol will donate preferentially at C₁ thereby giving rise to larger proportions of 2-ene compared with the NH₄⁺ cation which should be capable of donating at both ends of the mesomeric anion (14).

NH₄⁺ is probably virtually without steric hindrance, since it may be able to transfer H⁺ indirectly through the solvation shell of the anion, i.e. through a hydrogen-bonded solvent chain.

\[
\begin{align*}
\text{H} & \text{N} - \text{H} \\
\text{H} & \text{N} - \text{H} - \text{H} \\
\text{H} & \text{N} - \text{H} \\
\text{H} & \text{N} - \text{H} \\
\end{align*}
\]

There should therefore appear some differences in the ratio of products with each of the proton donors. Since such difference is either absent or negligible, it follows that the stereochemistry of the proton donor is unimportant here or that other factors are more important.
II.3 Reductions of Allylic Alcohols and Esters

The reduction of alkyl halides with solvated electrons gives initially radicals and halide anions. A similar reaction, though it is the gaseous state, is the "sodium flame" reaction, e.g. between gaseous sodium atoms and alkyl, allyl or vinyl halides. The transition state of this reaction is through the stages $R-X\cdot Na\rightarrow R\cdot X^-\cdot Na^+$. There is a linear relationship between bond energies and rates in simple alkyl halides. Vinylic halides have a higher activation energy, presumably because of mesomeric stabilisation of the halide.

The reverse is true of allyl halides, since delocalisation stabilises the transition state: $\text{CH}_2=\text{CHCH}_2\cdot \longrightarrow \text{Cl}^-\longrightarrow \text{Na}^+$. There is an indication with more polarisable groups, such as C≡N, that the transition state may be non-linear, in order to maximise charge interaction between Na$^+$ and the anionic transition state.\footnote{64}

Halides are also readily reduced in solution, because of the ease of formation of the halide anion. By contrast alcohols are not normally split (compare the low acidity of water with say, HCl). However, in the case of allylic alcohols, sodium and liquid ammonia was shown to produce fission, delocalisation of the allylic intermediate presumably being responsible. In order to produce complete fission, it is necessary to have another alcohol such as methanol present to act as a "buffer" in preventing formation of allyloxide, which cannot undergo fission because of the charge on the oxygen.

Allylic esters reduce far more readily than the corresponding alcohols, possibly because of the greater
ease of formation of the anionic leaving group, or possibly because of a different route of entry of the electron.

The effects of substitution show:\textsuperscript{64,44,45} (1) that a mesomeric entity of some sort (anion or radical, or both) is an intermediate, and (2) that increased degree of alkylation decreases the rate of fission to the point where many highly substituted alcohols are not split at all, and that arylation increases rate. The substitution can be at either end of the mesomeric intermediate, i.e., in the C from which OH is lost, or at the further end of the allylic double bond.

Sample cases are,\textsuperscript{44,45}
The last case is a particularly important one, since complete racemisation demonstrates the mesomeric nature of the intermediate, i.e. there is no "memory" of which end has lost OAc.

The products of the reaction (which as noted are carried out in presence of a proton source) are those to be expected of kinetic protonation of a mesomeric anion, and this aspect is discussed later. It is not initially clear whether the anion is a primary fission product; however, since two routes are possible:

\[
\text{ROH + e} \rightarrow \text{R}^- + \text{OH}^- \quad \text{and} \quad \text{ROH + 2e} \rightarrow \text{R}^- + \text{H}_2\text{O}^- + \text{H}^+ \]

Because of the inhibiting effect of alkyl substitution, which might be expected to inhibit anion formation, and also the necessary solvation of the carbanion (in contrast to the neutral radical), the process was first interpreted as a two-electron addition.\(^{65}\) This conclusion is however questionable on general grounds, since it requires the addition of a second negative electron to what must be a charged entity from the addition of the first one.

We are now inclined to interpret the mechanism according to (A) above, noting that the transition state is anionic, even though it leads to a neutral carbon radical, and the effects of substitution might be expected to be those observed to affect acidities of the hydrocarbon products. The relationship to such acidities was in fact early realised,\(^{44}\) and the relative ease of fission of alcohols RCMeOHCH=CH\(_2\) or RCMe=CHCH\(_2\)OH (above) was related
to the ease of bond migration of octene-1 into octene-2, through the allylic carbanion (II.1).

It was also expected, and proved in the case of geraniol and nerol\textsuperscript{45} (see also ref. 46) that the mesomeric intermediates would probably retain the existing stereochemistry at the initial double bond.

On the present view, therefore a representative reduction can be given as:

![Chemical structure diagram]

Two mesomeric anions (19) and (20) will result, both with the configuration of the original double bond position, and with the alternative configurations at the "new" double bond position. The ratio presumably depends on the nature of the R-groups, and possibly on the conformation of the alcohol induced by the "leaving group" (which could be different for the esters). If we label the carbon from which OH is lost as "a" and the allylic one as "b", then protonation will occur at relative rates in (19) and (20) at a,b determined again by the nature of R (and possibly by that of a counter ion, e.g. \text{Li}^+ or \text{K}^+). The proton source could also be a factor.

The observed facts are that protonation tends to occur at the less substituted end, and if this is \text{CH}_2, the
extent of protonation can be 90-95%. It also tends to occur at an end carrying Ar, but in competition between CH₂ and CHAr the former may dominate (see II.1 and II.2). With similar substitution, and with changes of stereochemistry, the position is much more complex, with usually a mixture produced. This mixture of position and stereoisomers is difficult to analyse, and when the original work was done, in the absence of efficient g.l.c., only preliminary conclusions could be drawn.

The present work was aimed at adding information on two points if possible, (1) whether 1e or 2e were added initially, and (2) what is the nature of the protonation products of the mesomeric anions formed. The process is an interesting supplement to that involving carbanion formation from the hydrocarbons, since most of the information available from simple olefins is obtained through bond-migrations, which is an intra-molecular process (see II.1) and not by kinetic protonation of anions, such as must be the case here.

Kinetic protonations have been carried out on salts from aryl-allyl anions (e.g. from propenyl or allylbenzenes) (see II.2) since in these cases base-exchange can be obtained with sufficiently strong bases (such as KNH₂-NH₃ or Na dimsonyl in DMSO). Further work has been carried out in that area also in this thesis (II.2).

Brown had already examined the fissions of some allylic nonenols to isomeric nonenes, but was unable to analyse the mixtures of products efficiently because of lack of appropriate g.l.c. equipment (which was not then available commercially). He was able to examine the ratio
total cis : total trans (using a AgNO₃ column) and the ratio 2-ene : 3-ene (using KMnO₄ - NaIO₄ fissions). He could not determine say the ratio cis-2-ene : trans-2-ene. Consequently the results are not discussed by him in any detail.

His results for nonenols and acetates are shown in Table III. The results of the present work are in Table IV.

Reduction of non-3-en-2-ol and non-3-en-2-yl acetate

**Table III**

Results previously obtained

<table>
<thead>
<tr>
<th>Compound</th>
<th>cis-Nonene</th>
<th>Non-3-ene</th>
</tr>
</thead>
<tbody>
<tr>
<td>trans-Non-3-en-2-ol</td>
<td>14.5</td>
<td>59.5</td>
</tr>
<tr>
<td>cis-Non-3-en-2-ol</td>
<td>47</td>
<td>33.5</td>
</tr>
<tr>
<td>trans-Non-3-en-2-yl acetate</td>
<td>10.5</td>
<td>55</td>
</tr>
<tr>
<td>cis-Non-3-en-2-yl acetate</td>
<td>47</td>
<td>38'</td>
</tr>
</tbody>
</table>

**Table IV**

Present Work

<table>
<thead>
<tr>
<th>Compound</th>
<th>trans-2-nonene</th>
<th>cis-2-nonene</th>
<th>trans-3-nonene</th>
<th>cis-3-nonene</th>
</tr>
</thead>
<tbody>
<tr>
<td>trans-Non-3-en-2-ol</td>
<td>51</td>
<td>-</td>
<td>49</td>
<td>-</td>
</tr>
<tr>
<td>cis-Non-3-en-2-ol</td>
<td>56</td>
<td>1.5</td>
<td>-</td>
<td>42.5</td>
</tr>
<tr>
<td>trans-Non-3-en-2-yl acetate</td>
<td>33</td>
<td>9</td>
<td>56.7</td>
<td>1.2</td>
</tr>
<tr>
<td>cis-Non-3-en-2-yl acetate</td>
<td>46</td>
<td>5.5</td>
<td>-</td>
<td>48.5</td>
</tr>
</tbody>
</table>
To begin with let us consider the cases where all of the products are defined:

\[ R = H \quad R = \text{Ac} \]

- [%]  \quad - [%]

\[ A \]

\[ B \]

\[ C \]

\[ D \]
There are some differences between alcohols and esters which may be partly errors in analytical method (~ ±5%) but are probably real, and may relate to differences in conformational effects. For A, B, D they are not large but for C the results are considerably different, including detection of a new isomer with the acetate. Although attempts were made as far as possible to characterise the starting-materials as pure isomers, some variation in results could be due to slight variations in this.

The route of entry of the electron to the ester could be through the carbonyl, and to the alcohol through the double bond. An extended transition state involving the carbonyl might well therefore lead to a different ratio of isomers at the "new" double bond position.

\[
\begin{align*}
C & \rightarrow C - \overset{\text{C}}{\text{C}} - C - OH \\
& \rightarrow C - \overset{\text{C}}{\text{C}} - C - OH \\
& \rightarrow C - \overset{\text{C}}{\text{C}} - C - OH \\
\end{align*}
\]

The most sensitive index is probably the production of the less stable configuration (cis) of the new double bond, but in that case it is not clear why in A and C the effect should be reversed.

A further obvious point is that the "new" double bond is predominantly produced in the trans-configuration, which would not be unexpected in view of the fact that the carbons of the allylic system are probably basically trigonal and that the trans isomer is therefore likely to be favoured for steric reasons. An alternative, less likely explanation is that the mesomeric anion is protonated in such a way as to leave the trans double bond in a trans-cis anion. This is
difficult to investigate, since each of the two possible intermediate anions, produced in unknown proportions, can give two products. The ratio of protonation at each end in a given anion, cannot therefore be decided on this evidence alone.

Before looking further at this, evidence from related fields may be considered. Allenes can apparently reduce directly, or through rapid isomerisation to acetylenes. The direct process presumably involves the dianion (24) which should be protonated at the more basic position to a mesomeric carbanion similar to those above.

\[
\begin{align*}
\text{C}=\text{C} & \quad \text{C} & \quad \text{G} & \quad \text{C} \\
\text{C} & \quad \text{C} & \quad \text{C} & \quad \text{C} \\
\text{C} & \quad \text{H} & \quad \text{G} & \quad \text{C} \\
\text{(24)} & \quad \text{(25)} & \quad \text{cis & trans}
\end{align*}
\]

If isomerisation occurs to an acetylene, only trans olefin would result. In fact a mixture of cis and trans has been obtained, with the trans normally greatly dominant, e.g. nona-1,2-diene to trans non-2-ene (93%), nona-2,3-diene to trans non-2-ene (49%), cis non-2-ene (1.5%), trans non-3-ene (48%), cis non-3-ene (1.4%). In the case of medium ring allenes, the pure cis isomer results, probably because of ring-strain. Insufficient examples have been studied to shed much light on the topic at issue.

Butadiene with Na-NH₃ gives mainly cis but-2-ene at low temperatures, with an increasing amount of trans as the temperature rises.

Although a monoanion is an intermediate the stereochemistry may have been determined at an earlier stage, in the radical anion and there could be a high proportion of
{
\[ \text{cis in this because of more efficient charge interaction with the carbon:} \]

Again, the less substituted position is that chiefly protonated. The only case where an indication of protonation in an unsymmetrical molecule can be observed is hexa-2,4-diene which gives hex-2-ene (65%) and hex-3-ene (35%), the stereochemistry not being defined. This result, if authentic, is puzzling at first sight since the more substituted end of the monoanion must be predominantly protonated to give the 2-ene.

A possible reason is the intermediate (a) carries an exo-Me and an endo-Et (with reference to the angle of the anion, presumably containing the cation) and protonation may occur at the position calculated to lead to greater relief of steric interaction. If this view is correct, then the products should have predominantly the opposite stereochemistry, as shown. This is susceptible to experiment. It is also an interesting indication of possibilities for the anions from fission reactions.

Turning back to the allylic reductions and assuming retention of initial stereochemistry,
A can give the intermediate anions

\[ A \]

\[ B \]

\[ C \]

\[ D \]

The problems to be discussed are (i) the possible ratios of the two anions in each case, and (ii) the possible products of protonation in the two possible positions.

Under (i) it seems likely that the less crowded isomer should result, i.e. the trans-trans. However, in the isomerisation of 1-enes into 2-enes by a base-catalysed process the cis isomer normally predominates (II.1). This was considered to be due\(^{62,70}\) to more favourable dipole interactions between alkyl \(R^+\) and the charge in the anion. With recent conclusions that alkyl, as a polarisable group, can actually stabilise negative charges, i.e. the induced dipole could be \(R^+\), this argument seems less convincing. Also, the migration is intra-molecular, which may introduce
factors concerned with easy proton migration. We provisionally assume, therefore, a dominant steric effect, i.e. $a > b$; $c > d$; $e > f$; $g > h$.

We also consider more closely the acetate results on two grounds: the yields are normally high in a rapid process, which would tend to eliminate complications due to possible impurities which are more readily reducible than the compound thought to be used, and as a much easier process it is less likely to involve possible complications.

A. The major products are alternative protonation products of (a), although the trans-isomer (22) can also arise from the alternative ion (b) together with the observed (21). The nearly equal ratio of (22) and (23) is therefore not due to equal protonations of (a) but to predominant protonation of (a) at the less substituted end, the extra trans 2-ene required to equalise arising from protonation of (b). It is not really possible to guess the ratios of (a) and (b) on this evidence, except that the result is readily explicable on $a > b$, especially the low yield of (21).

B. The two products are the alternative protonation products of (c), with no evidence of any intervention of the cis cis isomer (d). There is also a 2:1 protonation at the less substituted end.

C. Apart from chain-length, which is probably only a minor factor ($C_5$ instead of $C_4$) (d) is identical with (a); (f) differs from (b) in having the smaller chain endo-. The ratio $e : f$ might therefore be somewhat greater than $a : b$. The results (acetate) indicate the expected ratio of trans
3-ene > trans-2-ene, with a proportion of cis-2-ene comparable to that under A.

D. The results contrast somewhat with B, with which it should be comparable, in that some cis olefin derivable from (h) is present and the ratio of 2-ene to 3-ene is higher. The anion (d) is identical with (h) apart from the slight difference in chain length. A possible explanation is that ratio of c : d is higher than of g : h since c has the large group exo and the small one endo. It is notable that anion (h) appears to protonate only on the more highly substituted position, but this may be a failure of the analytical method due to the small amount of cis isomer present.

* With some minor discrepancies, and with the somewhat anomalous results for the alcohol (c), the initial postulates seem to explain the major features of the reaction.

Until a method is devised to produce a single anion of controlled configuration, the protonation ratio can only be a matter of guesswork.

To sum up: it appears that (i) steric configuration is retained in the initial double bond; (ii) that the least crowded mesomeric radical (and therefore the subsequent anion) is formed; (iii) that protonation tends to occur at the less alkylated situation, but differences in rates produced by change of Me for C₄H₉ or C₅H₁₁ are rather small; (iv) there is much greater tendency to produce a trans double bond in the new position rather than a cis-one; (v) the influence of configuration of the anion on the position of preferred protonation cannot
be decided at present but may be decided at least partly by preferential formation of the olefin which has less steric strain.

* Let us now analyse the less complete evidence of Brown,\textsuperscript{45} to see whether it could reasonably fit these conclusions (Li reductions)

\begin{itemize}
  \item \textbf{E.}
    \begin{itemize}
      \item \textit{cis}-nonene 17\%
      \item \textit{trans}-nonene 83\%
      \item non-2-ene 28\%
      \item non-3-ene 72\%
    \end{itemize}
  
  Assuming that all of the \textit{cis}-nonene is non-3-ene we deduce: \textit{cis}-non-3-ene 17\%, \textit{trans}-non-3-ene 55\%, \textit{trans}-non-2-ene 28\%. These figures are at least in qualitative agreement with A, where \(C_4\) replaces \(C_5\), although there is a discrepancy in the non-2-ene ratio. However using K instead of Li Brown\textsuperscript{45} found \textit{cis}-nonene 14.5\%, and non-3-ene 59\%, which would give much better agreement.

  Using the acetate (with Li) Brown\textsuperscript{45} found: \textit{cis}-nonene 8.5\%, non-3-ene 54.5\%, non-2-ene 45.5\%, which also calculate to reasonable agreement with (A).

  \begin{itemize}
    \item \textbf{F.}
      \begin{itemize}
        \item \textit{cis}-nonene 34\%
        \item \textit{trans}-nonene 66\%
        \item non-3-ene 69\%
        \item non-2-ene 31\%
      \end{itemize}
  \end{itemize}

  Assuming all non-2-ene to be \textit{cis}, the result would be \textit{cis}-non-2-ene 31-34\%, \textit{trans}-non-3-ene 66-69\%, in very
good agreement with (B). The acetate is also in good agree-
ment, and the results seem to show that C₄ or C₅ makes
little difference.

G.

\[
\text{cis-}{\text{nonene}} \quad 14.5% \\
\text{trans-}{\text{nonene}} \quad 85.5% \\
\text{non-3-ene} \quad 59.5% \\
\text{non-2-ene} \quad 40.5%
\]

Assuming all non-3-ene to be \textit{trans}, we can calculate:
\textit{trans}-non-3-ene 59.5%, \textit{cis}-non-2-ene 14.5%, \textit{trans}-non-2-ene 26%. The acetate gives similar figures. This is in good
agreement with the acetate of (C), but the alcohol figures
of (C) are in disagreement, and may therefore be incorrect.
In this case K gives very similar results to Li (\textit{cis}-nonene
11.5%, non-3-ene 56%).

H.

\[
\text{cis-}{\text{nonene}} \quad 47% \\
\text{non-3-ene} \quad 33.5%
\]

Assuming all non-3-ene to be \textit{cis}, we can calculate: \textit{cis}-
non-3-ene 33.5%, \textit{cis}-non-2-ene 13.5%, \textit{trans}-non-2-ene 53%.
There is qualitative agreement with (D), and a similar
result with K (\textit{cis}-nonene 44.5%, non-3-ene 36.5%) and
with the acetate (Li) (\textit{cis}-nonene 47%, non-3-ene 38%).

Agreement of results, although not as good as might
have been hoped, is sufficient to indicate that the basic
postulate on which they were calculated is likely to be
correct; that the steric configuration of the initial
double bond is unchanged.
Some of the discrepancies may be explicable on the basis of different specimens of alcohols and esters, which could have contained up to 5-10% of isomers without this being readily detectable. The following points are relevant to the results of table IV above:

*trans*-Non-3-en-2-ol was prepared by sodium-ammonia reduction of the acetylenic alcohol, which is known to be stereospecific. The *cis* isomer was prepared by hydrogenation of the acetylenic alcohol in methanol with a Lindlar catalyst. *trans*-Non-3-en-2-ol contained no trace of *cis* isomer (g.l.c.); *cis*-non-3-en-2-ol contained not more than 3.5% of the *trans* isomer.

The two allylic alcohols were acetylated with pyridine and acetic anhydride; this reagent is known not to produce allylic rearrangement of the alcohol during reaction. *trans*-Non-3-en-2-yl acetate contained not more than 2% of the *cis* isomer. *cis*-Non-3-en-2-yl acetate contained not more than 3.5% of the *trans* compound.

The reduction of the acetates was much more rapid than that of the alcohols.

For the reductive cleavage of allylic alcohols and allylic ester, the g.l.c. analysis of the product is most important and the exact conditions are given below. All analyses were made on Varian Aerograph 1702 model.
Non-3-en-2-yl acetates  Non-3-en-2-yl-ols  
Column: 5% QF1  Column: 5% QF1  
Temperature: 100°  Temperature: 100°  
Attenuation: 8  Attenuation: 8  
Gas Flow: 10  Gas Flow: 10  
Chart speed: 5 mm/min  Chart speed: 5 mm/min  
$t_R$, trans compound: 10 min  
$t_R$, trans alcohol: 4 min  
$t_R$, cis compound: 8 min  
$t_R$, cis alcohol: 3 min  

**Ratio of cis : trans**  
Column: silver nitrate (5%)/Glycol  
Temperature: 50°  
Gas Flow: 10  
Attenuation: 16  
Chart speed: 20 mm/min  
Injected sample size: 0.5-1.0 µ  
trans nonene $t_R$: 2 min  
cis nonene $t_R$: 2.75 min  

The trans isomer was isolated by injecting 1 µl sample at a time and collected in a U-tube immersed in acetone-dry ice.  

**Ratio of 2-nonene : 3-nonene**  
Column: 10% APL (5' x ¼" SS column)  
Temperature: 50°  
Attenuation: 1  
Gas Flow: 4  
Non-3-ene $t_R$: 17 min  
Non-2-ene $t_R$: 19 min
Combining the results of the analyses above the proportion of each isomer present was then worked out. All percentages were obtained by tracing peaks on to a light sheet, cutting out the area under each peak and weighing.

The nonenes were identified by using synthesised products which were made by hydrogenation of the appropriate acetylenes with metal in ammonia to give the trans-compound and with palladium-calcium carbonate to give the cis-compound.

Reduction of Cinnamyl Alcohols

Reductions of cinnamyl alcohols of type (26) can occur in two competing ways: reduction of the styrenoid double bond and cleavage of the allylic alcohol. This competition was observed by Birch, who found that, as expected, the cleavage reaction could be totally inhibited by forming the alkoxide first.

The present work was aimed to see whether substitution of the benzene ring by OMe in ortho- or para- notably affects the ratio of hydrogenolysis to double bond reduction. Ortho-OMe normally assists the formation of a negative charge in a benzylic situation, and p-OMe inhibits it (cf. hydrogenolysis of o-OMe benzyl alcohol and ring-reduction of p-OMe benzyl alcohol; they might be expected therefore to promote and hinder, respectively, both double-bond reduction and hydrogenolysis in type (26)). The question is whether both reactions are similarly affected, i.e. whether the ratio of reduced alcohol to hydrogenolysis product varies markedly.
The results are shown below.

(a) $R, R' = H$

- Na/NH$_3$ 100%
- Na/NH$_3$/EtOH 42% 58%

(b) $R' = OMe$, $R = H$

- Na/NH$_3$ 100%
- Na/NH$_3$/EtOH 44% 56%

(c) $R = OMe$, $R' = H$

- Na/NH$_3$ 100%
- Na/NH$_3$/EtOH 77% 15%

Lack of hydrogenolysis in the absence of added ethanol is obviously due to preferential salt formation. That some hydrogenolysis of (26a) occurred in previous work may have been due to the use of unpurified ammonia, with possible presence of water. In this work the solvent was redistilled from Na.

The second obvious point is that o-OMe instead of H makes virtually no difference to the ratio, whereas p-OMe not only alters the ratio considerably but introduces a new component into the products.

The probable mechanism here involves initial electron addition to the unsaturated system, probably to the anion-radical and then either protonation, or expulsion of hydroxyl anion.
The hydrogenolysis process seems to proceed via pathway (a) rather than (b) since the product is clearly that of kinetic protonation of the mesomeric anion, which cannot arise by route (b) at any rate in presence of buffering alcohol. (See II.2)

The reduction of the double bond can proceed either through process (b) or the alternative initial protonation:

\[
\begin{align*}
\text{ArCH}-\text{CH}-\text{CHCMe}_2\text{OH} & \quad \xrightarrow{\text{e}} \quad \text{ArCH}\text{-CH}-\text{CMe}_2\text{OH} \quad \xrightarrow{\text{ROH}} \quad \text{ArCH}_2\text{CHCMe}_2\text{OH} \\
\text{ArCH}_2\text{CHCMe}_2\text{OH} & \quad \xrightarrow{\text{ROH}} \quad \text{ArCH}_2\text{CH}_2\text{CMe}_2\text{OH}
\end{align*}
\]

The effect of p-OMe, because of charge-destabilisation in the benzylic position is likely to render (29) more important than (30), comparatively to the other examples.

\[
\begin{align*}
\text{MeO} & \quad \text{CH}\text{CHCMe}_2\text{OH} \quad \text{(29)} \\
\text{MeO} & \quad \text{CHCHCMe}_2\text{OH} \quad \text{(30)}
\end{align*}
\]
Protonation may be faster with a more basic anion, although a higher rate of proton-expulsion might also be expected. No very definitive conclusion can be drawn. The isolation of the conjugated hydrocarbon side-chain could be due to a similar effect on charge distribution in the anion.

\[
\text{MeO} \quad \text{MeO}
\]

It is somewhat surprising that the vinylbenzene escapes reduction, but the double bond is probably rather unreactive to electron-addition. The further point, which should be examined further, is why the allylic alcohol is apparently reduced in preference to the hydrocarbon.

The isolation of the conjugated hydrocarbon side-chain could be due to a similar effect on charge distribution in the anion.
This may be possibly due to donation of a proton from the OH, or possibly also to solvation of the radical anion, assisted by the solvation shell of the OH.

The following points are relevant to the results above:

The carbinols were obtained by the action of methylmagnesium iodide on the methyl ester of the corresponding cinnamic acid. The carbinol (26c) cannot be distilled without polymerisation. All the products were identified on the g.l.c. by comparing with authentic specimen.

The reduction of the carbinols with sodium in absence of alcohol result in the corresponding dihydroalcohol (27). The dihydroalcohol used for comparison was made by the palladium-charcoal-catalysed hydrogenation of each carbinol.

The hydrocarbons (15) and (13) were all identified by using the reaction products of the isomerisation reactions involving the olefins (13) (see II.2).

Since products have very different retention times, programmed temperatures (80°-100°, 5% Carbowax) were used for analysis.

The reduction of 1-phenyl-3-methyl-3-hydroxy-but-1-ene (26a) was repeated on a large scale to determine the yield from that type of reaction. The hydrocarbon (15a) and the
alcohol (27a) were obtained in 78% yield of which the former constituted 60%.

1-Heptene

This olefin was prepared by the action of excess magnesium bromide on allyl bromide, \textsuperscript{76} b.p. 94°C (150°C, 10 mm); 1.0 (s, 3H, Me), 1.3 (m, 6H, 2CH\textsubscript{2}), 2.84 (m, 3H, allylic), 4.06 (s, 3H, =CH\textsubscript{2}), 5.16 (s, H). Decahexaene and cross-2-heptene were obtained commercially, redistilled and had their purity checked by GC: 2-heptene: t\textsubscript{R} 9 min; decahexaene: t\textsubscript{R} 6 min (10\%).

1-Phenyl-1-buten-4-one

This was obtained by the action of benzylmagnesium bromide on allyl bromide\textsuperscript{76} b.p. 177°C, t\textsubscript{R} 3 min (150°C, 10 mm); 2.36 (s, 3H, Ph-CH\textsubscript{3}), 3.66 (m, 2H, allylic), 4.98 (m, 2H, =CH\textsubscript{2}), 7.80 (s, CH=), 7.86 (s, 5H, aromatic).

1,5-Hexadiene

This was obtained commercially and redistilled b.p. 50°C, t\textsubscript{R} 2.14 (m, 4H, methylenic), 2.0 (s, 4H, =CH\textsubscript{2}), 1.97 (s, 2H, =CH\textsubscript{2}).

2,3-Dimethyl-1,5-hexadiene

This was made by the condensation of methylallyl chloride over magnesium i.e. by the action of methylmagnesium chloride on methylallyl chloride\textsuperscript{77} b.p. 120°C, t\textsubscript{R} 1.86 (s, 6H, 2Me), 2.16 (s, 6H, methylenic), 2.76 (s, 6H, alkeninic).
II.4 EXPERIMENTAL

The potassium used was purified by cutting it in small pieces and refluxing in anhydrous dioxan.

Unless otherwise stated, all g.l.c. recordings were on a 20% Ucon column.

1-Heptene

This olefin was prepared by the action of butylmagnesium bromide on allyl bromide;\(^76\) b.p. 94°, \(t_R\), 6 min (50°); \(\delta\) 0.9 (t, 3H, Me), 1.3 (m, 6H, 3CH\(_2\)), 2.04 (m, 2H, allylic), 4.96 (m, 2H, =CH\(_2\)), 5.82 (m, CH=).

\(cis\)-2-Heptene and \(trans\)-2-heptene were obtained commercially, redistilled and had their purity checked by g.l.c., \(cis\)-2-heptene \(t_R\) 7 min, \(trans\)-2-heptene \(t_R\) 5 min (50°).

4-Phenyl-but-1-ene

This was obtained by the action of benzylmagnesium bromide on allyl bromide;\(^76\) b.p. 177°, \(t_R\) 3 min (150°, 10% APL); \(\delta\) 2.36 (m, 2H, Ph-CH\(_2\)), 2.66 (m, 2H, allylic), 4.98 (m, 2H, =CH\(_2\)), 5.80 (m, CH=), 7.96 (m, 5H, aromatic).

1,5-Hexadiene

This was obtained commercially and redistilled b.p. 59°, \(\delta\) 2.14 (m, 4H, methylenic), 5.0 (t, 4H, =CH\(_2\)), 5.82 (m, 2H, -CH=).

2,5-Dimethyl-1,5-hexadiene

This was made by the condensation of methallylchloride over magnesium i.e. by the action of methallylmagnesium chloride on methallylchloride;\(^77\) b.p. 137°, \(\delta\) 1.66 (s, 6H, 2Me), 2.16 (s, 4H, methylenic), 4.70 (s, 4H, olefinic).
Action of potassium amide on unsaturated hydrocarbons

The metal (1.6 gms or 0.04 mole) in ammonia (50 ml) was converted to the amide by the catalytic action of ferric nitrate under nitrogen. The hydrocarbon (0.01 mole) was added and the mixture stirred for 2 hours. Then water was added and the product taken up in ether (10 mls). The ether extract was washed thoroughly with water and with brine (once) and dried (MgSO₄). It was then analysed on the g.l.c.

Hept-1-ene after 2 hr gave a product whose g.l.c. (50°) gave three peaks corresponding to trans-hept-2-ene (11%, tR 5 min), hept-1-ene (81%, tR 6 min) and cis-hept-2-ene (8%, tR 7 min). After 4 hr, the percentages of the olefin in the order above were 29%, 48%, and 23% respectively; after 6 hr, these were 38%, 45% and 18% respectively.

4-Phenylbut-1-ene treated as above after 2 hr, gave a product b.p. 175-180° whose g.l.c. (150°, 10% APL) gave three peaks at tR 3 min (58%, 4-phenylbut-1-ene), tR 3.7 min (34%, 1-phenylbut-1-ene) and tR 4.8 min (8%, 1-phenylbut-1-ene). Some polymeric material was present in the products. After 4 hr, the peak at tR 3 min was (52%), at tR 3.7 min was (40%), and tR 4.8 min was (8%). More polymeric material was obtained here. After 6 hr, the peak at tR 3 min was (52%), at tR 3.7 min was (40%) and at tR 4.8 min was (8%). Considerable amount of polymeric material was obtained in this reaction.

2,5-Dimethylhexa-1,5-diene treated as above gave a product b.p. 135-147° whose u.v. spectrum (λmax 251 mm, ε 14,030) showed the reaction product to contain 2,5-dimethylhexa-2,4-diene tR 7 min (70°) after 2 hr. After 4 hr, the percentage of 2,5-dimethylhexa-2,4-diene rose to (70%)
(λ<sub>max</sub> 251 nm, ε 16,100). After 6 hr, only 2,5-dimethyl-hexa-2,4-diene was present (λ<sub>max</sub> 251 nm, ε 23,000). Pure 2,5-dimethylhexa-2,4-diene has λ<sub>max</sub> 251 nm, ε 23,000. The yield of the conjugated diene after 6 hr reaction was 80%.

Hexa-1,5-diene treated as above after 2 hr, gave a product b.p. 58-59° (λ<sub>max</sub> 217 nm, ε 16,170). This represents a 77% presence of hexa-2,4-diene. After 4 hr, the product (λ<sub>max</sub> 217 nm, ε 18,060) contained 86% hexa-2,4-diene. After 6 hr, hexa-2,4-diene was 95% in the product (λ<sub>max</sub> 217 nm, ε 19,950). (Pure hexa-2,4-diene has λ<sub>max</sub> ε 21,000.) The yield of the conjugated product was 90%.

**Preparation of l-phenyl-3-methylbut-1-ene (13a)**

Phenyltertbutylcarbinol was obtained by the grignard reaction of isobutylmagnesium bromide on benzaldehyde. The alcohol (5 g) was dehydrated by heating over KHSO<sub>4</sub> (4 g) in a 25 ml flask and collecting all product up to 210°. This was then washed thoroughly with water and once with brine. The product was dried (MgSO<sub>4</sub>) and distilled to give l-phenyl-3-methylbut-1-ene, 2.5 g, b.p. 42°/0.2 mm, λ<sub>max</sub> 252 nm, ε 10,300; δ 1.08 (d, 6H, Me), 2.47 (m, 1H, methine), 6.42 (m, 2H, olefinic), 7.4 (m, 5H, aromatic), t<sub>R</sub> 11.2 min (80°), m/e 146 (calc for C<sub>11</sub>H<sub>14</sub>, 146), IR showed no OH peak.

**Preparation of l-(o-methoxyphenyl)-3-methylbut-1-ene (13b)**

This was prepared from the corresponding carbinol following the procedure above. In this case the alcohol (5 g) which was a solid was ground together with KHSO<sub>4</sub> (4 g); the mixture was heated and the liquid coming off was collected up to 270°. Treated as above, distillation yielded 2.2 g of product b.p. 90°/1 mm, t<sub>R</sub> 3.1 min (150°), λ<sub>max</sub> 254
nm, ε 16,700, m/e 176 (calc for C_{12}H_{16}O, 176), δ 1.14 (d, 6H, Me), 2.29 (m, 1H, methine), 3.80 (s, 3H, OMe), 6.16 (q, 2H, olefinic), 7.05 (m, 4H, aromatic), IR shows no OH group.

Preparation of 1-(p-methoxyphenyl)-3-methylbut-1-ene (13c)

This was obtained from the corresponding carbinol by the procedure above b.p. 84°/1 mm, tR 3.9 min, λ_{max} 261 nm, ε 44,800, m/e, 176 (calc for C_{12}H_{16}O, 176), δ 1.09 (d, 6H, Me), 2.43 (m, 1H, methine), 3.74 (s, 3H, OMe), 6.12 (m, 2H, olefinic), 6.78 (m, 2H, aromatic), 7.25 (m, 2H, olefinic), IR shows no hydroxy peak.

Reactions of the olefins with potassamide in liquid ammonia

The olefin (6.8 mmoles) was stirred into a solution of potassamide (0.8 mmoles) in liquid ammonia (25 cc). The red colour of the salt was immediately formed in all cases. After stirring for ten minutes, the proton donor (NH₄Cl or tert-BuOH) was added until the red colour of the anion was destroyed. Water was added and the product was taken up in ether (10 cc). After washing with water (2 cc) and brine (once), the ether extract was dried (MgSO₄). The sample was then directly analysed on the g.l.c. (5% carbo wax). In all cases, the new product formed (15) was isolated by preparative g.l.c. and identified by n.m.r.

1-Phenyl-2-methylbut-1-ene (13a) treated as above and using NH₄Cl as proton donor gave unchanged product tR 11.2 min (80°), (32%), and 1-phenyl-3-methylbut-2-ene (15a) (68%), tR 9.8 min. Using tert-butanol as proton donor, the unchanged material was 47% and the new product 53%. The reaction was then repeated increasing the ratio
of base to starting olefin each time (see Table II). The new product, 1-phenyl-3-methylbut-2-ene was the sole product formed when 4 mole equivalents of base to one mole equivalent of starting olefin was used. It was purified by isolation from g.l.c. and identified by H\textsuperscript{1}n.m.r. \(\delta 1.74 \, (d, \, 6H, \, Me), \, 3.33 \, (d, \, 2H, \, methylene), \, 5.34 \, (t, \, 1H, \, olefinic), \, 7.18 \, (m, \, 5H, \, aromatic), \) no selective u.v. absorption. The yield from the last procedure was 60\%.

1-(o-methoxyphenyl)-3-methylbut-1-ene (13b) with one mole equivalent amount of base and \(\text{NH}_4\text{Cl}\) gave unchanged material (70\%) \(t_R\) 3.1 min (150\°) and 1-(o-methoxyphenyl)-3-methylbut-2-ene (30\%, \(t_R\) 2.7 min). Repeating the reaction and increasing the ratio of base to olefin gave increasing amount of the new product which was exclusively formed when the ratio of base was 4 mole to 1 mole equivalent of the starting olefin. The new product was from its n.m.r. \(\delta 1.76 \, (d, \, 6H, \, Me), \, 3.33 \, (d, \, 2H, \, methylene), \, 3.81(s, \, 3H, \, OMe), \, 5.32 \, (m, \, 1H, \, olefinic), \, 7.00 \, (m, \, 4H, \, aromatic), \) 1-(o-methoxyphenyl)-3-methylbut-2-ene (15b). The yield from the last procedure was 65\%.

1-(p-methoxyphenyl)-3-methylbut-1-ene (13c) treated in the same way as described above using 1 equivalent amount of the olefin, was recovered unchanged \(t_R\) 3.9 min, (150\°). When 4 equivalent amount of base was used to one mole equivalent amount of olefin, the unchanged product was 70\% \(t_R\) 3.9 min and the new product (30\%) \(t_R\) 3.5 min using ammonium chloride as the proton donor. The new product 1-(p-methoxyphenyl)-3-methylbut-2-ene isolated on the g.l.c. had \(\delta 1.52 \, (d, \, 6H, \, Me), \, 3.53 \, (d, \, 2H, \, methylene), \, 3.76 \, (s,
3H, OMe), 5.32 (m, 1H, olefinic), 6.78 (m, 2H, aromatic), no selective u.v. absorption.

Reduction of 3-hydroxy-1-phenyl-3-methylbut-1-ene (26a)

The carbinol was made by the action of methylmagnesium iodide (from 2.5 g Mg and 14.8 g methyl iodide) on methyl cinnamate. The product 2.5 g had b.p. 100°/0.01 mm, $\lambda_{\text{max}}$ 252 nm, $\epsilon$ 17,400, $\nu_{\text{max}}$ 3380, 1150 cm$^{-1}$, $\delta$ 1.38 (s, 6H, Me), 2.3 (s, OH), 6.40 (q, 2H, olefinic), 7.16 (m, 5H, aromatic). $t_R$ 6.8 min (150°).

The carbinol (1 g) in ethanol (0.64 g) was added to redistilled liquid ammonia (15 ml) and sodium metal (0.32 g) was added. Reduction was completed within 5 min. The product was taken up in ether, washed with water and dried. It was examined on the g.l.c. and found to contain 1-phenyl-3-methyl-but-2-ene (58%) $t_R$ 9.8 min (80°), and the dihydroalcohol 2-hydroxy-4-phenyl-2-methyl-n-butane (42%). $t_R$ 3.8 min (150°). The two products were identified by comparing with authentic specimens. The butene used for comparison was obtained from isomerisation reactions of 1-phenyl-3-methyl-but-1-ene (13a) described above. The dihydroalcohol was obtained by hydrogenating the unsaturated carbinol over palladium-charcoal and had no u.v. absorptions, $\nu_{\text{max}}$ 3370, 1035 cm$^{-1}$, $\delta$ 1.28 (s, 6H, Me), 1.60 (s, OH), 1.78 (m, 2H, methylenic), 2.70 (m, 2H, benzylic), 7.20 (s, 5H, aromatic). The reaction was repeated on larger scale starting with 20 g of the carbinol. Two fractions of product were isolated (i) b.p. 95°/15 mm (8.5 g) which was 1-phenyl-3-methylbut-2-ene and (ii) b.p. 84°/0.5 mm (6.4 g). This latter compound was the dihydro-
alcohol above (27a). The yield of the products was 78%.

When the carbinol (5 g) was treated with sodium (1.6 g) in liquid ammonia (90 ml), a red colour was obtained which disappeared in 15 min. The only product obtained b.p. 84°/0.5 mm (3 g) corresponded to the dihydroalcohol 2-hydroxy-4-phenyl-2-methyl-but-2-ene (27a).

**Reduction of 3-hydroxy-1-(o-methoxyphenyl)-3-methylbut-1-ene (26b)**

This carbinol was made by the action of methylvanadimagnesium iodide on the corresponding methyl cinnamate, b.p. 108°/0.06 mm, \(t_R\) 3 min (200°), \(\lambda_{max}\) 253 nm, \(\varepsilon\) 15,360, 

\[\nu_{max} 3300, 1155 \text{ cm}^{-1}, \delta 1.42 (s, 6H, Me), 1.84 (s, OH), 3.90 (s, OMe), 6.34 (d, 1H, olefinic), 7.00 (m, 4H, aromatic), 7.40 (q, 1H, OMePhCH=).\]

The carbinol (1.2 g) was treated with sodium and ethanol as described above. The g.l.c. gave two products. The first one \(t_R\) 2.7 min (150°), was 56% and corresponding to 1-(o-methoxyphenyl)-3-methylbut-2-ene and the second \(t_R\) 1.8 min (200°) corresponded to the dihydroalcohol. The identification was done as already described above. The dihydroalcohol 2-hydroxy-4-(o-methoxyphenyl)-2-methyl-n-butane had no selective u.v. absorption, \(\nu_{max}\) 3360, 1050 cm\(^{-1}\), \(\delta\) 1.28 (s, 6H, Me), 1.76 (2H, \(\underline{\text{CH}_2\text{CMe}_2\text{OH}}\)), 2.68 (m, 3H, OH and OMePhCH\(^2\)), 3.69 (s, 3H, OMe), 7.00 (m, 4H, aromatic).

When the carbinol was reduced with sodium in the absence of alcohol, the red colour formed disappeared in 45 min. The only product isolated was the dihydroalcohol (27b).
Reduction of 3-hydroxy-1-(p-methoxyphenyl)-3-methylbut-1-ene (26c)

This carbinol was made by the action of methylmagnesium iodide on the methyl ester of the corresponding cinnamic acid. It could not be distilled without polymerisation. It was obtained as a solid m.p. 40°, $\lambda_{\text{max}}$ 261 nm, $\epsilon$ 20,000, $t_R$ 2.1 min (200°), $\nu_{\text{max}}$ 3400, 1150 cm$^{-1}$, $\delta$ 1.40 (s, 6H, Me), 2.12 (s, OH), 3.80 (s, 3H, OMe), 6.40 (q, 2H, olefinic), 6.90 (m, 2H, aromatic), 7.37 (m, 2H, aromatic).

The carbinol (26c) treated with sodium and ethanol in liquid ammonia in the same way as described above gave three products on the g.l.c. The product $t_R$ 3.9 min, (150°), (8%), corresponded to 1-(p-methoxyphenyl)-3-methylbut-2-ene. The product $t_R$ 2.9 min (200°) corresponded to the dihydroalcohol (27c) which was made by palladium-charcoal catalysed hydrogenation of the carbinol (26c), $\nu_{\text{max}}$ 3380, 1040 cm$^{-1}$, no selective u.v. absorption, $\delta$ 1.30 (s, 6H, Me), 1.80 (m, 2H, $\text{CH}_2\text{CMeOH}$), 2.06 (s, OH), 2.70 (m, 2H, OMePh$\text{CH}_2$), 3.80 (s, 3H, OMe), 6.80 (m, 2H, aromatic), 7.12 (m, 2H, aromatic).

The reduction of the carbinol (27c) in the absence of alcohol gave only the dihydroalcohol. The red colour of the reaction mixture was destroyed in 16 hours.

Preparation of $\alpha\beta$-Non-3-en-2-ol

Hept-1-yne (64 g) was converted to heptynylmagnesium bromide in ether solution, which was condensed with acetaldehyde, giving 70 g of non-3-yn-2-ol, b.p. 58°/0.5 mm. The acetylenic alcohol (35 gms, 1/4 mole) and quinoline (0.5 gms) were dissolved in methanol (100 mls) and hydrogen-
ated over 3.5 gms of Lindlar catalyst until 99% of the theoretical amount of hydrogen had been absorbed. The catalyst was removed by filtration and methanol evaporated off. The residue was dissolved in pentane and washed with dilute acetic acid, and freed from ketonic impurities by washing repeatedly with an aqueous solution of hydroxylamine hydrochloride and sodium acetate. Removal of pentane and distillation gave 27 grams of cis-non-3-en-2-ol, b.p. 69°/3.5 mm. Found m/e 142 (calc for C₉H₁₈O, 142). The g.l.c. shows it to be at least 97% pure. The infra-red spectrum showed no trace of the trans isomer (962 cm⁻¹).

**trans-Non-3-en-2-ol**

Non-3-yn-2-ol (14 gms, 0.1 mole) was added to redistilled liquid ammonia (300 mls) and the solution stirred whilst sodium (7 gm, 0.305 mole) was added gradually. After 1 hour the excess blue colour was destroyed by adding solid ammonium chloride then water. The resulting aqueous solution was extracted with pentane, and the pentane layer washed with water and dried over MgSO₄. Removal of pentane in vacuo and distillation through an 8" Vigreux column gave trans-non-3-en-2-ol (12 gms), b.p. 60°/1.5 mm, m/e 142 (calc for C₉H₁₈O 142). G.l.c. shows no trace of the cis isomer.

**cis-Non-3-en-2-yl Acetate**

cis-Non-3-en-2-ol (6.45 gm) was refluxed for 75 min with pyridine (25 ml) and acetic anhydride (10 ml). The solution was cooled, diluted with water (50 ml) and pentane (20 ml) added. The pentane later was thoroughly extracted with water until the odour of pyridine was imperceptible,
and dried over MgSO₄. Pentane was removed in vacuo, and the residue distilled, the fraction boiling at 58°/1.2 mm, (7 gms, 84%) being collected. This was cis-non-3-en-2-yl acetate, ν_max 1240, 1735 cm⁻¹. Found m/e 184 (calc for C₁₁H₂₀O₂, 184). This was not less than 98% pure, (g.l.c.). An identical method was used to prepare trans-non-3-en-2-yl acetate.

Reduction of cis- and trans-Non-3-en-2-ol

The alcohol (7 gms, 1/20th mole) was dissolved in redistilled liquid ammonia (200 ml) and dry methanol (19.2 gms, 0.6 mole). Lithium (105 moles) was added gradually, and the solution stirred until no blue colour remained (1 hr). Water (200 ml) and pentane (50 ml) were added and the pentane layer separated off and washed 3 times with water. This solution was dried (MgSO₄) and passed through a short column of 'H' alumina (100 gms); pentane was removed by distillation through a Dufton column. The residual nonene mixture was analysed for cis-trans and position isomerism as described. Further elution of the alumina column with ether gave traces of unchanged starting material. The yield of the olefins was 30% for the trans compound and about 29% for the cis compound.

Reduction of cis-Non-3-en-2-yl Acetate

cis-Non-3-en-2-yl acetate (1.47 gms, 0.008 moles) was dissolved in liquid ammonia (60 ml) and dry methanol (1.28 gms, 0.04 moles). Lithium (225 mgs, 0.032 moles) was added, and the solution stirred until no blue colour remained (30 min). Water (50 ml) and pentane (20 ml) were added. The pentane layer was washed thoroughly with
water, dried, and evaporated. The recovered product (1 gm) was analysed on the g.l.c. The procedure was repeated using trans-non-3-en-2-yl acetate. Both procedures gave a yield of about 55% of the nonene mixture.

11.1 Action of AuH₂ on Cyclohexadiene

Examinations have been made of some of the reactions of carbene produced by platinum-carbonyl from cyclohexadiene. These reactions include dehydrogenation, disproportionation, and alkylation. Examples are the dehydrogenation of methylcyclohexene-1,2-diene and of 1-methylcyclohexene-1,2-diene in toluene, the disproportionation of cyclohexene-1,2-diene to benzene and cyclohexene and the reaction of isolated bromide in ammonia with cyclohexene-1,2-diene.

Reductions of benzoid compounds by metals and alcohols in liquid ammonia or saline involve the addition of two electrons and one proton, to give mesomeric systems of
CHAPTER III.

SOME EXAMINATIONS OF CYCLOHEXADIENYL ANIONS.

The reduction of benzenoid compounds by metal ammonia or metal amine solutions has received much attention over the past few years. However, no prior examination has been made of the factors operating when such reductions are carried out under strong basic conditions when the primary reduction products—usually the unconjugated dihydrobenzenoid compound—may be in contact with strongly basic anions for a considerable length of time. Under these conditions, unwanted reaction products may be formed due to a number of factors. Two of such factors—dehydrogenation and disproportionation—have been examined through the action of potassiumamide in liquid ammonia on several dihydrobenzenes.

III.1 Action of KNH$_2$ on Cyclohexadienes

Examinations have been made of some of the reactions of carbanions produced by proton-removal from cyclohexadienes. These reactions include dehydrogenation, disproportionation and alkylation. Examples are the dehydrogenations of 1-methylcyclohexa-1,3-diene and of 1-methylcyclohexa-1,4-diene to toluene, the disproportionation of cyclohexa-1,3-diene to benzene and cyclohexene and the reaction of isobutyl-bromide in ammonia with cyclohexa-1,4-diene.

Reductions of benzenoid compounds by metals and alcohols in liquid ammonia or amine involve the addition of two electrons and one proton, to give mesomeric anions of
the type (d)\(^7\) which are kinetically protonated predominantly to form the unconjugated diene such as (e).

It has been postulated\(^{32,33}\) and there is considerable evidence\(^{32}\) for, protonation at point of highest charge density in any mesomeric anion. In the case of U-shaped anions, as in benzene case, this is in the middle of the system\(^8\). As pointed out earlier, the view of irreversible protonation or alkylation at the point of highest charge density holds if the transition state of the reaction is highly polarised as is frequently true for addition of protons from fairly acidic sources to carbanions and also of readily polarisable halides in mesomeric anion alkylation processes\(^{32,34}\).

Under conditions where proton-addition is reversible, thermodynamically more stable conjugated isomers would be expected. It was shown\(^{33}\) that 1-methoxycyclohexa-1,4-diene
(f) and 1-methoxycyclohexa-1,3-diene (h) can be equilibrated in favour of the latter through the salt (g). Reaction of either (f) or (h) with excess of potassamide in ammonia generated (g), converted by kinetic protonation into (f). The OMe has an acidifying influence, and the salt from 1,3-dimethoxycyclohexa-1,4-diene was efficiently alkylated in connection with steroid synthesis. Other substituents such as Me may not have a definitive effect on acidity and both 1-methylcyclohexa-1,4-diene and 1-methylcyclohexa-1,3-diene could give mixtures of salts by proton abstraction from several positions.

To examine further the situation, the products of reactions with potassamide in ammonia of several cyclohexadienes and related compounds have been examined and the results are given below:

2. RESULTS.

**TABLE 1.**

<table>
<thead>
<tr>
<th>DIENES</th>
<th>KNH₂ moles equiv.</th>
<th>Reaction Time hr.</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclohexa-1,3-diene</td>
<td>3</td>
<td>2</td>
<td>benzene 53%; cyclohexene 47%</td>
</tr>
<tr>
<td>Cyclohexa-1,4-diene</td>
<td>3</td>
<td>2</td>
<td>benzene + cyclohexene 15%; cyclohexa-1,4-diene 85%</td>
</tr>
<tr>
<td>Cyclohexa-1,4-diene</td>
<td>12</td>
<td>3</td>
<td>benzene 50%; cyclohexene 19%; cyclohexa-1,4-diene 31%</td>
</tr>
<tr>
<td>DIENES</td>
<td>$\text{KMN}_2$ mole equiv.</td>
<td>Reaction Time (hr.)</td>
<td>PRODUCTS</td>
</tr>
<tr>
<td>--------------------------------</td>
<td>-----------------------------</td>
<td>---------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>1-Methylcyclohexa-1,4-diene</td>
<td>3</td>
<td>2</td>
<td>toluene 83%; 1-methylcyclohexene 10%; 3- and/or 4-methylcyclohexene 7%.</td>
</tr>
<tr>
<td>1-Methylcyclohexa-1,3-diene</td>
<td>3</td>
<td>2</td>
<td>toluene 90%; methylcyclohexenes 10%.</td>
</tr>
<tr>
<td>2-Methyl-5-isopropyl-cyclohexa-1,3-diene</td>
<td>4</td>
<td>6</td>
<td>1-methyl-4-isopropylbenzene 47%; unchanged material 53%.</td>
</tr>
<tr>
<td>2-Methyl-5-isopropyl-cyclohexa-1,3-diene</td>
<td>4</td>
<td>24</td>
<td>1-methyl-4-isopropylbenzene 100%.</td>
</tr>
<tr>
<td>1,5-Dimethylcyclohexa-1,4-diene*</td>
<td>3</td>
<td>6</td>
<td>1,3-dimethylbenzene (m-xylene) 100%.</td>
</tr>
<tr>
<td>1,3-Dimethylcyclohexa-1,3-diene*</td>
<td>3</td>
<td>6</td>
<td>1,3-dimethylbenzene 80%; unchanged material 20%.</td>
</tr>
<tr>
<td>1,4,5,8-Tetrahydro-naphthalene</td>
<td>4</td>
<td>3</td>
<td>1,2,3,4-tetrahydro-naphthalene 37%; Napthalene 10%; 1,2,3,7,8,9-hexahydronaphthalene 12%; unchanged material 35%; unidentified product 6%.</td>
</tr>
<tr>
<td>DIENES</td>
<td>KNH₂ mole equiv.</td>
<td>Reaction Time hr.</td>
<td>PRODUCTS</td>
</tr>
<tr>
<td>----------------------------</td>
<td>-----------------</td>
<td>-------------------</td>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td>1,4,5,8-Tetrahydro-</td>
<td>4</td>
<td>6</td>
<td>1,2,3,4-tetrahydro-naphthalene 33%;</td>
</tr>
<tr>
<td>naphthalene</td>
<td></td>
<td></td>
<td>Naphthalene 24%;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1,2,3,7,8,9-hexahydronaphthalene 27%;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>unchanged material 16%.</td>
</tr>
<tr>
<td>1,2,3,4,5,8-Hexahydro-</td>
<td>4</td>
<td>6</td>
<td>1,2,3,4-tetrahydro-naphthalene 84%;</td>
</tr>
<tr>
<td>naphthalene</td>
<td></td>
<td></td>
<td>1,2,3,7,8,9-hexahydronaphthalene 15%;</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1,2,3,4,5,6,7,8-octahydronaphthalene &lt;1%.</td>
</tr>
</tbody>
</table>

* These results were obtained by earlier workers¹⁶ and the ratio of products in the case of 1,3-dimethylcyclohexa-1,3-diene was obtained from ultra-violet absorption measurements and not from g.l.c. Not recorded on the table is the reaction of cyclohexa-1,3-diene and benzophenone (9) which we have found under the influence of KNH₂ in ammonia to give benzene (38%) and benzhydrol (62%) and only a trace of cyclohexene. The products were identified on the g.l.c. by comparison with authentic specimen.
The results were monitored by g.i.c. and mass spectra. The analyses quoted are the proportions in the total products deduced from g.i.c. data. The quantities of 9,10-dimethylanthracene used in each diene case and the hydrodesulfurization procedure were the same in all cases except in one which might be due to low solubility rather than to reactivity. Structure assignments to the products were in most cases done by comparing the retention times on the g.i.c. with an authentic specimen which was synthesized or was commercially obtained.

At the end of each reaction, the product was taken up in ether, washed with water, dried, and examined immediately on the g.i.c.

A curious common theme to all reactions was that hydrogenation of the products observed in solvent was not to be expected, but it would indicate that only disproportionation occurred. The reaction involving cyclohexene-1,3-diene (15, 16) is that in which equal molar quantities of cyclohexene and benzene should be produced. But since the latter predominated, the disproportionation could only take place through dehydration. Another interesting feature in the relative ease of subsequent reactions in the 1,3-diene quantitation...
The results were monitored by g.l.c., 'H n.m.r., ultraviolet and mass spectra. The analyses quoted are the proportions in the total products deduced from g.l.c. data. The quantities of KNH₂ quoted were used on one equivalent quantity of each diene. Some of the hydrocarbons were not very soluble in ammonia, and unreacted material in some cases might be due to low solubility rather than to low reactivity.

Structure assignments to the products were in most cases done by comparing the retention times on the g.l.c. with an authentic specimen which was synthesised or was commercially obtained.

At the end of each reaction, the product was taken up in ether, washed with water, dried, and examined immediately on the g.l.c.

A feature common to all the results was that dehydrogenation was observed in every reaction. At first sight, it would seem that only disproportionation occurred in the reaction involving cyclohexa-1,3-diene (1), if that is true, calculation shows that

\[
\begin{align*}
\text{cyclohexa-1,3-diene} & \rightarrow \text{cyclohexene} + \text{benzene} \\
\end{align*}
\]

equal mole quantities of cyclohexene and benzene should be produced. But since the latter predominated, the explanation could only come through dehydrogenation. Another interesting feature is the relative ease of the dehydrogenation of 1-methylcyclohexa-1,4-diene which was quantitatively
dehydrogenated (with small disproportionation) under the conditions above. Another unconjugated diene (13) dehydrogenated readily.

The substituted conjugated cyclohexa-1,3-dienes e.g. 1-methylcyclohexa-1,3-diene, 1,3-dimethylcyclohexa-1,3-diene all dehydrogenated for the most part.

Cyclohexa-1,4-diene (4) showed less willingness to dehydrogenate or disproportionate compared with its substituted or conjugated counterparts above.

In the reaction of 1,4,5,8-tetrahydronaphthalene (16), the preponderance of 1,2,3,4-tetrahydronaphthalene (tetralin) indicated that isomerisation was the main process but considerable disproportionation also occurred. The original 1,4,5,8-tetrahydroderivative must lose 4H in forming naphthalene, and since the hexahydroderivatives requires the addition of 2H, the balance of products indicates that little if any of the naphthalene was formed by direct loss of hydride. The reaction of 1,2,3,4,5,8-hexahydronaphthalene showed trace of disproportionation by giving very little 1,2,3,4,5,6,7,8-octahydronaphthalene; hydride loss predominated in this instance; naphthalene and 1,2,3,4-tetrahydronaphthalene were both identified on the g.l.c. by comparing them with authentic specimens which were readily available. Naphthalene had $t_R$ 33 min and 1,2,3,4-tetrahydronaphthalene, had $t_R$ 19.5 min (150°, 20% carbonwax).

The hexahydronaphthalene (18) was identified from its n.m.r. spectrum which showed 3 olefinic protons $\delta$ (CDCl$_3$) 5.59, 2H and 6.0, 1H, m/e, 134 (C$_{10}$H$_{14}$) and u.v. spectrum $\lambda$ 236 nm, $\epsilon$ 15,100. (Literature gave $\lambda$ 236 nm, $\epsilon$ 15,140)
This hexahydronaphthalene (18) was also synthesised\textsuperscript{54} and was identical to that obtained in the reaction product here ($t_R$ 14.9 min (50°)).

1,2,3,4,5,6,7,8-octahydronaphthalene (21) was identified by comparing with an authentic specimen made by lithium ethylamine reduction of naphthalene.\textsuperscript{86}

Full details on the mechanisms and significance of the above results are discussed below:

DISCUSSION.

The isomerisations, dehydrogenations and disproportionations observed in the results above are pertinent to the study of products of metal-ammonia reductions if conditions are basic enough to generate the required carbanions. These factors are now discussed in detail.

DISPROPORTIONATION:

The results above (Table 1) show that it has now been found that the action of a strong base such as potassamide in liquid ammonia promotes the disproportionation of cyclohexadienes to benzene and cyclohexene, thus confirming the earlier deduction that cyclohexa-1,3-diene disporportionates in this way\textsuperscript{16}. The mechanism probably involves the attack of the carbanion generated on the starting material as illustrated below:

\begin{equation}
\text{Cyclohexadiene} + \text{NH}_2 \rightleftharpoons \text{Carbanion} + \text{NH}_3
\end{equation}
That hydride transfer is involved (step ii) is supported by the fact that benzene and benzhydrol were produced when cyclohexa-1,3-diene was added to potassamide solution in liquid ammonia followed by benzophenone in equimolecular proportions.

Base catalysed disproportionation of cyclohexadienes into benzene and cyclohexene in dimethylsulphoxide and of 1,4-dihydronaphthalene into naphthalene and 1,2,3,4-tetrahydronaphthalene in the same medium were studied earlier.

Carbon-carbon hydride transfers are well known in acid media and are important in hydrocarbon conversions such as isomerisation and alkylation. However, very little work has been done in the area of base-catalysed carbon-carbon hydride transfers. Pines reported several examples of disproportionations involving hydride transfers using various sodium catalysts in which the reaction system is clearly heterogenous and the nature of the reactive intermediate dubious.

Kinetics of disproportionation of cyclohexa-1,3-diene
was studied by Schriesheim et al. This involved the action of potassium tert-butoxide in dimethylsulfoxide on the diene. The result observed is presented below:

\[ \frac{(C_0 - C)}{C} \]

\[ \text{Time Hours} \]

Co = Initial concentration of cyclohexadiene

C = Concentration of cyclohexadiene at time t

These observed kinetics lead to the postulation of a mechanism where hydride transfer was considered rate determining i.e.

\[ \text{slow} \]

\[ \text{fast} \]
Since no cyclohexene is produced in the reaction of cyclohexa-1,3-diene and benzophenone in the present work, it follows that the latter is a much better hydride acceptor. The stability of the intermediate anion is also probably important and

![Chemical structure](image)

will be much more stable than the cyclohexenyl anion because one negative charge is located on oxygen in the former. In the base-catalysed disproportionation studies in dimethylsulphoxide, using equimolar quantities of butadiene and cyclohexadiene, cis- and trans-2-butene were formed.

![Chemical reaction](image)

The rate of butene formation was faster than that of cyclohexene indicating that butadiene was a preferred hydride acceptor as compared to cyclohexadiene. Anthracene and ace-naphthalene were also found to be efficient hydride acceptors, resulting in the formation of the hydrogenated analog, 9,10-dihydroanthracene and acenaphthene.
In this case the hydrogenated aromatics were produced to almost the total exclusion of cyclohexene.

Thus very roughly it is possible to equate the effectiveness of the hydride acceptor with the stability of the anion formed during hydride transfer. Butadiene was found better than cyclohexadiene because it gives a stable anion containing CH₂; anthracene and acenaphthalene were found extremely effective because the resulting anions were stabilized through the aromatic system. The anion derived from benzophenone above is better stabilized than the cyclohexenyl anion because the charge is located on the electronegative atom, oxygen.

This may then explain why substituted cyclohexadienes such as 1-methylcyclohexa-1,3-diene (6) and 1,3-dimethylcyclohexa-1,3-diene (15) do not disproportionate. Hydride transfer as proposed above should involve anions
in the case of (6) and (15) respectively. The inductive effects of the methyl group and steric inhibition of resonance and solvation are likely factors to reduce the stability of such anions thus making the cyclohexadienes (6) and (15) inefficient hydride acceptors.

Other dienes such as cyclohexa-1,4-diene and 1-methylcyclohexa-1,4-diene cannot act as efficient hydride acceptors since anions of the type

![Chemical structure](image)

which should be involved in the carbon-carbon transhydrogenation are in effect probably similar to an ordinary double bond unless there is some overlap of orbital between the negative charge and the double bond.

![Chemical structure](image)

The results however indicate that cyclohexa-1,4-diene itself disproportionated to some extent. This may be explained upon the fact that the 1,4-diene itself must in this case establish equilibrium with the 1,3-diene by protonation of the salt by the ammonia but only very slowly.
The deduction by Schriesheim and co-workers\textsuperscript{87} that the isomerisation between 1,3- and 1,4-cyclohexadienes was sufficiently rapid so that either isomer would lead to the same result is therefore inconsistent with the results of the present research.

Dehydrogenation Reactions

The regeneration of the aromatic material as the main reaction in the action of KNH\textsubscript{2} in liquid ammonia on a compound such as 1-methylcyclohexa-1,4-diene (5) can be explained on the basis of hydride loss from the mesomeric anion generated.
The result shows that 1-methylcyclohexa-1,4-diene dehydrogenates more readily than cyclohexa-1,4-diene. It was earlier deduced\textsuperscript{16} that 1-methylcyclohexa-1,4-diene dehydrogenated to the aromatic material by potassamide in ammonia and it was further pointed out\textsuperscript{82} that while the more acidic 1,3-dimethoxycyclohexa-1,4-dienes gave very stable salts, 1-methoxycyclohexa-1,4-dienes were dehydrogenated after being left for several hours.

The above information shows that the tendency to lose hydride seems to be in an inverse relationship to the acidity of the 1,4-diene from which the mesomeric anion is derived. This means that the more stable the carbanion generated, the less is the tendency to dehydrogenate. The dehydrogenation could be due to destabilisation of the anion by the substituent (for solvation and possibly inductive reasons) and consequently larger free energy change in hydride loss and probably greater rate.

The order of acidities of cyclohexa-1,4-dienes can be deduced from the information above.

\[ R = \text{OMe} > H > \text{Me}. \]  
This order also corresponds to that observed by qualitative examinations of the acidities of the dienes by inspection of the colour of the anion due to a fixed proportion of amide. With \( R = \text{OMe} \) or \( H \), the salts are stable for considerable periods. With \( R = \text{Me} \), decomposition rapidly occurs with loss of hydride.
Relative Stabilities of Some Pentadienyl Carbanions.

Since much mention has been made of the stabilities of the intermediate carbanions above, it is important to discuss the factors affecting the stability of such anions.

Pentadienyl carbanions have been proposed as intermediates in nucleophilic aromatic substitution in Birch reductions and in base catalysed isomerisation of 1,3- and 1,4-dienes. The factors affecting pentadienyl carbanion stability will strongly influence the rates of reactions in which the rate determining transition state resembles the pentadienyl carbanion (e.g. base-catalysed diene isomerisations).

Birch and co-workers have obtained qualitative evidence that alkyl groups destabilize pentadienyl carbanions, and they attribute this more to steric hindrance to solvation than to the inductive effect of the alkyl group.

It was pointed out later that the shapes of pentadienyl carbanions have effects on their stabilities.

Through studies on isomerisation of hexahydronaphthalene, it was found that the U-shaped pentadienyl carbanions are more stable than other planar types with similar substitution by about 2-5 kcal/mole. It was suggested that the stabilisation might be due to the ease of solvation of the U-shaped carbanions by metal cations (due to the placement of $M^+$) or to $\pi$-orbital overlap.
The mechanism whereby 1,2,3,4,5,8-hexahydronaphthalene (20) gave 1,2,3,7,8,9-hexahydronaphthalene (18) (see Table 1, above) as one of its products can be written through the various pentadienyl carbanions above.

(a) There is loss of proton by action of base.

(b) There occurs addition of proton from ammonia.

(c) There is loss of hydride to a conjugated diene.

(d) There is loss of hydride as an ion.

(e) This is isomerisation by a combination of (a) and (b).

The fact that 1,2,3,4-tetrahydronaphthalene (17) was the main product, and 1,2,3,4,5,6,7,8-octahydronaphthalene (21) was obtained in trace amounts, indicates that the main path of the reaction is that through step (d). That dehydrogenation is the main process here indicates that the acidity of the diene (20) is not high and thereby producing unstable carbanion. In support of the last statement, it was quantitatively shown that the rate constant of isomerisation of cyclohexa-1,4-diene to cyclohexa-1,3-diene (via 24) with potassium t-amyloxide at 95° was larger than that for the isomerisation of (20) to (30) via (25) by a
factor of 22.1 corresponding to a difference in $\Delta F^+$ for the two reactions of 1.75 kcal/mole. The destabilisation of the anion (29) was pointed out to be primarily due to the alkyl substituent on carbon 1 of the pentadienyl system.

The isolation of the hexahydronaphthalene (18) other than (30) is consistent with the finding that transoid dienes were found much more stable than cisoid ones (see Chapter I).

The results (Table 1) show that isomerisation is the main process in the action of potassamide in liquid ammonia on 1,4,5,8-tetrahydronaphthalene. Using the consideration of relationships between structure and acidities in allylic hydrocarbon acids already developed, an acceptable series of bond migrations through mesomeric anions can be written to give the intermediates necessary in the above reactions.
(a) There is loss of hydride, either as an ion or by transfer to a conjugated diene.
(b) This represents gain of 2H by donation as above.
(c) There occurs loss of a proton by action of base.
(d) There is addition of proton from ammonia.
(e) This is isomerisation by combination of (c) and (d).

An alternative mechanism for the production of 1,2,3,4-tetrahydronaphthalene (17) through (32) is
This last mechanism cannot be the major path since it cannot explain the ratio of naphthalene to 1,2,3,4-tetrahydro-naphthalene but at least some of the products can come through this path. A similar mechanism for the disproportionation of 1,4-dihydronaphthalene by the action of potassium tert-butoxide in dimethylsulphoxide was proposed.88
Importance of Results.

The dehydrogenations, disproportionations and isomerisations observed are very important in understanding some of the observed secondary processes in Birch reductions. When these reductions are carried out under conditions which are basic enough to generate the mesomeric anions of the type above, secondary reduction products may be obtained due to the factors above.

A good case to consider here is that of naphthalene. In the reduction of naphthalene with sodium in ammonia at the boiling point \(^9^6\), it was found that four atoms of sodium were taken up per molecule, the eventual product being 1:2:3:4-tetrahydronaphthalene. It was assumed that a tetrasodium addition product was formed. Later \(^9^7\), it was shown that the initially-formed sodium addition product abstracts protons from the ammonia to give 1:4-dihydronaphthalene (32) which is isomerised by the sodium amide
formed in the process to the conjugated 1,2-dihydronaphthalene through the sodium salt. The 1:2-dihydronaphthalene is then reduced further by two more sodium atoms to tetrahydronaphthalene.

\[
\begin{array}{c}
\text{(19)} \quad \text{\rightarrow} \quad \text{(32)} \quad \text{\rightarrow} \quad \text{(33)} \\
\end{array}
\]

It is now clear that there is an alternative mechanism to this. The present work indicates that the generation of an anion such as (33) will lead to disproportionation by hydride transfer from (33) to (32) or (34).

\[
\begin{array}{c}
\text{(19)} \quad \text{\rightarrow} \quad \text{(34)} \\
\end{array}
\]

The production of tetrahydrobenzenes from benzenes by the action of calcium hexammine, Ca(NH₃)₆, observed by Kazanskii and his co-workers⁹⁸-¹⁰⁰, were explained on the basis of secondary reductions⁷⁸. The primary products were undoubtedly the same as those obtained from the sodium-
alcohol-ammonia reduction - (unconjugated dihydrobenzenes) -
and these were then conjugated probably by the influence of
calcium amide, and then further reduced. The reduction of
isolated benzene rings to the tetrahydrobenzenes is now also
explicable in terms of hydride transfer. The conjugation
of a dihydrobenzene probably by calcium amide as suggested
above produces the conjugated diene which can accept hydride
from the intermediate mesomeric anion to generate the tetra-
hydroproduct as discussed earlier.

The use of lithium in different amines on some aromatic
hydrocarbons gave tetrahydro-derivatives\(^5\). Such results have
not been easy to explain\(^82,101\). It is however now evident
that the disproportionation can lead to the formation of
cyclohexene from benzene if cyclohexadienyl anion is gener-
ated as it could have been under the experimental conditions.

In the reduction processes, if the hydride elimination
(dehydrogenation) is sufficiently rapid compared with the
protonation of an anion of the type

\(\begin{array}{c}
\text{(which is almost certainly an intermediate in the aromatic}
\text{reductions), the overall result will be the catalytic}
\text{evolution of hydrogen gas, the aromatic material being}
\text{recovered unchanged. In other words overall reduction may}
\text{be aborted and the extent of reversal could differ with the}
\text{structure of the anion. The anion (37) for example is quite}
\end{array}\)
stable, probably more so than (38) which could therefore undergo reversal to a greater extent. In cases where different anions result from protonation in two different ortho or meta-positions in substituted systems, the final reduction product could therefore be decided not by the relative rates of initial protonation in the alternative positions but by rates of reversal. In simple cases the efficiency of reduction is high and the effect is unlikely to be important, but it might also be an explanation of the difference in rates of reduction of (39) and (40). The former is reducible in good yield to the 1,4-dihydro-derivative with only a small excess of lithium and ethanol in ammonia, the latter requires about 80 equivalents of metal with ethanol to produce 40-50% yield of the 3,9-dihydro-derivative, although the metal rapidly disappears and hydrogen is evolved. The intermediate anion (41) may be unstable, expelling a hydride ion to regenerate (40), leading to inefficient reduction.

Dehydrogenation and disproportionation may be in part responsible for some of the divergent results obtained in the
reduction of polycyclic aromatic hydrocarbons. In the case of dihydrobenzenes, carbanion formation appears to require the presence of amide anion, but with more acidic reduced polycyclic aromatic compounds even alkoxide anion might be sufficient to cause further reactions, particularly if the reaction is prolonged.

The reduction of polycyclic compounds are sometimes quite complex, the products depending on the exact conditions and the ratio of reducing agent used. Even naphthalene which on complete reduction with metal and alcohol in ammonia produces 1,4,5,8-tetrahydronaphthalene\(^{42,103}\) cannot be stopped at the 1,4-dihydro-stage with any degree of efficiency, despite the slower intrinsic rate of reduction of the dihydro-compound. In these reductions, the products obtained are likely to be sensitive to exact experimental conditions one of which is the period of the time involved and whether the mixture is left after metal is all consumed. Under such a condition, dehydrogenation and disproportionation are factors likely to alter the nature of the reduction products.

There is therefore no doubt that the result of the present study is at least significant both experimentally and theoretically in throwing more light on the nature of secondary processes that may accompany Birch reductions of aromatic compounds. The factors discovered in the present work may lead to unwanted secondary reaction products and an understanding of these factors will provide methods of eliminating them and reducing the amount of unwanted products accompanying these reductions.
III.2 Alkylation Reactions.

Further information as to the nature of anions produced may be obtained by examining the products of alkylation, although the situation is complicated by their mesomeric nature and the possibility of alkylation in more than one position.

The results under Table 1 (III.1) suggested that cyclohexa-1,4-diene produced a relatively stable anion in $\text{KNH}_2 - \text{NH}_3$ and in line with that, the cyclohexa-1,4-dienyl anion was alkylated. The results of the alkylation reactions is given below:

**Table II**

<table>
<thead>
<tr>
<th>DIENE</th>
<th>ALKYL HALIDE</th>
<th>$\text{KNH}_2$ MOLE EQUIV.</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Cyclohexa-1,4-diene</td>
<td>methyl</td>
<td>2</td>
<td>3,6-dimethylcyclohexa-1,4-diene (42), 80%; 5,6-dimethylcyclohexa-1,4-diene (43), 20%.</td>
</tr>
<tr>
<td></td>
<td>iodide</td>
<td>(2 mole equiv.)</td>
<td></td>
</tr>
<tr>
<td>B. Cyclohexa-1,4-diene</td>
<td>isopropyl</td>
<td>1</td>
<td>3-isopropylcyclohexa-1,4-diene (44), 70%; 5-isopropylcyclohexa-1,3-diene (45), 30%.</td>
</tr>
<tr>
<td></td>
<td>bromide</td>
<td>(1 mole equiv.)</td>
<td></td>
</tr>
<tr>
<td>C. Cyclohexa-1,4-diene</td>
<td>isobutyl</td>
<td>2</td>
<td>3-isobutylcyclohexa-1,4-diene (46), 32%; 5-isobutylcyclohexa-1,3-diene (47), 8%; 5,6-diisobutylcyclohexa-1,3-diene (49), 20%;</td>
</tr>
<tr>
<td></td>
<td>bromide</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DIENE</td>
<td>ALKYL HALIDE</td>
<td>KNH₂ MOLE EQUIV.</td>
<td>PRODUCTS</td>
</tr>
<tr>
<td>-------</td>
<td>--------------</td>
<td>------------------</td>
<td>----------</td>
</tr>
<tr>
<td>C.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>D. 3-Isobutyl-cyclohexa-1,4-bromide (46)</td>
<td>isobutyl</td>
<td>2</td>
<td>3,6-diisobutylcyclohexa-1,4-diene (48), 32%; 2,5,6-triisobutylcyclohexa-1,3-diene (50), 8%.</td>
</tr>
<tr>
<td>E. 1-Methyl-cyclohexa-1,4-iodide (5)</td>
<td>methyl</td>
<td>2</td>
<td>2,3-dimethylcyclohexa-1,4-diene (53), 64%; 1,3-dimethylcyclohexa-1,4-diene (54), 36%.</td>
</tr>
<tr>
<td>F. 1,4-Dihydrobenzoic acid bromide (51)</td>
<td>n-butyl</td>
<td>4</td>
<td>1,n-butyl-1,4-dihydrobenzoic acid (51).</td>
</tr>
</tbody>
</table>
In order to determine whether this product could cause conjugation with 5-methylcyclohexa-1,4-diene and 2,4-dimethylcyclohexa-1,4-diene were examined under the experimental conditions here.

3. Structure (44) was confirmed from its pmr which gave 6 aliphatic protons (6.91) and also in 1H by nmr analysis. The compound (45) was shown to be present from the fact that the reaction product, after dehydrogenation, afforded 5-methylcyclohexa-1,4-diene, which was obtained in 50% yield.
In order to check whether this reagent itself can cause conjugation of cyclohexa-1,4-dienes, the reaction with 1-methylcyclohexa-1,4-diene and 2,4-dimethylcyclohexa-1,4-diene were examined. No phthalic ester resulted under the experimental conditions here.

B. Structure (44) was assigned from its n.m.r. which gave 4 olefinic protons (δ 5.66) and also had m/e 122 (Calc for C₉H₁₄, 122), no u.v. absorption. The compound (45) was shown to be present from the fact that the reaction product mixture had λ_{max} 259 nm, ε 1200. The reaction product mixture gave (by Alder-Rickert reaction) dimethylphthalate (15%) yield. The reaction product was dehydrogenated (Pd-C) to isopropylbenzene which was obtained in 50% yield.
C. This reaction gave products separated into four fractions by fractional distillation. Fraction (1) b.p. 60°/16 mm had $t_R$ 2.2 min (80%) and $t_R$ 3 min (30%). The product at $t_R$ 2.2 min was separated by preparative g.l.c. and showed no u.v. absorption. It had 4 olefinic protons ($\delta$ 5.73) m/e 136 ($C_{10}H_{16}$). Dehydrogenation of this fraction gave isobutylbenzene. The product $t_R$ 2.2 min therefore corresponded to 3-isobutylcyclohexa-1,4-diene (46). The compound (47) was shown to be present in the fraction from the presence of a peak $t_R$ 3 min constituting 20% of the fraction. Alder-Rickert reaction on the mixture gave dimethylphthalate (20% yield). The fraction further had $\lambda_{max}$ 259 nm, $\varepsilon$ 1500. The yield of isobutylbenzene was 28%. This yield increased to 50% when one equivalent of each reagent was employed.

The second fraction b.p. 110°/20 mm had $t_R$ 6.2 min (150°) $\lambda_{max}$ 260 nm, $\varepsilon$ 8900, m/e 192 ($C_{14}H_{24}$), n.m.r. showed 4 Me peaks ($\delta$ 0.09) and 4 olefinic protons ($\delta$ 5.7). The fraction (2 g) was converted into dimethylphthalate (1.5 gms). All these evidences support the structure assigned to (49). The yield of this product was 10%.

The third fraction b.p. 60°/0.5 mm had $t_R$ 9 min (150°) and contained only 3,6-diisobutylcyclohexa-1,4-diene (48) from the n.m.r. spectrum evidence which gave 4 Me peaks ($\delta$ 0.91, 12H), and four olefinic protons ($\delta$ 5.63), m/e 192 ($C_{14}H_{24}$), no u.v. absorption and no Alder-Rickert reaction product. The yield was 17%.

The fourth fraction b.p. 93°/0.5 mm had $t_R$ 21 min, m/e 248 ($C_{18}H_{32}$), $\lambda_{max}$ 263 nm, $\varepsilon$ 7000, $\delta$ 0.91 (m, 18H, CMe$_2$),
5.29 (m, 1H, =CH), 5.69 (m, 2H, HC=CH); the Alder-Rickert product had m/e 250 (C_{14}H_{18}O_4) corresponding to a dimethyl isobutylphthalate. These evidences support the assigned structure (50) corresponding to 2,5,6-triisobutylcyclohexa-1,3-diene. The yield was 3%.

D. When the product from first fraction above (C) was treated again with 2 mole equivalents of KNH₂ and isobutylbromide in liquid ammonia, it gave unchanged material (35%), the diene (48) (40%), and 5,6-diisobutylcyclohexa-1,3-diene (49) (25%). These products were identified on the g.l.c. by comparing with the reaction products above.

E. The methylation of 1-methylcyclohexa-1,4-dienyl anion in liquid ammonia gave a product b.p. 135° which gave only one peak on the g.l.c. The methylated product showed no u.v. absorption. Dehydrogenation gave o-xylene (64%) and m-xylene (36%). From this evidence and from the mechanism of the methylation discussed later, the product contained about (64%) of 2,3-dimethylcyclohexa-1,4-diene (53) and 36% of 1,3-dimethylcyclohexa-1,4-diene (54). The yield of the xylenes was (34%).

F. The alkylation of a number of derivatives of 1,4-dihydrobenzoic acids had been carried out earlier. The butylation of 1,4-dihydrobenzoic acid here gives only one product assigned the structure (52) from its n.m.r. spectrum δ 0.59 (t, 3H, Me), 1.3 (m, 4H, CH₃CH₂Me), 1.7 (m, 2H, CH₂-CH₂CH₂Me), 2.64 (m, H₂C-C=), 5.82 (m, HC=CH), 12.08 (s, COOH), m/e 180 (C₁₁O₂H₁₆, 180); no selective u.v. absorption in the region 2200-2800 nm. The yield was 41%.

More information on the nature of the anions produced was obtained by further examining the products of alkylation...
of anions derived from naphthalene; while the anions above had been generated by base-catalysed proton removal, the anions here had been obtained by electron addition by a metal. That is, the naphthalene was reductively alkylated. 2-Methoxynaphthalene was used so that the results will add further information on the substituent effects of the methoxy group. Although dianions are probably generated in the reactions below, final products are derived from mono-anions (see discussions below).

RESULTS.

TABLE III.

Reductive methylation of methyl-β-naphthyl ether (55)

<table>
<thead>
<tr>
<th>Methyl-β-naphthyl Ether Conc. in moles</th>
<th>Metal Conc. in moles</th>
<th>Ammonia mls</th>
<th>Cosolvent ml</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A .034</td>
<td>Na, 0.12</td>
<td>150</td>
<td>thf, 75</td>
<td>1-methyl-2-tetralone, 47%; 1,4-dimethyl-2-tetralone, 34%; tetralin, 6%; others*, 13%.</td>
</tr>
<tr>
<td>B .034</td>
<td>Na, 0.12</td>
<td>150</td>
<td>DME, 75</td>
<td>1-methyl-2-tetralone, 49%; 1,4-dimethyl-2-tetralone, 36%; others*, 15%.</td>
</tr>
<tr>
<td>C .034</td>
<td>Na, 0.12</td>
<td>150</td>
<td>thf, 15</td>
<td>1-methyl-2-tetralone, 15%; 1,4-dimethyl-2-tetralone, 52%; tetralin 13%; others*, 20%.</td>
</tr>
<tr>
<td>Methyl-8-</td>
<td>Metal Conc. in</td>
<td>Ammonia</td>
<td>Cosolvent</td>
<td>PRODUCTS</td>
</tr>
<tr>
<td>naphthyl Ether</td>
<td>moles</td>
<td>mls</td>
<td>ml</td>
<td></td>
</tr>
<tr>
<td>----------------</td>
<td>---------</td>
<td>--------</td>
<td>---------</td>
<td>----------</td>
</tr>
<tr>
<td>D .034 Na, 0.18</td>
<td>150 thf, 15</td>
<td>1-methyl-2-tetralone, 22%; 1,4-dimethyl-2-tetralone, 55%; tetralin, 3%; others*, 20%.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E .034 Na, 0.31</td>
<td>150 ether, 75</td>
<td>1-methyl-2-tetralone, 35%; 1,4-dimethyl-2-tetralone, 28%; tetralin, 9%; others*, 28%.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F .034 K, 0.18</td>
<td>150 thf, 15</td>
<td>1-methyl-2-tetralone, 23%; 1,4-dimethyl-2-tetralone, 60%; others*, 17%.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G .034 Li, 0.12</td>
<td>150 thf, 75</td>
<td>1-methyl-2-tetralone, 10%; 1,4-dimethyl-2-tetralone, 10%; tetralin, 45%; 2-tetralone, 35%.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H .034 Li, 0.55</td>
<td>150 thf, 75</td>
<td>tetralin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* These are minor products (3-5 compounds) which were not identified. Percentages do not represent yields but the proportion of each compound in the reaction product as determined by g.l.c. analysis.

All reactions were carried out at -78°C and the methylated products were identified as ketones (58) and (59).
The dimethylated compound was also identified as its naphthalene derivative (60).

The major products in all the procedures were the products (56) and (57) identified as the ketones (58) and (59).

In all the procedures, the ketone (58) was isolated by converting it to its semicarbazone which had m.p. of 190° corresponding to the literature value for the m.p. of an authentic specimen.

This semicarbazone was hydrolysed back to the ketone which had b.p. 90°/0.3 mm, \( \nu_{\text{max}} \) 1710 cm\(^{-1}\), m/e 160 (calc for \( \text{C}_{11}\text{H}_{12}\text{O} \), 160), \( \delta \) 1.48 (d, 3H, Me), 1.53 (t, 2H, \( \text{CH}_{2}\text{CH}_{2}\text{C}=\text{O} \)), 2.06 (t, 2H, \( \text{CH}_{2}\text{C}=\text{O} \)), 2.49 (s, 2H, >CH-), 7.21 (s, 4H, aromatic). All these evidences supported the structure assigned (58). The yield (by procedure B) was 37%.

The compound (57) was identified as its ketone (59). This ketone did not give a semicarbazone. It was isolated from other products by preparative g.l.c. and its structure was assigned from the following evidence, \( \nu_{\text{max}} \) 1710 cm\(^{-1}\), m/e 174 (calc for \( \text{C}_{12}\text{H}_{14}\text{O} \), 174), \( \delta \) 1.43 (m, 6H, Me), 2.5 (m, 2H, methine), 3.42 (m, 2H, methylenic), 7.26 (d, 4H, aromatic).

The compound (57) was also identified as its naphthalenic derivative (60). The dehydrogenation of products of reductive alkylation (procedures A - F) using Pd-C in decalin gave a solid m.p. 68°. This corresponded to the m.p. of 1,4-dimethyl-2-methoxynaphthalene (60). Further this solid had m/e 186 (\( \text{C}_{13}\text{H}_{14}\text{O} \), 186), \( \delta \) 2.57 (d, 6H, Me), 3.86 (s, 3H, OMe), 7.05 (s, 1H, aromatic), 7.36 (m, 2H, aromatic),
7.9 (m, 2H, aromatic). The solid had t<sub>R</sub> 8.7 min (60°, 3% S.E. 30) corresponding to the retention time of 1,4-dimethyl-2-methoxynaphthalene obtained by the procedure of Wolthius.

It is interesting to find that lithium (procedures G and H) gave tetralin as the major product. Tetralin was identified by comparing with an authentic specimen on the g.l.c. Similarly, β-tetralone was identified.

The full significance of the alkylation results are discussed below:

\[
\begin{align*}
&\text{(55)} & \text{(56)} & \text{(57)} \\
&\text{(58)} & \text{(59)} & \text{(60)} \\
&\text{(61)}
\end{align*}
\]
III.2 DISCUSSION.

The mechanism for the alkylation of cyclohexadiene (4) to give the observed products can be written as

![Chemical structures](image)

The dialkylation product e.g. (66) can be further alkylated by a repetition of the process e.g.

![Chemical structures](image)

This last path explains the formation of trialkylated products such as 2,5,6-triisobutylcyclohexa-1,3-diene (50).

It has been shown\(^{34}\) that carbon alkylations are always irreversible and are therefore kinetically controlled. Such alkylations have been shown\(^{107}\) to proceed via "SN\(_2\)" process and as such exhibit strong preference for bond formation in the transition state. Oxygen alkylation on the other hand has been found\(^{34}\) to proceed via an SN\(_1\) mechanism and is reversible. Protons can add reversibly or irreversibly\(^{32}\) to a mesomeric anion of the type above and therefore the picture and the nature of products becomes clearer by comparing the results above with irreversible
proton addition to similar anions.

**Position of Addition of Alkyl Groups to a Mesomeric Anion.**

The results above (Table II) show that alkylations occur chiefly in the centre of the U-shaped pentadienyl carbanion. The isopropylation, for instance gave (63, \( R = \text{iPr} \)) (70%) and (64, \( R = \text{iPr} \)) (30%). Since calculation has shown that U-shaped anion carries the highest charge in the centre, the results suggest that irreversible addition of alkyl groups occurs to the charge in its most stable position. Such a conclusion accords with the original suggestion by Birch\(^{32}\) that in protonation by irreversible addition, the \( \text{H}^+ \) adds predominantly to the charge in its most stable position: in the case of mesomeric allylic ions to the least alkylated end or most arylated end of the system. This suggestion of course amounts to the same to the Hughes-Ingold rule already discussed (see II.1 and II.2).

To conclude that alkylations such as carried out have occurred at the site of highest charge density is to make the situation considerably simple. In the interconversions of allyl and propenylbenzene\(^{108}\) although the former is more acidic by a factor of one to two powers of 10, kinetic protonation of the anion gives about (80%) of the conjugated isomer. This result can be related to the type of transition state involved. It has been pointed out\(^{32}\) that the addition of an addendum to the point of highest charge-density is to be expected only if it requires little activation energy. The possible type of transition states have already been outlined above (II.1).
It has already been mentioned (III.1) that a distinction has been made \(^3\) between U-shaped pentadienyl anions as in (62) or (65) and "sickle" and W-shaped anions as in open chain systems with trans-cis and trans-trans stereochemistry. The U-shaped anions e.g. (62) and (65) which are apparently more stable by about 2-5 k.cal/mole for reasons already mentioned, are found considerably simpler with regard to their reactions.

In a study of the equilibrium below \(^3\), using potassium tert-amyloxide as catalyst, the 1,3-diene predominates over the 1,4-diene (2.2:1). Using deuterium labelling it was found that \(k_2/k_1 = 8\) and \(k_1/k_2 = -0.05\), that is, the less stable 1,4-diene is produced 8 times as fast by protonation in the centre of the system, corresponding to an energy difference of 1.52 k.cal/mole for the transition states for protonation of (62) at (a) (\(^a\)) and at each (b) (\(^b\)).
The alkylations present no unexpected features. The anion (62, \( R = H \)) from dihydrobenzene is capable of alkylation in the centre of the system to give (63) and at an end to give (64) (cf. butylation and isopropylation, Table II). Proton abstraction from the less substituted allylic position of (64) will produce the same salt as that formed from (63). The ratio of alkylation at the end of the system is higher compared with the centre than is the case with protonations. As discussed already\(^{34}\), this is not unexpected since this is due to the differing natures of the transition states.

The alkylation of 1,4-dihydrobenzoic acid (51) (Table II) shows that alkylation takes place in the centre of the mesomeric anion i.e. in 1 position only. It has also been found that kinetic protonation of the compound below occurs\(^{33}\) in the 1-position.

\[
\begin{array}{c}
\text{COOK} \\
\text{H}^+ \\
\text{H, COOK}
\end{array}
\]

The action of a substituent such as the carboxylic group which is charge stabilising is probably to alter the energy of the transition state in such a way as to allow exclusive alkylation or protonation (irreversible) to take place only in the 1-position. A similar result was obtained\(^{33}\) for the methylation and kinetic protonation of the anion derived from 1-methoxycyclohexa-1,4-diene where the addition (irreversible) occurred in the 2-position ortho to the methoxy group. The methoxy group probably stabilises the charge by its inductive effects.
In all the examples quoted above, two anionic isomeric forms are possible

\[
\text{COOH} \quad \text{and} \quad \text{OMe}
\]

The anionic form (68) is more stable than (69) because of charge stabilisation, therefore (68) is produced by H\(^+\) removal from the dihydrobenzoic acid.

The original assumption\(^\text{33}\) essentially on intuitive grounds was that charge density would be greatest in the centre of the system in (70) and related species and the removal of proton from the 2- rather than the 5-position of (72) was thought to depend on the inductive effect of the methoxy group. However the situation has been more recently somewhat rationalised. A number of MO calculations on charge distribution has been made\(^\text{109,110}\) but the situation is far from being as simple in the general case as was originally imagined.\(^\text{33}\) Alkyl substituents, for example instead of being electron-repelling when attached to anions, behave as polarisable groups, which may be electron-stabilising.\(^\text{111}\)

The results of methylation of 1-methylcyclohexa-1,4-diene (5) shows that the reaction proceeds via the two possible anionic isomeric forms:
This shows that the methyl group exercises less control on the position from which proton is abstracted by base when compared with the methoxy group. The result however suggests that the form (73) predominates since more o- than m-xylene was obtained. The result however shows that methylation occurs exclusively in the centre of the U-shaped pentadienyl anion in both cases.

Medium effects on alkylation and kinetic protonation of mesomeric anions.

The results of interconversions of allyl and propenylbenzene mentioned above was found to depend on the solvent. Kinetic protonation of the anion gave in liquid ammonia 85-90% conjugated isomer (MeOH or NH₄⁺), in ether 50% (MeOH) and in pentane 26%, probably due to extent of ion-pairing.

The reductive alkylation of naphthalene by sodium and lithium has been reported in detail. The following results were obtained:

The ammonia solvent was used with various other cosolvents including tetrahydrofuran (thf), ether and dimethoxyethane (DME).
In the present work a substituted naphthalene has been examined under similar conditions and the results essentially (see Table III above) are as:

The ratio of mono- to di-methylated product varies with the nature of cosolvent used with ammonia.

Although it has been pointed out\(^{49}\) that dianions appear as probable intermediates in these alkylations, the final products nevertheless correspond to monoanions which are kinetically protonated by ammonia or methylated.

The observed metal effect was explained for the reductive methylation of naphthalene\(^{49}\) in terms of greater tendency of lithium than sodium to form solvent-separated rather than contact ion pairs in solution and the more
facile protonation of the former by the medium. In this hypothesis (Harvey and Rabideau)\textsuperscript{49}, the monolithio anion \((\text{Li}^+/\text{NCH}_3)\) formed on initial alkylation of the dilithio dianion \((2\text{Li}^+, \text{N}^-)\) is solvent-separated and susceptible to protonation by ammonia to form the monomethylated product (see eq. 2 below) whereas the corresponding monosodio anion exists as an intimate ion pair \((\text{Na}^+, \text{NCH}_3)\) able to persist in the medium sufficiently long to undergo a second alkylation leading to formation of the dialkylated product (eq.1)

\[
\begin{align*}
2\text{M}^+, \text{N}^- & \rightarrow \text{M}^+, \text{NR} \rightarrow \text{NR}_2 + \text{MX} \quad \text{------------------------ (1)} \\
\text{MX} + \text{M}^+/\text{NR} & \rightarrow \text{NH}_3 \quad \text{HNR} + \text{MNH}_2 \quad \text{--- (2)}
\end{align*}
\]

\((\text{M}^+ = \text{Na, Li}; \text{ N} = \text{Naphthalene}; \text{ R} = \text{CH}_3)\)

With regard to the present work, the results of the reductive alkylation of 2-methoxynaphthalene can be explained as being due to the fact that the position next to OMe should give most stable, i.e. least basic charge (compare dihydroanisole case above). The results are therefore probably due to partial protonation at the most basic position followed by methylation.

The dimethyl could be produced by methylation of the surviving dianion in either order.
The failure of lithium to give the methylated products makes it difficult to compare the results with those of reductive methylation of naphthalene. However, since sodium gives a reasonable amount of dimethylated product under all the conditions employed here (Table III), it is clear that intimate ion pairs are at least present as intermediates. This is in agreement with the earlier view already outlined. The ratio of mono- to dimethylated product is related to the ratio of the amount of solvent-separated ion pairs present to that of intimate ion pairs. In other words, whether an anion such as (76, R = H, or R = OMe) is protonated to monomethylated product or methylated to a dimethylated one depends on the extent of solvation of the cation. Therefore in the irreversible addition of an addendum to a mesomeric carbanion, solvation is an important factor to be taken into account.

The results with lithium is unexpected. The reaction with lithium probably involves the sequence of reactions outlined below.
One theoretical importance of the results (Tables II and III) is that the original conclusions that addition of alkyl groups like irreversible proton additions, to a mesomeric carbanion takes place in the most stable position of the charge still largely seems to hold. Where both alkylation and kinetic protonations are possible, solvation may be a deciding factor. While substituents like OMe and COOH show definite effects on kinetic acidity, the effect of alkyl groups is less definite.

One practical application of the alkylation results is the ready synthesis of substituted cyclohexadienes and of the corresponding alkylbenzenes. It also provides new ways of making substituted β-tetralones and methyl-β-naphthyl ethers.
III.3 EXPERIMENTAL.

Cyclohexa-1,4-dienes were obtained by standard Birch reductions. G.l.c. results were checked by the use of authentic compounds when available; these are marked *. The potassium used was purified by cutting in small pieces and refluxing in anhydrous dioxan. Unless otherwise stated all hydrocarbons were examined on 20% Ucon column and phthalic esters on 5% QFI. Naphthalenic compounds were on 3% SE30 or 20% Carbonwax columns.

Dienes with Potassamide in Ammonia:

Potassamide was obtained from the metal in pure ammonia by the catalytic action of ferric nitrate.16 The diene was added to the solution and stirred under nitrogen for 2 hours unless otherwise indicated. Ammonium chloride was then added, followed by water; the product was taken up in a little pentane, washed with water, dried (MgSO₄) and the pentane carefully removed, or in the case of very volatile products the extract was examined directly by g.l.c.

Cyclohexa-1,4-diene (0.5 g) and potassamide (0.5 g of metal) in ammonia (30 ml) gave unchanged diene* (31%) tᵣ 9.4 min, benzene* (50%) tᵣ 8.1 min and cyclohexene* (19%) tᵣ 6 min (column: Uncon oil 20%, 50°).

Cyclohexa-1,3-diene, made from cyclohexene, had λ_max 258 nm., (ε 8000) and showed one peak on g.l.c., tᵣ 7.2 min. Reacted as for the 1,4-diene the product contained benzene* (53%), tᵣ 8.1 min and cyclohexene (47%) tᵣ 6 min.
Reaction of cyclohexa-1,3-diene and benzophenone

Cyclohexa-1,3-diene (0.5 gms) was added to potassamide (0.5 gms of metal) in ammonia (30 ml) followed by benzophenone (1.1 gms). After two hours, water was added and the product taken up in pentane and treated as above. The product contained benzene* (38%) $t_R$ 8.1 min, (50°), benzhydrol* (62%) $t_R$ 8 min (100°) and a trace of cyclohexene* $t_R$ 6 min (50°). Programme temperatures were used.

1-Methylcyclohexa-1,4-diene showed one peak, $t_R$ 19.5 min (50°), δ 4.60 (1H, C=CH), 4.31 (b.s., 2H, CH=CH). Reacted as above the product contained toluene* (83%) $t_R$ 18.3 min, 1-methylcyclohexene* (10%) $t_R$ 11.6 min, and a peak due to 3- and/or 4-methylcyclohexene* (7%) $t_R$ 8.9 min (50°). The mixed methylcyclohexenes for comparison were made by the lithium-ethylamine reduction of toluene.\textsuperscript{112}

1-Methylcyclohexa-1,3-diene, $\lambda_{max}$ 263 nm (ε 6500), δ 1.85 (s, 3H, Me), 2.10 (b.s., 4H, 2CH$_2$), 5.65 (m, 3H, =CH), was made from 3-methylcyclohex-2-enone by the tosylhydrazone procedure.\textsuperscript{113} The initial product contained some toluene and was purified by preparative g.l.c., $t_R$ 12.3 min (50°), $\lambda_{max}$ 263 nm, (ε 6500). Reacted as above the product was chiefly toluene*, $t_R$ 18.3 min with traces of the above methylcyclohexenes*.

Commercial (-)-α-phellandrene was redistilled, b.p. 66°/16 mm. From g.l.c. it contained p-cymene (3%) $t_R$ 7 min but consisted essentially of one peak at $t_R$ 5.5 min (130°). α-Phellandrene (1 gm) and potassamide (from metal 1.1 gm) were reacted in ammonia for 24 hours, the only organic product being p-cymene*, b.p. 46°/4 mm, $t_R$ 7 min, identical
in 'H n.m.r. spectrum with the authentic compound: δ 1.2 (d, 6H, Me₂C), 2.84 (m, CH), 7.8 (s, 4H, ArH). Shorter periods of time resulted in recovery of some starting material.

1,4,5,8-Tetrahydronaphthalene, m.p. 54°, showed one peak at t_R 26.5 min on CW (20%) at 150°, δ 2.5 (b.s., 8H, 4CH₂), 5.63 (b.s., 4H, CH=CH). The hydrocarbon (0.5 gms) was reacted with potassamide (from 0.6 gms of metal) in ammonia for 3 hr to give 1,2,3,4-tetrahydronaphthalene* (37%), t_R 19.5 min, unchanged material* (35%) t_R 25.6 min, naphthalene* (10%) t_R 33 min, 1,2,3,7,8,9-hexahydronaphthalene (12%) t_R 14.9 min, and unidentified peak constituted (6%) t_R 20 min. The 1,2,3,4-tetrahydronaphthalene was isolated by preparative g.l.c. and had an identical 'H n.m.r. spectrum to authentic material. The hexahydronaphthalene was isolated by preparative g.l.c. and contained 1,2,3,7,8,9-hexahydronaphthalene, m/e, 134 (calc for C₁₀H₁₄, 134), λ_max 236 nm, (ε 14,500), δ 1.66 (m, 4H, methylenic), 2.14 (m, 7H, methylenic and methine hydrogen), 5.59 (m, 2H, olefinic), 6.0 (d, 1H, olefinic). Authentic material has λ_max 236 nm (ε 15,140). The 1,2,3,7,8,9-hexahydronaphthalene obtained by heating 1,2,3,4,5,8-hexahydronaphthalene with potassium tert-amyl oxide at 184° for 24 hr had t_R 14.9 min (150°) and was identical with the hexahydronaphthalene above.

Continuation of the amide-ammonia reaction by 6 hr gave a product containing less starting material* (16%), 1,2,3,4-tetrahydronaphthalene*, (33%), naphthalene*, (24%), and 1,2,3,7,8,9-hexahydronaphthalene*, (27%).
1,2,3,4,5,8-Hexahydronaphthalene (from Birch reduction of 1,2,3,4-tetrahydronaphthalene) [5 gms] δ 5.68 (b.s., 2H, CH=CH) was reacted with potassamide (from 3.5 g of metal) in ammonia (200 ml) for 6 hr. to give chiefly 1,2,3,4-tetrahydronaphthalene* (84%), 1,2,3,7,8,9-hexahydronaphthalene* (15%), tR 14.9 min and a small peak due to 1,2,3,4,5,6,7,8-octahydronaphthalene* (<1%). The last compound was identified by comparison with a specimen made by lithium ethylamine reduction of naphthalene. 86

Alkylations - The diene was added to potassamide in ammonia and after 10 min, alkyl halide was rapidly added. Reaction was very rapid and the mixture was worked up in the usual way immediately the red colour had disappeared.

Cyclohexa-1,4-diene -

(a) The diene (20 gms) was reacted with potassamide (from metal 19.5 gms) and methyl iodide (71 gms). The product b.p. about 120° (12 gms) showed 3 peaks on g.l.c. The predominant g.l.c. peak (70%), tR 7.3 min (60°) was separated. It showed m/e 108 (C₈H₁₂), λ_max 260 nm (ε 2,000), δ 1.08 (m, 6H, Me), 2.65 (m, 2H, CH), 5.57 (envelope, 4H, =CH). Dehydrogenation (Pd-C) gave o-xylene* (20%) tR 7.3 min (3% S.E. 30) (120°) and p-xylene* (80%) tR 6.1 min. Alder-Rickert reaction on the product (2 gms) gave dimethylphthalate (0.5 gms) tR 3.0 min (180°) identical with authentic specimens. The yield of o-xylene was (6%) and p-xylene (24%). The total product from the alkylation showed some product m/e 122, corresponding to trimethylcyclohexadiene.
(b) The diene 10 gms was reacted with potassamide (1 equiv. or from 4.9 gms metal) and isopropyl bromide (15.4 g). The product (8 gms) b.p. 44°/15 mm had m/e 122 (calc for C₉H₁₄, 122), tᵣ 3.2 min (125°), δ 0.9 min (d, 6H, Me₂C), 1.7 (m, 1H, HCMe₂), 2.64 (m, 3H, HC=CH₂), 5.66 (m, 4H, HC=CH). Dehydrogenation gave isopropylbenzene*, tᵣ 3.9 min. It is therefore 3-isopropylcyclohexa-1,4-diene. The Alder-Rickert reaction gave a 15% yield of dimethylphthalate. This showed that the 1,4-diene (44) is contaminated with a little of the 1,3-diene (45), λₘₐₓ 259 nm, ε 1200. The yield of isopropylbenzene was 50%.

The diene (20 gms) was reacted as above and the product was separated into 4 fractions. The first fraction (10 gms) b.p. 60°/16 mm, had tᵣ 2.2 min (80%) and 3 min (20%). The peak at tᵣ 2.2 min had m/e 136 (C₁₀H₁₆), δ 0.88 (m, 6H, Me₂), 5.73 (m, 4H, =CH). Dehydrogenation gave isobutylbenzene*. Alder-Rickert reaction on the fraction (2 gms) gave dimethylphthalate (0.5 gms). The fraction had λₘₐₓ 259 nm, ε 1,500. The fraction therefore contains about (20%) 5-isobutylcyclohexa-1,3-diene and (80%) 3-isobutylcyclohexa-1,4-diene. The yield of isobutylbenzene was 28%.

The second fraction (5 gms), b.p. 110°/20 mm had tᵣ 6.2 min, λₘₐₓ 260 nm, ε 8,900, δ 0.09 (m, 12H, 2CMe₂), 1.47 (m, 6H, CH₂), 2.3 (m, 2H, CH), 5.7 (m, 4H, =CH), m/e 192 (C₁₄H₂₄). The fraction (2 gms) was converted into dimethylphthalate* (1.5 gms). It was therefore 5,6-di-isobutylcyclohexa-1,3-diene. The yield was 10%.

A third fraction (8 gms) b.p. 60°/0.5 mm, had tᵣ 9 min and showed no selective absorption in the region 240-260 nm,
134 0.91 (d, 12H, CMe₂), 5.63 (b.s., 4H, =CH), m/e 192 (calc. for C_{14}H_{24}). It was therefore 3,6-diisobutylcyclohexa-1,4-diene. The yield was 17%.

The fourth fraction (2 gms), b.p. 93°/0.5 mm had t_R 21 min, m/e 248 (C_{18}H_{32}), \lambda_{max} 263 nm, \varepsilon 7,000, \delta 0.91 (m, 18H, CMe₂), 5.29 (m, 1H, =CH), 5.69 (m, 2H, HC=CH); the Alder-Rickert product had m/e 250 (C_{14}H_{18}O_4) corresponding to a dimethyl isobutylphthalate. From this evidence, the fraction is 2,5,6-triisobutylcyclohexa-1,3-diene. The yield was about (3%).

When 1 equivalent of potassium amide and one equivalent of isobutyl bromide was used, the yield of the monoisobutylated product above was (50%).

Cyclohexa-1,4-diene was reacted with potassamide (10 equiv.) and isobutyl bromide (15 equiv.) to give a mixture of the diisobutylcyclohexadienes (57%), and the monoisobutylcyclohexadienes, b.p. 60°/16 mm (above) (43%), identified by g.l.c. comparison with the substances above. The last mixture was reacted with potassamide (2 equivalents) and isobutyl bromide (2 equivalents) to give unchanged material* (35%), t_R 2.2 min (150°), 5,6-diisobutylcyclohexa-1,4-diene (30%) t_R 9 min, and 5,6-diisobutylcyclohexa-1,3-diene (22%), t_R 6.2 min and all were identified by g.l.c. comparisons with the substances above.

Methylation of 1-Methylcyclohexa-1,4-diene - To a stirred solution of potassamide (from the metal, 6 gms) in pure ammonia (250 ml) was added 1-methylcyclohexa-1,4-diene (15 gms). After 8 min, methyl iodide was added as rapidly as
was practicable, to discharge the red colour. Worked up as usual, the product (6 gms) b.p. 135°, showed no u.v. absorption. The product was dehydrogenated using Pd-C, and the product examined by g.l.c. (120°) showed two xylene peaks, that due to o-xylene t_R 7.3 min (64%) and that due to m-xylene t_R 6.1 min (36%). The structure of the latter was further confirmed by n.m.r. δ 2.32 (s, 6H, Me), 7.0 (m, aromatic). The yield of the xylenes was 34%.

Methylation of 1,4-Dihydrobenzoic acid

Benzoic acid (20 gms) in ammonia (1000 ml) and ethanol (200 ml) was reduced by the action of sodium (12.4 gms) according to the procedure of Kuhne and Lambert. The product, b.p. 105°/0.01 mm weighed 24.9 gms. Lack of conjugation of the double bonds was confirmed by the absence of a light absorption maximum in the region 2200-2800 nm, δ 2.66 (m, 2H, H₂C-C=), 3.75 (m, 1H, HC-COOH), 5.84 (m, CH=CH), 11.89 (s, COOH).

1,4-Dihydrobenzoic acid (10 gms) was added to potassium amide (from 6 gms of the metal) in ammonia (200 ml) and bromobutane (30 gms) in ether (20 ml) was cautiously added. Water (50 ml) was added and the ammonia allowed to evaporate. Ice water was added to the residue and then acidified with 10% HCl. The product was then extracted with ether. The ether extract was washed with water and brine and dried (MgSO₄). Upon removal of ether, the residue was distilled to give a product b.p. 115°/0.2 mm (6 gms), δ 0.89 (t, 3H, Me), 1.3 (m, 4H, CH₂CH₂Me), 1.7 (m, 2H, CH₂-CH₂CH₂Me), 2.64 (m, H₂C-C=), 5.82 (m, HC=CH), 12.08 (s, COOH), m/e 180.
(C\textsubscript{11}O\textsubscript{2}H\textsubscript{16}, 180); no selective u.v. absorption in the region 2200-2800 nm. From the evidence above, the structure corresponds to 1-n-butyl-1,4-dihydrobenzoic acid. The yield was 41%.

**Reductive methylation of methyl-β-naphthyl ether**

A solution of sodium (0.12 mole) in redistilled liquid ammonia (150 ml) was cooled to -78°. β-Naphthyl methyl ether (.034 mole) dissolved in dry tetrahydrofuran (75 ml) was stirred in (5 min). After 10 min, methyl iodide was added as rapidly as the reaction allowed until the red colour of the solution disappeared. Water was carefully added and the product was extracted with ether. The ether extract was washed with water (2 times), brine (once) and dried (MgSO\textsubscript{4}). After removal of ether, the residue was heated with 2NHCl for 30 min, cooled and extracted with ether. The ether extract was treated as above and the residue distilled b.p. 110°/0.5 mm. This gave two main peaks on the g.l.c. at t\textsubscript{R} 3 min (47%) and t\textsubscript{R} 3.5 min (34%) (150°). Other 4 minor peaks including tetralin (6%) constitute the rest percentage. The infra-red spectrum of the mixture (υ\textsubscript{max} 1710 cm\textsuperscript{-1}) showed it to contain mainly some saturated ketone. The mixture (5 gms) was then converted to the semicarbazone. This was highly insoluble in all common solvents and was heated for some time with ethanol and filtered off washed thoroughly with ethanol and dried (3 gms). It had m.p. of 190° which corresponded to literature value for the m.p. of 1-methyl-2-tetralone semicarbazone.\textsuperscript{105}

The semicarbazone was hydrolysed with 2NHCl by heating for
30 minutes. The oily product was extracted with ether, washed with water and brine and dried (MgSO₄). Distillation gave a product b.p. 90°/0.3 mm and weighing 2 gms. This had ν_max 1710 cm⁻¹ and m/e, 160 (calc for C₁₁H₁₂O, 160), t_R 3 min (150°), δ 1.48 (d, 3H, Me), 1.53 (t, 2H, CH₂CH₂C=O), 2.06 (t, 2H, CH₂C=O), 2.49 (s, 2H, CH-), 7.21 (s, 4H, aromatic). The dinitrophenylhydrazone had m.p. 150°. The information above showed that this ketone was 1-methyl-2-tetralone. The yield was 37%.

**1,4-Dimethyl-2-tetralone**

The results above show that the 1,4-dimethyl-2-tetralone did not form semicarbazone. This ketone was nevertheless isolated by preparative g.l.c. from the reaction products above, t_R 3.5 min (150°), ν_max 1710 cm⁻¹, m/e, 174 (calc for C₁₂H₁₄O, 174), δ 1.43 (m, 6H, Me), 2.5 (m, 2H, methine), 3.42 (m, 2H, methylene), 7.26 (d, 4H, aromatic).

**1,4-Dimethyl-2-methoxynaphthalene**

The product of the reductive alkylation above (5 gms) was refluxed with stirring in decalin (redistilled) containing 10% palladium - charcoal catalyst (1 gm) for 24 hrs. At the end of the reaction, the mixture was filtered and the catalyst washed through with dry tetrahydrofuran. Decalin and tetrahydrofuran were distilled off under reduced pressure and the residue distilled b.p. 125°-130°/2 mm. The fraction at 130°/2 mm solidified. More solid product was obtained from the lower boiling fraction when left in the cold. The solid product was recrystallised
three times from methanol and the crystals (2 gms) had m.p. 68°. This corresponded to the m.p. of 1,4-dimethyl-2-methoxynaphthalene. It had m/e 186 (C_{15}H_{14}O, 186), δ 2.57 (d, 6H, Me), 3.86 (s, 3H, OMe), 7.05 (s, 1H, aromatic), 7.36 (m, 2H, aromatic), 7.9 (m, 2H, aromatic). The product was also found to correspond to 1,4-dimethyl-2-methoxynaphthalene, t_R 8.7 min (160°). This last compound was obtained by the procedure of Wolthius. From the above evidence, it followed that the product corresponded to 1,4-dimethyl-2-methoxynaphthalene. The yield (overall) of the naphthalene was 30%.

Other reactions recorded on the table of results (Table III, III.2) were carried out in the same way. 2-Tetralone and tetralin were identified by comparing with authentic specimens.
CHAPTER IV

IV.1 Some Carbanionoid Reactions of Aromatic Systems

The original idea was two-fold (1) to examine the effects of nucleophiles on the dipolar system in which benzynes seem to react with ionic reagents, (2) to examine possible uses in synthesis.

In the case of a substituted compound such as polarisation can occur as

In the formation of dehydrobenzene, the rate determining step is removal of the most acidic (kinetically) proton; reaction of the aryne as polarised probably are chiefly determined by the negative charge situation. From the fact that \( \text{NH}_2^- \) in \( \text{NH}_3 \) reacts as seems to indicate that polarisation is assisted by the OMe to form an adjacent negative charge. The alternative benzyne (3,4-dehydroanisole) gives a mixture.

It seemed of interest to find out whether other
nucleophiles behaved similarly and phenols and phenol ethers of m-substitution are not easy to make in other ways.

In view of rather poor yields, and some unexpected products, the work was not continued on the envisaged original lines, which involved particularly halobenzene derivatives, e.g. O-dichlorobenzene.

The results are in agreement with other observations which indicate ready formation of an ortho-anion to OMe, e.g. ortho-lithiation of anisole.

**Benzynes, structure and reactions**

In view of the reactions described later, it is necessary first to discuss the nature and some reactions of "benzyne".

The benzyne intermediate has also been called dehydrobenzene, o-phenylene, and cyclohexadienyne and a general term "aryne" has also been applied in the case of substituted benzyynes. Formulation of the intermediate has been written in a variety of ways, 115-117

![Diagram of benzynes](image)

each of which has certain advantage over the others in defined contexts. It is generally agreed that the aromatic character of the cyclic system in the aryne intermediates is
Models of the electronic structure show that the ring strain is not excessively high and can be compared with that in the cyclopropene rings. The existence of a bent excited acetylene has been quoted in favour of the existence of the benzyne intermediate. Simplified calculations indicate the bond lengths shown except those indicated as 1.44Å should perhaps be smaller by 0.03Å.

Returning to the reactions of benzyynes, more recently Cram et al. reported the isolation of a small amount of by-product, 4-methylmercapto-5-hydroxy-2,2-paracyclophane with potassium tert-butoxide in dimethylsulphoxide. Further, Kise and co-workers have found that aryne intermediates reacted with dimethylsulphoxide to yield a mercaptophenol-type of compound together with other products. Reacting bromobenzene with potassium tert-butoxide in dimethylsulphoxide, they isolated phenyl tert-butyl ether (52%), o-methyl mercaptophenyl phenyl ether (5%), o-methylmercaptophenol (7%), phenol (8%), and diphenyl ether (6%), and tarry material. The reaction of chlorobenzene with dimsyl-sodium was also observed to give o-methylmercaptophenol (2%). The formation of o-methylmercaptophenol and o-methylmercaptophenyl phenyl ether is presumed to involve the 1,2-dipolar addition of dimethylsulphoxide to benzyne as illustrated below:
o-Methylmercaptophenol (14%) and polymethylene have been found among the products formed in the decomposition of benzenediazonium-2-carboxylate with 10 mol. equivalents of dimethylsulphoxide in a large amount of benzene solution when heated for 27 hours at 45-55°C. The formation of o-methylmercaptophenol in this reaction seems to support the idea that benzyne is formed as an intermediate and the subsequent addition of dimethylsulphoxide to it leads to the formation of the mercapto-compounds. A similar 1,2-dipolar addition of dimethylsulphoxide to an acetylenic compound has been reported.

In the case of benzene only one product is possible, but with polycyclic compounds, or substituted benzenes, substitution effects are observed.

It was thought that further examination of substituent effects might shed more light on (a) the mechanism in detail, and (b) the synthetic possibilities of the reaction.
If the aryne reacts in the dipolar form

(possibly induced by the proximity of the DMSO dipole)
the results may give further indications of the relative
ease of formations of the two possible dipoles with
substitution of the ring, e.g.

\[
\begin{align*}
\text{OR} & \quad \text{Me} \\
\text{O} & \quad \text{Me} \\
\text{S} & \quad \text{Me}
\end{align*}
\]

or

\[
\begin{align*}
\text{OR} & \quad \text{Me} \\
\text{O} & \quad \text{Me} \\
\text{S} & \quad \text{Me}
\end{align*}
\]

There is evidence already from reactions of other
anions,\textsuperscript{51,52,125,126} e.g. \(\text{NH}_2^-\), that polarisation occurs
at any rate on approach of the anion, e.g.

\[
\begin{align*}
\text{OMe} & \quad \text{NH}_2 \\
\rightarrow
\end{align*}
\]

\[
\begin{align*}
\text{OMe} & \quad \text{NH}_2
\end{align*}
\]

\[
\begin{align*}
\text{OMe} & \quad H^+ \\
\rightarrow
\end{align*}
\]

\[
\begin{align*}
\text{OMe} & \quad \text{NH}_2
\end{align*}
\]
An extensive study of the reactions of bromo-naphthalene and potassium tert-butoxide and tert-butyl alcohol in dimethylsulphoxide has been made recently.\textsuperscript{127-129} The reaction of 1-bromonaphthalene and potassium tert-butoxide in tert-butyl alcohol-dimethylsulphoxide mixed solvent was found\textsuperscript{127} to give the products below:

\[
\begin{align*}
\text{Br} & \quad \text{DMSO} \quad \text{K-o-t-Bu} \quad \text{HO-t-Bu} \\
\end{align*}
\]

The apparent ratio of \( \alpha \) to \( \beta \) products (1:4) from a 1-naphthylene reaction is considerably different from that (1:2) found when 1-naphthylene was prepared by a different procedure.\textsuperscript{130}

The reaction of 1- and 2-bromonaphthalene with potassium tert-butoxide in a tert-butanol-dimethylsulphoxide solvent mixture was found\textsuperscript{128} to give not only tert-butyl 1- and 2-naphthyl ethers and naphthols but also eleven other identifiable products including 1-methyl mercapto-2-naphthol (5) and 2-methyl mercapto-1-naphthol (6). The tert-butyl naphthyl ethers were found to decompose to the corresponding naphthols at higher temperatures (140\(^\circ\)) but were found however to be much more stable at lower temperatures (70\(^\circ\)).
The formation of 1- and 2-naphthols from the reaction of 1-bromonaphthalene and potassium tert-butoxide in a tert-butanol dimethylsulphoxide solvent mixture was also reported by some earlier workers. 127

1,2-Dehydronaphthalene was named as the intermediate from the fact that the ratio of 1:2-tert-butyl naphthyl ethers was the same whether 1- or 2-bromonaphthalene was used. The formation of the methyl-mercaptanaphthols was interpreted as a probable addition of dimethylsulphoxide to the intermediate in the same way as has been mentioned above. 123 The resulting adduct is believed to eliminate methylene (in the form of polymethylene) to form the observed products. The observed preponderance of 1-methyl-mercapto-2-naphthol (5) over the 2,1-isomer (6) was not explained.

The ratio of (5) to (6) depends on the exact conditions. With 1 mole of 1-bromonaphthalene, 2 moles of potassium tert-butoxide in tert-butanol (3 moles), dimethyl-
sulphoxide (15 moles) mixture at 80°, the ratio of (5) to (6) was about 9. It is important to discuss the intermediate anions.

The formation of 1,2-dehydronaphthalene from 1-bromonaphthalene involves removal of the 2-H

\[ \text{H} \quad \text{B} \rightarrow \text{H} \quad \text{B} \rightarrow \text{H} \]

The generation of the same intermediate from 2-bromonaphthalene involves the abstraction of the 1-H

\[ \text{H} \quad \text{B} \rightarrow \text{H} \quad \text{B} \rightarrow \text{H} \]

Since in naphthalene 1-H is more acidic\textsuperscript{11,131} than 2-H, the process may be faster with 2-bromonaphthalene (which has a 1-H) than for 1-bromonaphthalene (which has a 2-H).

The fact that (5) predominated over (6) showed readier polarisation to give

\[ \text{H} \quad \text{B} \rightarrow \text{H} \quad \text{B} \rightarrow \text{H} \]

This may indicate that \( \odot \) requires more stabilising by the ring system (since it is \( \alpha \)) than does \( \oplus \). Another possibility involves steric effects.

Ortho and para-bromoanisoles.

These were examined with sodium dimysyl in attempts to elucidate some of the problems noted. An outline of the results, including proofs of structure is:
RESULTS

A.

\[\text{OMe} \xrightarrow{\text{Br}} \text{OMe} \xrightarrow{\text{OH}} \]  

B.

\[\text{OMe} \xrightarrow{\text{Br}} \text{OMe} + \text{OMe} \]
C.

In all cases, the dimethylosulphide used was carefully purified by refluxing over sodium and then distillation. It was then reduced to the mer sulphide and stored over calcium hydride in an atmosphere of dry hydrogen. The reactants used on an equivalent basis.

\[
\begin{align*}
  \text{Br} & \quad \text{OMe} \\
  \text{(19)} & \quad \text{Me} \\
  \quad \rightarrow \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{OH} & \quad \text{SMe} \\
  \quad \text{(20)} & \quad \text{Me} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{MeS} & \quad \text{OH} \\
  \quad \text{(21)} & \quad \text{Me} \\
\end{align*}
\]

D.

The reaction of 4-bromo anisole with potassium tert butylate in dimethylsulphoxide gave about 85% 4,6-dihydroxy-2-methyl phenol (8) with a Rf value of 0.33. The 

\[
\begin{align*}
  \text{Me} & \quad \text{OMe} \\
  \text{(26)} & \quad \text{Br} \\
  \rightarrow \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \text{OH} & \quad \text{SMe} \\
  \quad \text{(27)} & \quad \text{Me} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{Me} & \quad \text{OMe} \\
  \quad \text{(28)} & \quad \text{Me} \\
\end{align*}
\]

The 3,5-dimethoxy-4-hydroxy-2-methyl phenol was identified by comparing with the authentic sample. The p.P. in the 3,5-dimethoxy-4-hydroxy-2-methyl phenol is 3.69, by comparing with the authentic sample.
In all cases, the dimethylsulphoxide used was carefully purified by refluxing over calcium hydride for about one-quarter hour and then distilling over calcium hydride under reduced pressure and storing over calcium hydride.

Four mole equivalents of base was used on one mole equivalent of bromide.

A. The reaction of 2-bromoanisole (7) with sodium dimethylsulphoxide in dimethylsulphoxide gave the phenol (8) in 27% yield. The phenol was identified by its I.R. $\nu_{\text{max}}$ 3370 cm$^{-1}$ and by the fact that its methyl ether (a) had m/e 184 (C$_9$H$_{12}$O$_2$S, 184). The n.m.r. spectrum of the methyl ether gave one methylmercapto peak at $\delta$ 2.36. Desulphurisation of the phenol (8) with Ranel nickel gave 3-hydroxyanisole (10) which was identified on the g.l.c. ($t_R$ 3 min), by comparing with the authentic specimen.

B. The product from the reaction of 4-bromoanisole with potassium tert-butoxide in dimethylsulphoxide gave only about 10% of the phenol (8), the main product being 3-hydroxyanisole (10).
contained approximately equal amounts of (13) and (14). Desulphurisation gave a product which has the same $t_R$ as a mixture of 3- and 4-hydroxy anisole. However these were not separable.

C. The reaction of 2-methyl-4-bromoanisole gave a phenolic product (about 20% yield) which had $\nu_{\text{max}}$ 3370 cm$^{-1}$. It was converted to the methyl ether which gave two equal peaks on the g.l.c. (160°) $t_R$ 7 min and 9 min. The n.m.r. of the methyl ether gave SMe peaks at $\delta$ 2.3 and had m/e 198 (C$_{10}$H$_{14}$O$_2$S). Desulphurisation of the methyl ether gave two equal peaks on the g.l.c. $t_R$ 3 min and $t_R$ 4 min (200°) which corresponded to 2-methylresorcinol methyl ether and 2-methylhydroquinone methyl ether respectively; these last two compounds were commercially available.

D. The phenolic product obtained from the reaction of 3-methyl-4-bromoanisole was converted into its methyl ether which had m/e 198 (C$_{10}$H$_{14}$O$_2$S), and showed SMe resonances at $\delta$ 2.36 (n.m.r. spectrum). The g.l.c. gave two peaks at $t_R$ 6.4 min (47%) and 8.5 min (53%). Desulphurisation of the methyl ether mixture gave 3-methylresorcinol methyl ether $t_R$ 3 min (47%) and 2-methylhydroquinone methyl ether (53%), $t_R$ 4 min (200°). This showed that the phenolic product contained 53% of the methylmercaptophenol (29) and 47% of the methylmercaptophenol (30).

The reaction of 2-bromotoluene or bromobenzene gave very poor yield of the methylmercaptocompounds (<5%, n.m.r., and g.l.c.). The reaction of 2- and 4-bromobenzoic acid ethyl ester failed to give any methylmercapto compound.

The mechanism and importance of these results are
discussed in detail below:

DISCUSSION

The generation of "arynes" by reacting aryl halides with amide ions has been studied in detail. Cram and co-workers have shown that the elimination of hydrogen bromide from bromobenzene can be effected using potassium tert-butoxide and that the reaction is greatly enhanced when dimethylsulphoxide is used as a solvent. Phenyl tert-butyl ether is obtained as a product. Corey and Chaykovsky have shown that the reaction of chlorobenzene with dimyslsodium, prepared from dimethylsulphoxide and sodium hydride or sodium amide, gave as main products benzyl methylsulphoxide and benzhydryl methyl sulphoxide.

Both reactions are presumed to involve prior formation of "benzyne" which then reacts with the respective strong bases to form the final products.

Reviewing the results of the present work, it is apparent in the reaction of bromoanisoles with sodium dimethylsulphoxide that a dehydroaromatic is the intermediate. This is evidenced by the fact that a 4-bromoanisole such as 3-methyl-4-bromoanisole gave rise to a mixture of products (27) and (28).

Such a view is in line with that already established by earlier workers.
The methylmercaptophenol (8) obtained from the reaction of o-bromoanisole with sodium dimethylsulphoxide in DMSO is probably formed by a dipolar addition of dimethylsulphoxide to 2,3-dehydroanisole as shown below:

\[
\begin{align*}
\text{OMe} & \leftrightarrow \text{OMe} + \text{SM}_2 \\
\text{OMe} & \rightarrow \text{OMe} + \text{O} \quad \text{elimination methylene}
\end{align*}
\]

Such a mechanism has also been suggested by Cram and Day, Kise et al, and Bradshaw and co-workers. The resulting adduct is believed to eliminate methylene (in the form of polymethylene) to give the observed products. Polymethylene has in fact been found among the products formed in the decomposition of benzenediazonium-2-carboxylate in dimethyl sulphoxide, a reaction shown to involve benzyne as intermediate. The influence of the substituent in these reactions is not readily understood. The dehydroaromatic bond in dehydrobenzene is probably easy to polarise. It is therefore to be expected that as soon as a charged particle or a dipole approaches dehydrobenzene, a partial ionic structure is thereby induced which otherwise contributes only little to the ground state of dehydrobenzene.
This dipolar structure will facilitate polar addition. The straightforward addition of nucleophiles to dehydrobenzene leads to one product.

\[ R^- + \text{dehydrobenzene} \rightarrow R \]

However, if the dehydroaromatic intermediate is not symmetric with regard to the dehydrobond, addition of nucleophiles leads in principle to two isomeric products, e.g. the reaction of p-bromoanisole with sodium dimethylsulphoxide in dimethylsulphoxide gave two products (13) and (14). Another example is the attack of the amide anion in liquid ammonia on 4-methoxybenzyne.\(^5^2\)

The ratio of isomers formed depends on the electronic effect of the substituent \( R \) and on the steric requirements and nucleophilicity of the attacking species.

The gross differences in the isomer ratio observed with various substituents in a dehydroaromatic intermediate are certainly a consequence of the electronic and steric demands of each particular substituent present. These effects are expected to be more marked if the substituent is directly adjacent to the dehydro-bond (compare 4 and 2 bromoanisole in the results above) and thus frequently one isomer is formed. With 4-substituted dehydrobenzenes, the diminished substituent effect leads to the formation of both possible isomers at approximately equal rates. This is seen
in the reaction products obtained from p-bromoanisoles above. These substituent effects may be explained on the basis of electronic effects.

The formula below shows that the orbital at which polar additions occur are orthogonal to those of the aromatic \(\pi\)-system, including the \(\pi\)-electrons at the substituent. To a first approximation mesomeric effects of the latter will therefore influence only the aromatic \(\pi\)-system, but not the reactive bond. This bond has contact with the substituent merely by the system of \(\sigma\)-bonds and is hence predominantly susceptible to inductive influences only. The inductive effect will direct the approaching nucleophile into such a position that the resulting negative charge on the nucleus is best stabilised by the substituent. In other words, the more acidic of the two possible products predominates.\(^{137}\)

An alternative consideration would be that the concerted addition of a reagent to benzyne such as can be accomplished by a molecule having nucleophile and electrophilic centres will be a very exo-thermic process, and it is appropriate to consider that the geometry and electron distribution in the transition state approximate those in the ground state molecules.\(^{138}\) Accordingly the isomer ratio obtained is kinetically controlled and reflects the electron density at the two carbon atoms of the former triple
bond which is polarised by the inductive effect of the substituent.

In the addition of nucleophiles to dehydroheterocycles such as 2,3-dehydropyridine which have the hetero atom adjacent to the dehydro-bond, the experiment is in agreement with the latter hypothesis. However, with substituted dehydrobenzene derivatives, both theories lead to the same conclusion.

Considering 2,3-dehydroanisole

\[
\begin{align*}
\text{OMe} & \quad \text{(33)} \\
\text{R} & \quad \text{(34)}
\end{align*}
\]

it is seen that when the stability of the resulting adduct is the decisive factor (thermodynamic control) (34) should be formed in preference to (35) since the negative charge is better stabilised in (34). When the electron density at the two ends of the dehydro bond determines the addition ratio (kinetic control), the nucleophile should attack still at the 3-position because of its lower electron density.

The formation of the 2-methylmercapto-3-hydroxyanisole (8) by the attack of dimethylsulphoxide on the 3-position of 2,3-dehydroanisole is in agreement with the discussion above and in line with earlier results; for instance, the amide anion in liquid ammonia attacks in the 3-position of 2,3-dehydroanisole, to give 3-methoxyaniline\textsuperscript{51} and the reaction below\textsuperscript{139} also results mainly in 3-substituted products.
The results from p-bromoanisoles (12), (19) and (26) are less easy to interpret. Apart from the inductive effect mentioned above, the methoxy group has another possible influence in the 4-position namely the mesomeric effect (compare II.2 and II.3).

The inductively-electron attracting effect of the methoxy group in 4-methoxybenzyne would decrease the total electron density at the 4-position (36a).

The methoxy group donates electrons strongly by its mesomeric effect and thus confers a partial negative charge to the aromatic π-orbital in the 4-position (36b). This partial negative charge inductively influences the orthogonal orbital of the dehydro bond and reinforces the direct inductive effect of the substituent. It therefore follows that both inductive and mesomeric effects should help stabilise the negative charge in the 3-position, i.e. both effects should help cause polarisation as shown:

Results do not accord with this, but only on the assumption that the polarised form above (37a) and the
alternative (37b) give the same yield of the required product. The total yield of this is so low that a faster alternative reaction on one of the forms could explain the result, i.e. if (37b) gives the product noted more efficiently than (37a) which does something else. Similar results to that obtained above were reported in the reaction of the amide anion on 4-methoxy benzyne in liquid ammonia which gave the ratio of p- to m-anisidines of about 1.

The reaction of bromobenzene and 2-bromotoluene or 4-bromotoluene gave very little of the required product but mostly polyaromatic. It seems therefore that the unsubstituted benzyne and the methyl-substituted one are rapidly undergoing other types of reactions than with dimethylsulphoxide. For instance, it has been found that benzyynes show a tendency to dimerise which falls in the order shown. 

\[
\begin{align*}
\text{OMe} & > \text{Me} \quad > \quad \text{CF}_3 \\
& \sim \quad > \\
> \quad \text{Me} & > \\
\text{OMe} \quad > \quad \text{Cl} \quad > \quad \text{NO}_2 \quad > \\
& \quad \text{NO}_2
\end{align*}
\]
It therefore seems that dimerisation competes with attack by nucleophiles, and that the ease of nucleophilic attack is determined by the inductive effect of the substituents. Thus, in a compound such as 2,3-dehydroanisole where the inductive effect of the methoxy group helps to stabilise the negative charge, the yield of the methylmercaptophenol is fair. The failure of 2- and 4-bromo-benzoic acid ester to react with dimethylsulphoxide under the conditions used for the anisoles above is not readily apparent.

In order to throw more light on the effect of the methyl group on "benzyne" reaction the compounds (19) and (26) were also examined under the reaction conditions above. The result is similar to that of 4-bromoanisole.

The formation of the products (27) and (28) in almost 1:1 ratio shows that the methyl group exerts very little (if any) influence on the electron density at each end of the orthogonal bond, in fact, the relative electron density at the 2- and 3-position of toluene has been calculated\textsuperscript{132} and potassium amide in liquid ammonia has been found to add to 2,3-dehydrotoluene with only a slight preference for the position meta to the methyl group.\textsuperscript{51} The results further show that the 5-position is much more acidic than the 3-position in 2-methyl-4-bromoanisole (19).

The action of base on halobenzenes with 2H adjacent to bromine initiates the benzyne formation by removal of one
of them, presumably the more acidic in the case of unsymmetrical compound such as (19). The case of 2-bromonaphthalene has already been noted, it being fairly clear that the 1-position is more acidic than the 3-position (the acidities of α- and β-hydrogens in naphthalene has been examined and it has been shown that the α-position is more acidic).

The reason why only dehydroanisoles and naphthalynes give the methylmercapto compounds is not so far explicable. It could be possibly a question of the stability of the benzyne which may be a reverse of its reactivity towards outside reagents. The benzyne could become more selective because of greater stability. If such stability is due to electron withdrawal, then benzynes derived from bromobenzoic acid esters should be stable and therefore should give the products. This has not been observed. However, if mesomeric electron donation produces such stability, then benzynes substituted by OMe should be stable. The same is possible with dehydronaphthalene but not with alkyl-substituted benzynes.

In the case of (26), proton abstraction may be sterically hindered from the 3-position and could also be reduced in rate if the inductive effect (Me+) is important. Proton removal from 5- is therefore more likely. This is in agreement with the fact that 4-position of toluene is more acidic than the 2-position.

Other factors which could have affected the isomer ratio obtained in the results include steric effects and the nucleophilicity of dimethylsulphoxide.

It is obvious that any bulky substituent adjacent
to the dehydro bond will interfere with ortho-addition of a bulky nucleophile. However, in the exothermal addition of a nucleophile to any dehydro-aromatic intermediate, the transition state is reached when the new bonds are only slightly formed and still very extended. Steric effects on the isomer ratio should therefore not be of great importance.

When confronted with a weak nucleophile, the selectivity of the dehydro-aromatic intermediate may come into full operation. On the other hand, the better a nucleophile the more it will react at the first encounter and will thus suppress the selectivity of the polarised dehydro-bond. In the limiting case an excellent nucleophile should yield statistical addition, with a para/meta-ratio of 1:0. This has been found to be so in the addition of hydroxide to 3,4-dehydrotoluene at 340°C. Such a factor may be in part responsible for the isomer ratios obtained in the reactions of the p-bromoanisoles above.

One other point which also needs mentioning is the fact that no addition of dimethylsulphinyl carbanion to the benzyne is observed here as well as in other reactions described earlier, despite the fact that this carbanion must be present during the reaction.

Corey and co-workers have reported the addition of dimethylsulphinyl carbanion to benzyne derived from chlorobenzene. It should be mentioned however that these people first generated the carbanion and carried out the rest of the reaction at room temperature. In the present work the reaction was carried out at about 60-70° and it
might be that under such a condition the dimethyl-sulphinyl carbanion decomposed into some other products. For example it was suggested that the thermal decomposition of methyl-sulphinyl carbanion can occur by the mechanism proposed below. 129

\[
\begin{align*}
\text{CH}_3\text{SOCH}_2^- & \rightarrow \text{CH}_2 + \text{CH}_3\text{SO}^- \\
2\text{CH}_3\text{SO}^- & \rightarrow \text{CH}_3\text{S}^- + \text{CH}_3\text{SO}_2^-
\end{align*}
\]

The effects of substituents on the formation of methylmercaptophenols, in competition with other reactions, is not so far explicable. A substituent such as OMe which seems to produce reasonable yields, might act by its inductive effect in stabilising the \( \text{SO}^- \) part of the system (as shown by reaction of this ortho to the OMe in the 2,3-benzyne). However in this case, since the p-OMe also reacts, it should be important in this case, yet there is little or no distinction between the p- and m-positions.

Alkyl bromobenzenes should react like bromobenzene on this view, but bromobenzoic acids (or esters) should, because of anion-stabilising effects behave rather like OMe.
First let us look at possible explanations of other products of the reactions (IV.1). The reaction of 1- and 2-bromonaphthalenes were found to give 1- and 2-naphthols among other products as already outlined above. In the reaction of benzyne and dimethylsulphoxide using potassium-tert-butoxide, it is mentioned above\textsuperscript{123} that phenol was obtained (8\%) as one of the products. Two possible explanations have been given for the formation of phenols in the butoxide-dimethylsulphoxide reaction. One involves reaction of the dimethylsulphoxide as below:\textsuperscript{123}

\[
\text{benzyne} + \text{Me}_3\text{SO}^+ \xrightarrow{\text{Base}} \text{phenol}
\]

A more attractive hypothesis, put forward by Cram and co-workers\textsuperscript{133} and illustrated by the paracyclophane derivatives is:
In order to examine the possible formation of phenolic products by ether fissions, reactions of some phenolic ethers with potassium tert-butoxide in dimethylsulphoxide were also examined. (Table 1 shows the results)

**TABLE 1**

<table>
<thead>
<tr>
<th>ETHER</th>
<th>TIME hr</th>
<th>TEMPERATURE</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-Ethoxyanisole (38)</td>
<td>4</td>
<td>65°</td>
<td>2-Ethoxyanisole 82%; 2-Hydroxyanisole 18%.</td>
</tr>
<tr>
<td>2-Ethoxyanisole (38)</td>
<td>96</td>
<td>65°</td>
<td>2-Ethoxyanisole 12%; 2-Hydroxyanisole 88%.</td>
</tr>
<tr>
<td>m-tert-Butylanisole (39)</td>
<td>4</td>
<td>65°</td>
<td>m-tert-Butoxyanisole 75%; 3-Hydroxyanisole 25%.</td>
</tr>
<tr>
<td>2-(2-Phenylethoxy)-anisole (40)</td>
<td>4</td>
<td>65°</td>
<td>2-Hydroxyanisole 100%.</td>
</tr>
<tr>
<td>2-(2-Phenylethoxy)-anisole (40)</td>
<td>1/4</td>
<td>25°</td>
<td>2-Hydroxyanisole 100%.</td>
</tr>
</tbody>
</table>
Compounds (38)-(41) were freshly prepared and used immediately. Their reactions with potassium tert-butoxide in dimethylsulphoxide were carried out using excess of the base under nitrogen. The phenolic product of the cleavage reactions was taken up in ether at the end of the reaction, dried quickly and analysed immediately on the g.l.c.

The phenol (42) or (17) was identified by comparing with authentic specimen on the g.l.c.

Under similar conditions (65°) used for all the reactions, the compounds 2-(2-phenylethoxy)-anisole (40) and ethyl 3-(2-methoxyphenoxy)-propionate (41) cleaved much more rapidly than the other two (38) and (39). Under less severe conditions, i.e. at room temperature, the two
compounds (40 and (41) still disappeared totally. This means that the conditions given for the two compounds (40) and (41) are not minimal for total cleavage.

More details about the significance of these results are discussed below:

IV. 2 DISCUSSION

On examining the results in Table 1, it is clear that under the condition employed, the methoxy group remains intact, that is, a methyl ether is not affected. The fact that the ethoxy group is sensitive to cleavage under the conditions means that a hydrogen β to the oxygen of the ether linkage is essential. This is probably due to the fact that removal of proton from the β-position permits ready elimination. Removal of proton from the α-position does not permit such ready elimination (it would have to generate a carbene). This enables a reasonable mechanism to be proposed for the cleavage:

That such a mechanism is operating is supported by the fact that in the base-catalysed decomposition of tert-butylphenyl ethers at high temperature (140°), Bradshaw et al observed a gas leaving the solution. This gas is
probably isobutylene.

In the production of the phenol (below) from the bromide, Cram and Day\textsuperscript{122} proposed the addition of tert-butoxide anion to the benzyne intermediate followed by an intramolecular elimination reaction to give the phenol and isobutylene. This has already been outlined:

It is even possible that base regenerates the ortho-anion which then abstracts the $\beta$-hydrogen. This means that the $\beta$-hydrogen is not directly removed by the base.

Under the reaction conditions (IV.1), all the mechanisms may be operating.

That the removal of the $\beta$-hydrogen is rate determining is shown in the results (table 1). The acidifying substituents COOEt and C\textsubscript{6}H\textsubscript{5} greatly enhance the acidity of the $\beta$-hydrogen and this is reflected in the much faster rate of cleavage of the ethers (40) and (41) compared with (38) and (39). This further justifies the outlined mechanism.
That the tert-butyl-2-methoxyphenyl ether (39) is cleaved at a more rapid rate than the ethyl-2-methoxyphenyl ether (38) is not unexpected. The former has nine hydrogens β to oxygen while the latter has only 3. This situation leaves the base with more easy choice of which proton to abstract in the case of (39) than in the case of (38).

The result here is potentially important in synthetic work in that in cases where there are two ether groups, one of them methoxy, a selective cleavage can be performed in which the methyl ether is left. Also when phenolic groups are protected in the form of ethers, other than methoxy, this may provide a suitable way of removing the protective group.
All g.l.c. examinations were carried out on a SE-30 column (3%); n.m.r. spectra were recorded in deuterochloroform.

**Reaction of o-Bromoanisole and Sodium Dimethylsulphoxide**

To stirred pure dimethylsulphoxide (100 ml) was added sodium hydride (5.02 g) over 15 min under nitrogen. 2-Bromoanisole (10 g) was slowly added and the temperature kept at 60-65° for 1.5 hr. Water was then cautiously added and the solution was extracted with ether to remove neutral products, which contained some starting material (g.l.c. $t_R$ 3 min, 155°). The aqueous solution was acidified and the product was extracted with ether, washed with water and dried (MgSO₄). The ether was distilled off to leave a dark yellow oil soluble in 2N KOH and weighed 2.5 g. This could be distilled 84°/1 mm to give a lighter-coloured product but this operation is accompanied by some decomposition or polymerisation. This product ($t_R$ 6 min, 155°) appeared from the spectral data: $\nu_{\text{max}}$ 3370 cm⁻¹, $\delta$ 1.25 (s, 3H, SCH₃), 3.88 (s, 3H, OCH₃), 6.54 (m, 2H, m to SCH₃), 7.18 (t, 1H, p to SCH₃), 7.02 (s, 1H, OH), to be essentially 3-methoxy-2-methylthiophenol (2). The yield was 27%.

**Methyl ether of 3-methoxy-2-methylmercaptophenol**

The phenol (8) (0.5 g) was methylated by refluxing overnight with sodium hydroxide (0.4 g), water (0.8 ml) and dimethylsulphate (0.5 ml). The crystals formed were recrystallised from ether and had m.p. 80° and weighed 0.2 g. Methylation of the phenol (8) was also effected by its repeated treatment with diazomethane. The spectral
data: $t_R$ 7.4 min (155°); $\delta$ 2.36 (s, 3H, SCH$_3$), 3.88 (s, 6H, OCH$_3$), 7.54 (d, 2H, m to SCH$_3$), 8.18 (t, H, p to SCH$_3$), corresponded to 1,3-dimethoxy-2-methylmercaptobenzene.

3,5-Dinitrobenzoate of 3-methoxy-2-methylmercaptophenol

The phenol (0.5 g) in pyridine (2 ml) was heated on steam bath with about 0.5 g 3,5-dinitrobenzoyl chloride for 20 min. Hydrochloric acid (0.5 N) was added to complex the pyridine and the mixture extracted with ether. The extract was washed with bicarbonate and water, dried and evaporated. The solid was recrystallised from ethyl acetate/methanol: m.p. 146-148°; m/e 364 (calc for C$_{15}$H$_{13}$O$_7$SN$_2$, 364); $\delta$ 2.26 (s, 3H, SCH$_3$), 3.98 (s, 3H, OCH$_3$), 6.9 (m, 2H, m to SCH$_3$), 7.3 (t, 1H, p to SCH$_3$), 9.37 (m, 3H, protons of dinitrobenzoate ring).

Desulphurisation of 3-methyl-2-methylmercaptophenol (8)

The phenol (1 g) was refluxed with Raney nickel (15 g) in ethanol for 4 hr. The catalyst was filtered off and the ethanol removed. The product was examined on the g.l.c. (160°). Its retention time ($t_R$ 3 min) was identical to that of 3-methoxyphenol.

Reaction of 4-bromoanisole (12) with sodium dimethylsulphoxide

The procedure was carried out as above. The phenolic product was obtained in 25% yield, and had b.p. 87-90°/0.1 mm, $\nu_{max}$ 3370 cm$^{-1}$; it contained two compounds (g.l.c. 150°), $t_R$ 6.2 and 6.8 min respectively. The n.m.r. spectrum showed two methylmercapto peaks at $\delta$ 2.2 and 2.3, and two methoxy
peaks at $\delta$ 3.73 and 3.75. Furthermore, the intensities of the peaks comprising each pair are roughly equal thereby showing a mixture of about equal proportions of the isomeric 3-SMe, 4-OH (14) and 4-SMe, 3-OH (13) compounds are present. The phenolic mixture was converted into a mixture of the methyl ether as described above. The etheric mixture b.p. 80-85°/0.1 mm had m/e 184 (C$_9$H$_{12}$O$_2$S). The n.m.r. spectrum showed two SMe resonances at $\delta$ 2.34 and $\delta$ 2.36 of about equal intensities. Desulphurisation of the phenolic product as described above gave a product which corresponded to a mixture of 3- and 4-hydroxyanisole on the g.l.c. However these were not separable. The yield of the phenolic product was (25%).

**Reaction of 2-methyl-4-bromoanisole with sodium dimethyl-sulphoxide**

The procedure was carried out as described for o-bromoanisole. The phenolic product b.p. 100-105°/0.05 mm, had $\nu_{\text{max}}$ 3370 cm$^{-1}$. It was converted directly to the methyl ether in the way described above. The methyl ether b.p. 90-94°/0.1 mm had m/e 198 (C$_{10}$H$_{14}$O$_2$S) and gave two equal peaks on the g.l.c. at $t_R$ 7 min and 9 min (160°). The n.m.r. gave SMe peak at $\delta$ 2.3. Desulphurisation of the methyl ether gave two equal peaks on the g.l.c. at $t_R$ 3 min and $t_R$ 4 min (200°). The peak at $t_R$ 3 min corresponded to 2-methylresorcinol methyl ether and the one at $t_R$ 4 min corresponded to 2-methylhydroquinone methyl ether respectively. These last two compounds were commercially available. The phenolic product was obtained in 20% yield.
Reaction of 3-methyl-4-bromoanisole with sodium dimethylsulphoxide

The procedure was carried out in the same way as described for o-bromoanisole. The phenolic product $v_{\text{max}}$ 3370 cm$^{-1}$ was converted into the methyl ether in the usual way. The methyl ether 90-95$^\circ$/0.1 mm had m/e 198 ($C_{10}H_{14}O_2S$). The n.m.r. spectrum gave SMe resonances at $\delta$ 2.36. The g.l.c. gave two peaks at $t_R$ 6.4 min (47%) and 8.5 min (57%) (160$^\circ$). Desulphurisation of the methyl ether mixture gave 3-methylresorcinol methyl ether (47%) $t_R$ 3 min and 2-methylhydroquinone methyl ether (53%) $t_R$ 4 min (200$^\circ$). This showed that the phenolic product contained (53%) of the methylmercaptophenol (29) and (47%) of the methylmercaptophenol (30). The yield of the phenolic mixture was (20%).

Preparation of 2-ethoxyanisole (38)

This was obtained by ethylating sodium 2-methoxyphenolate in ethanol with ethyl bromide$^{145}$: m/e 152 (calc for $C_9H_{12}O_2$, 152); $\delta$ 1.41 (t, 3H, Me), 3.80 (s, 3H, OMe), 4.02 (m, 2H, OCH$_2$), 6.85 (s, 4H, aromatic).

m-tert-Butoxyanisole (39): was prepared by the reaction of o-bromoanisole with potassium-tert-butoxide in dimethylsulphoxide; b.p. 76-77$^\circ$/1.5 mm, m/e, 168 (calc for $C_{10}H_{16}O_2$, 168); $\delta$ 1.41 (s, 9H, Me), 3.81 (s, 3H, OMe), 6.67 (m, 3H, aromatic), 7.20 (m, 1H, aromatic). Debutylation gave only m-hydroxyanisole (g.l.c.).

2-(2-Phenylethoxy)-anisole (40): was prepared by alkylating sodium 2-methoxyphenolate with 1-bromo-2-phenylethane$^{145}$; b.p. 126$^\circ$/0.5 mm, m/e 212 (calc for $C_{15}H_{16}O$, 212), $\delta$ 3.12 (t,
2H, CH₂), 3.82 (s, 3H, OMe), 4.18 (t, 2H, OCH₂), 6.86 (s, 
4H, aromatic), 7.26 (s, 5H, aromatic); t_R 3.5 min (210°).

Ethyl 3-(2-methoxyphenoxy)-propionate (41): was prepared 
by phenolating ethyl acrylate with sodium 2-methoxyphenolate 
(Hall and Stern 146); b.p. 120°/0.6 mm, m/e 224 (calc for 
C₁₂H₁₆O₄, 224); δ 1.20 (t, 3H, CH₃), 2.23 (t, 2H, OCH₂CH₂COO), 
2.68 (t, 2H, COOCH₂CH₃), 4.0 (s, 3H, OMe), 4.15 (t, 2H, 
OCH₂CH₂), 6.85 (m, 4H, aromatic); t_R 2.3 min (200°).

Reaction of the ethers with potassium tert-butoxide in 
dimethylsulphoxide

The ether (3.3 moles) was added to potassium tert­ 
butoxide (8.9 moles) in dimethylsulphoxide (15 ml) under 
nitrogen and the temperature of the oil bath was maintained 
at the required temperature. Stirring was continued over 
a given time (see the table of results) after which water 
was added and the aqueous mixture acidified with hydro­ 
chloric acid. The product was taken up in ether (7 ml), 
washed and dried (15 min, MgSO₄) and examined on the g.l.c. 

2-Ethoxyanisole treated as above after 4 hr (65°), 
gave unchanged material 82% (t_R 3 min, 110°) and o-methoxy­ 
phenol 18%. After 96 hr (65°), unchanged material was 12% 
and the phenol 78%.

m-tert-Butoxyanisole treated as above after 4 hr (65°), 
gave unchanged material 75% and o-methoxyphenol 25% (t_R 3.5 
min, 140°).

2-(2-Phenylethoxy)anisole (40) gave after 4 hr (65°) 
only 2-methoxyphenol. When the procedure was carried out 
at room temperature for only 15 min, the result remained the 
same. Prepared on a larger scale, 2-methoxyphenol was
obtained in 80% yield.

Ethyl 3-(2-methoxyphenoxy)-propionate (41) gave the same results as for 2-(2-phenylethoxy)-anisole above (see table of results). The yield of the phenol here was 90%.
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