STUDIES OF BASE - CATALYSED PROTIODEIODINATION OF ARYL IODIDES.

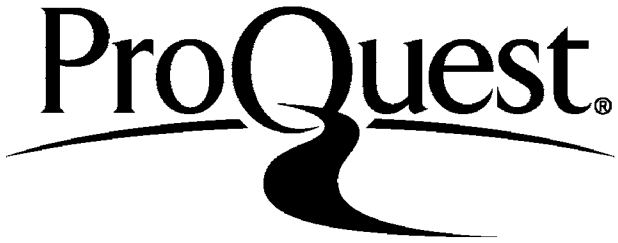
A thesis presented for the degree of Doctor of Philosophy in the Faculty of Science of the University of London.

by

CLIVE MOORE.

November, 1981.

Bedford College, London.



ACKNOWLEDGEMENTS

I would like to extend my unfeigned gratitude to my supervisors, Dr. R. Bolton and Dr. J.P.B. Sandall, for their initial suggestion of this research topic, and their incessant enthusiasm and forebearance throughout the period of this work.

I am also indebted to the Science Research Council for the award of a grant for this research.

Finally, I would like to thank Mrs.Irene Fraser for typing this thesis.

ABSTRACT.

The rates of the methoxide ion induced protiodeiodination of a number of polychloroiodoarenes in dimethyl sulphoxide-methanol (9:1, v/v) have been measured at 323·2K. Chlorine substituents activate all positions in the order, o-Cl > m-Cl > p-Cl, although the more fully substituted polychloroiodoarenes show much weaker substituent effects.

The true reagent effecting the reactions appears to be the dimsyl anion, and the rates of reaction in some cases reach and exceed that expected of an encounter-controlled process. This may account for the major decrease in efficiency of further activating substituents.

The extent to which concomitant methoxydehalogenation occurs has been checked partly by product analysis and partly by comparison with the rates of methoxydechlorination of some allied polychlorobenzenes. Methoxydehalogenation is an expected mode of reaction in a number of cases. Only in studies of some non-ortho-substituted compounds is extensive methoxydehalogenation observed. The presence of an ortho-chlorine substituent promotes the protiodeiodination reaction to the exclusion of methoxydehalogenation.

The addition of fluorene to the reaction medium to provide a second and competing carbanion causes the formation of 9,9'-bifluorenylidene whose presence suggests the intermediacy of 9-iodofluorene. This and a number of other observations suggest that the mechanism of the reduction involves the loss of iodine as $I^{\delta+}$ towards a suitable nucleophile and that, despite the similarity of reaction conditions, the $S_{RN}1$ mechanism is not operating in these systems.

CONTENTS.

1. INTRODUCTION.

1.1. CLASSIFICATION OF REACTIONS.

Two types of processes are distinguishable in aromatic substitution reactions.

(a) When two species come together during processes of bond formation, both bonding electrons come from just one of the species, and subsequently, when bond breakage occurs, both electrons depart with one of the fragments. Generally, all intermediates in such reactions have an even number of electrons. These processes are known as heterolytic reactions.

$$C_6H_6 + Br^+ \longrightarrow C_6H_5Br + H^+ \qquad (1)$$

Within heterolytic processes, there are two further distinctions. If the process is initiated by a species which attacks sites of relatively high electron density, it is said to be an electrophilic process, and the species which attacks is said to be an electrophile, as shown in equation (1).

If the process is initiated by a species seeking to donate electrons to sites of relatively low electron density, a nucleophilic reaction takes place, and the attacking species is termed a nucleophile, as illustrated in equation (2).

$$C_2H_5O^- + O_2N{\cdot}C_6H_4{\cdot}Cl \longrightarrow O_2N{\cdot}C_6H_4{\cdot}OC_2H_5 + Cl^- \qquad (2)$$

(b) A number of important series of reactions are those involving species containing an odd number of electrons. Such reactions proceed through an intermediate with an odd number of electrons and are classified as homolytic reactions, shown in equation (3).

$$Ph\cdot + C_6H_5X \longrightarrow Ph{\cdot}C_6H_4{\cdot}X + H\cdot \qquad (3)$$

1.1.1. AROMATIC SUBSTITUTION REACTIONS.

There are obvious broad analogies between addition to olefinic compounds and substitution in aromatic compounds. In both types of reaction, a new σ-bond has to be established with the p-orbital of a carbon atom participating in a molecular π-system. In both types of reaction, this can be done by attacking, with a suitable reagent, an electron deficient region suitably exposed by an electropolar displacement of the π-system.

1.1.2. FREE RADICAL PROCESSES.

In a free-radical substitution process,

$$R\text{-}X \longrightarrow R\text{-}Y \qquad (4)$$

there must first be cleavage of substrate RX so that R• radicals are produced. This may happen by a spontaneous cleavage,

$$R{:}X \longrightarrow R^{\bullet} + X^{\bullet} \qquad (5)$$

or may be caused by light or heat; or more often, cleavage is induced by abstraction of a fragment (X in equation (6)) by an attacking radical.

$$RX + W^{\bullet} \longrightarrow R^{\bullet} + WX \text{ (e.g., W = Br, X = H)} \qquad (6)$$

W• is produced by adding a compound such as a peroxide which spontaneously forms free radicals. Such a compound is called an initiator. Once R• is formed, it may go to product in a number of ways; by abstraction,

$$R^{\bullet} + YW \longrightarrow RY + W^{\bullet} \text{ (e.g., Y = W = Cl)} \qquad (7)$$

or by coupling with another radical,

$$R^{\bullet} + Y^{\bullet} \longrightarrow RY. \qquad (8)$$

Disproportionation of radicals produces a saturated and an unsaturated species, exemplified by equation (9),

$$2RCH_2CH_2\cdot \longrightarrow RCH_2CH_3 + RCH{:}CH_2\cdot \qquad (9)$$

Dimerization is also a mode of reaction of free radicals,

$$2R\cdot \longrightarrow RR. \qquad (10)$$

1.1.3. ELECTROPHILIC PROCESSES.

In aromatic systems, the π-electron system provides a high electron density around the aromatic ring. Due to this high electron density, electrophilic attack is preferred, the electrophile being a positive ion or the positive end of a dipole or induced dipole.

The best known aromatic substitution reactions such as nitration, halogenation, and the Friedel-Crafts' reactions, are of the electrophilic type.

It was first suggested by Euler[1] that the active species in nitration was the nitronium ion, NO_2^+. Variation of the freezing point of mixtures of dinitrogen pentoxide, N_2O_5, and water over a range of concentrations encompassing the formation of nitric acid, showed[2] that appreciable self-dehydration occurred according to equation (11).

$$2HNO_3 \rightleftharpoons NO_2^+ + NO_3^- + H_2O \qquad (11)$$

Cryoscopic measurements of the more usual nitrating reagent, nitric acid plus sulphuric acid, showed[3] four particles present in solution, consistent with the formation of NO_2^+, the addition of sulphuric acid allowing a further mode of ionisation (equation (12)).

$$HNO_3 + H_2SO_4 \rightleftharpoons NO_2^+ + HSO_4^- + H_2O \qquad (12)$$

Raman spectra of nitric acid[4] show two weak bands at 1050 and 1400 cm^{-1}. These were not attributable to either of the

acid molecules in the HNO_3/H_2SO_4 nitrating mixtures.[5,6] The band at 1400 cm^{-1} was assigned to the NO_2^+ ion, and the 1050 cm^{-1} band attributed in cases concerning HNO_3 and N_2O_5, to the nitrate ion.[7,8] In H_2SO_4, the 1050 cm^{-1} band was attributed to the bisulphate ion, from the ionisation shown in equation (13)).

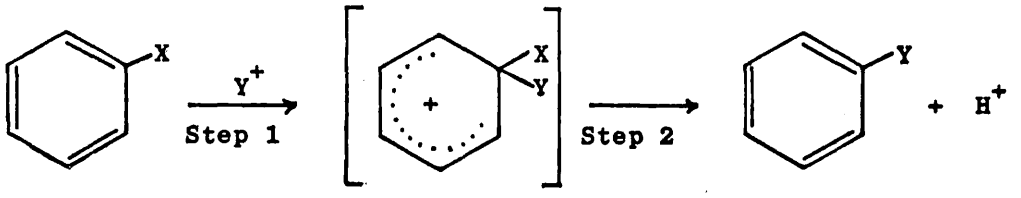
$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^- \qquad (13)$$

The concentration of NO_2^+ ions in HNO_3, determined by infra-red spectroscopy, was increased markedly by the addition of sulphuric acid;[9] up to 10% water does not affect the concentrations of NO_2^+ ions.[10,11,12] Further dilution reduces the concentration of these species, which is not detectable (< 1%) in solutions containing < 85% H_2SO_4. Concentrations containing > 89% by weight of sulphuric acid, causes the complete ionisation of nitric acid to NO_2^+ ions. Martinsen[13,14] observed the occurrence of a maximum in the rate of nitration, for nitration in sulphuric acid of 89-90% concentration.

The structure determination of solid NO_2ClO_4[15] and N_2O_5[8] by X-ray crystallography revealed the two compounds to contain the ions ClO_4^- and NO_3^- respectively; but in addition, both were found to contain the same linear, triatomic species. From the stoichiometry of these compounds, the species was thought to be the nitronium ion. Although complete structural determinations of these compounds have not been reported, the Raman spectrum of each shows an absorption at 1400 cm^{-1}, consistent with the spectra reported for the NO_2^+ ion.

The large majority of aromatic electrophilic substitutions proceed by a variant in one general mechanism with respect to the substrate. In this mechanism, the electrophile attacks in the first step, giving rise to a positively charged intermediate, and the

leaving group (the proton being the most common in aromatic electrophilic substitution) departs in the second step, as shown in Scheme 1.



Scheme 1.

(The dotted line in the intermediate structure indicates partially formed or broken bonds.)

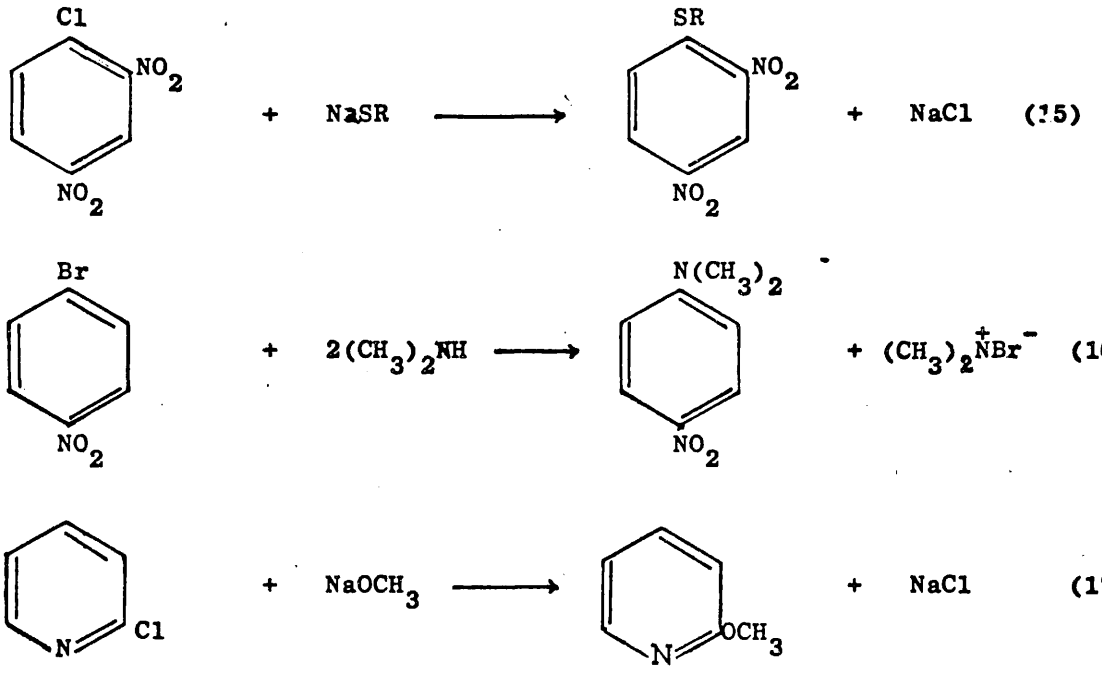
In nitration, if the substitution involved a single step, it would necessarily be rate-determining. Since this involves breaking a C-H bond, a kinetic isotope effect would be observed. Melander[16] first sought this isotope effect, but unsuccessfully. This proves step 2, in the two step sequence (Scheme 1), not to be rate-determining. Thus, nitration by the nitronium ion is a two stage process, the first step being rate-determining.

1.1.4. NUCLEOPHILIC PROCESSES.

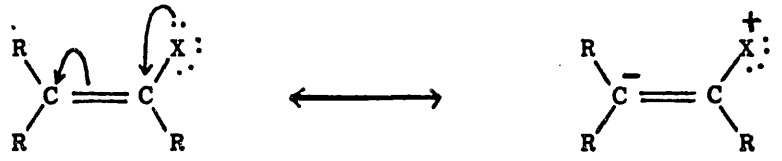
In nucleophilic substitutions, the attacking reagent (the nucleophile) brings an electron pair to the substrate to form the new bond, and the leaving group (nucleofuge) comes away with an electron pair. This is represented by equation (14).

$$RX + Y^- \longrightarrow RY + X^- \qquad (14)$$

Reactions (15), (16) and (17) depict some familiar nucleophilic aromatic substitutions.

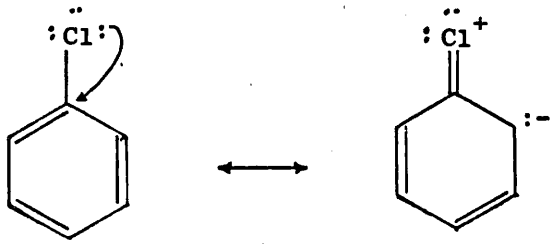


It has been implied in organic textbooks that simple vinyl halides are unreactive towards S_N1 type solvolytic reactions.[17] The lack of reactivity of vinyl and aryl halides has been ascribed not only to transition state destabilisation reflecting the relative energies of vinyl, aryl and alkyl carbocations, but also to the lowered ground state energies of vinyl and aryl halides. The latter has been attributed to the increased σ-bond strength[18] of the carbon-halogen bond due to change in hybridisation of carbon from sp^3 in alkyl halides to sp^2 in vinyl halides, as well as to the partial double bond in the mesomeric form of the vinyl halides[19] (structures I and II).



I II

An analogous situation is possible in aryl halides (structures III and IV).

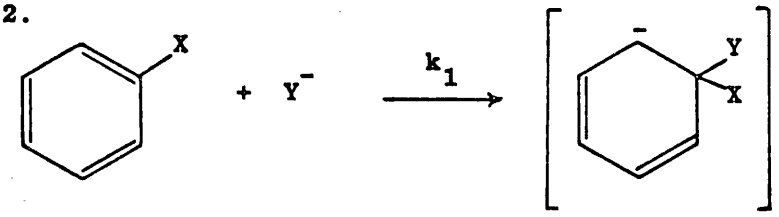


III IV

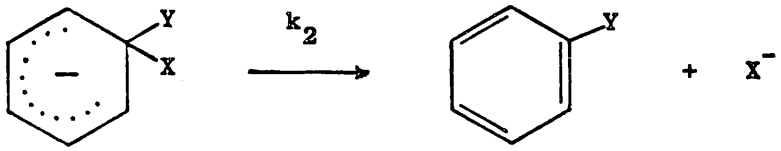
As the meagre reactivity of vinyl and aryl halides is due to the low stability of the intermediate cations as well as to the greater bond strength of the carbon-halogen bond in these systems, nucleophilic substitution reactions may be easier when the intermediate anions are stabilised by suitably situated substituents, and this is generally the case.

By far the most important mechanism for nucleophilic aromatic substitution consists of two steps. This mechanism is illustrated in Scheme 2.

Step 1.



Step 2.



Scheme 2.

The first step is usually, but not always, rate-determining when Y^- is a 'hard' nucleophile and the solvent is aqueous or protic (e.g., methanol).

In nucleophilic substitutions, hydrogen is seldom replaced, the replaceable groups ordinarily being halogen atoms and other groups capable of resonance stability as anions.

1.1.5. EFFECTS OF SUBSTITUENTS IN HETEROLYTIC AROMATIC SUBSTITUTION.

The reactions of compounds are largely determined by their functional groups. One must realise that rate constants and positions of equilibria associated with the reactions of functional

groups may be strongly dependent upon other groups present in the reacting molecules. Rates and equilibria are often markedly affected by changes in the carbon skeleton or by the introduction of additional substituents which themselves suffer no net change. Thus, a nitro group placed in the para-position in benzoic acid causes an increase in the dissociation constant for the acid from $K = 6{\cdot}46 \times 10^{-5}$ for benzoic acid,[20] to $K = 3{\cdot}93 \times 10^{-4}$ for p-nitrobenzoic acid.[20]

Two dissimilar atoms, bonded together, set up a dipole moment between them. The extents of these dipoles, which may be altered by other groups present in the system, have a considerable bearing upon the courses of many reactions.

To discuss substituent effects, we need two fundamentals; (i) a standard state, and (ii) mechanisms for transmitting the effect to the reaction site.

The standard state is taken as the behaviour of the fully hydrogenated (parent) system, that is, hydrogen is the standard substituent.

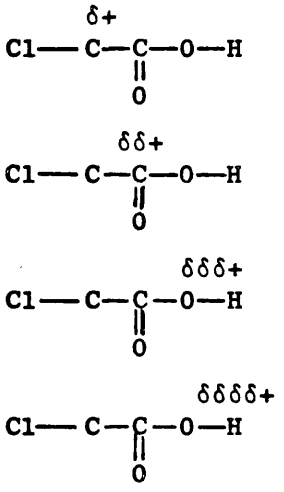
In attempting to correlate structure and reactivity, three mechanisms by which substituent effects may be transmitted to the reaction centre electrically can be distinguished. Either the π-electrons may be involved, in which case there is conjugative (mesomeric) relay, or the σ-electrons are perturbed (giving rise to inductive relay), or the effect may be transmitted across solvent molecules (field effects).

1.1.6 THE INDUCTIVE EFFECT.

The electrical dissymmetry, arising from unequal sharing of electrons between unlike atoms, that is, from electronegativity or electropositivity, could be propagated along a chain of bound atoms

(like or unlike) by a mechanism of electrostatic induction. This is called the inductive mechanism of electron displacement.

This effect is well exemplified in the acidity of acetic acid, which is vastly increased by successive substitution of hydrogen by chlorine, the reason being the marked C-Cl dipole, which induces charge upon the adjacent atoms. The effect is then relayed throughout the system through the σ-bonds. This causes higher acidity of the hydrogen atom, which is reflected in the dissociation constants of the chloroacetic acids.[21] A representation of the inductive effect of chlorine substitution in acetic acid is outlined in Scheme 3.



Scheme 3.

Since the effect is relayed by induction, its magnitude should decrease as the distance (number of atoms) between the dipole and the reacting group increases. Although increasing the length of the alkyl chain attached to the $-CO_2H$ fragment (in acetic acid) does not materially alter the dissociation constant, the dissociation constants of the ω-chloroacids drop regularly.[22] The inductive effect therefore dies out fairly quickly as successive atoms are interspersed between the dipole and the reaction centre.

It must also be noted that in an aromatic or other conjugated system, a change in the electronegativity of the attached atom must

also affect the electron distribution in the π-system.

1.1.7. THE FIELD EFFECT.

These are due to electrostatic interactions between a charged or partially charged atom and a reaction centre, and are seen to operate in the same direction as the inductive effect.

Equilibrium properties have been successfully discussed in terms of the field effect; notably, the ionisation constants of saturated dibasic acids.[23,24]

Ridd and his co-workers have made a quantitative study of the nitration of aniline and its N-methylated derivatives. It appears[25,26,27,28] that nitration occurs via the anilinium ions, and in the series $PhNMe_3^+$, $PhNHMe_2^+$, $PhNH_2Me^+$, $PhNH_3^+$, there is smooth increase in the reactivity of the para-position over that of the meta-, though the differences are small when compared with the powerful, overall deactivating influences of these substituents. The change from $-NH_3^+$ to $-NMe_3^+$ decreases the rate of para-nitration even more than the rate of meta-; a marked contrast to the effect of going from methyl to t-butyl in the isoelectronic alkyl series.

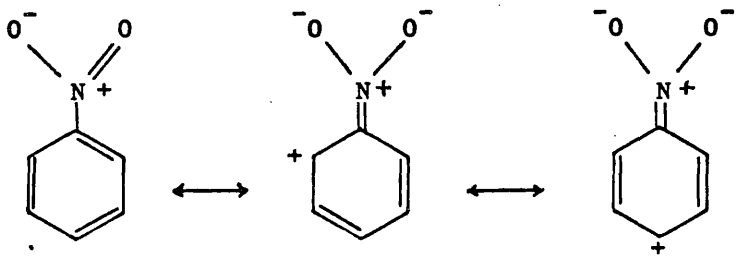
The closely similar reactivities of the para- and meta-positions of these cations reveal a substituent effect which causes deactivation of the ring without much discrimination between para- and meta- positions. Such substituent effects are seen as arising from the field effect.

The extent of m-substitution in the nitration of the three substrates $Ph(CH_2)_nNMe_3^+$ (n = 0-3),[29] was not in accord with the view that the poles act inductively through the methylene chain, but was reminiscent of the way in which a methylene group affected the dissociation constants of dicarboxylic acids.[30]

Thus, the substituent effects of both positive and negative poles are evidently, in the main, consequences of direct electrostatic interactions.

1.1.8. THE MESOMERIC EFFECT.

It is widely accepted that two apparently isolated double bonds, as in 1,3-butadiene, can act as one continuous π-orbital, and that the three formal bonds in benzene, are in fact, one molecular π-orbital. If a group is attached to such a conjugated system, and if the p-orbital overlap can occur between the attached atom (X) and the π-system in the conjugated structure, electron density within the structure may alter. If a group X repels electrons from the overlapping p-orbital into the π-system, increases in electron density will occur at alternate carbon atoms in the conjugated structure. Unlike the inductive effect, this mesomeric effect is transmitted through π-bonds with very little loss of intensity. An illustration of this mesomeric effect is in the resonance structures for nitrobenzenes, structures V, VI and VII.



V VI VII

The substitution of a nitro-group on a benzene ring results in withdrawal of π-electron density from the ring, especially from the ortho- and para- positions. An important characteristic of mesomeric effects is that they are transmitted largely to alternate atoms in the conjugated system.

The mesomeric effect of a group operates only when the group is directly connected to an unsaturated system, so that, for example,

in explaining the effect of the CH_3O- group on the reactivity of $-CO_2H$ in $CH_3O \cdot CH_2 \cdot CH_2 \cdot CO_2H$, only the inductive effect of the CH_3O- group need be considered. This is one way of separating the effects. In $CH_3O \cdot CH{:}CH \cdot CO_2H$, where conjugation arises, both must be considered.

1.1.9. NOMENCLATURE.

By convention, groups which are more powerful electron attractors than the hydrogen atom are said to exhibit negative inductive (-I) effects, whereas those which are poorer electron attractors than hydrogen display positive inductive (+I) effects.

Groups that supply electron density to conjugated systems by mesomeric effects are designated +M in character, and those groups designated as -M withdraw electron density from such systems.

1.1.10. ADDITIVITY IN AROMATIC ELECTROPHILIC SUBSTITUTION.

Substituents in aromatic compounds are known to affect the reactivity and orientation of electrophilic substitutions. Aromatic compounds are sometimes described as being 'reactive' and others 'less reactive'. A group of aromatic compounds could be arranged in order of reactivity merely by measuring their rates of reaction under similar conditions.

Some relative rates of nitration of various benzene derivatives are given in Table 1. These relative rates are totals for all nuclear positions and are expressed with respect to the total rate of nitration of benzene as unity.

If these rates are combined with the proportions of each isomer produced, it is possible to calculate relative rates of attack on each individual nuclear position. The results of this combination of relative rates and orientation ratios are given in Table 2.

Table 1. Relative rates of mononitration of benzene derivatives.

Aromatic Compound	Rate	Reference
Benzene	1·00	
Toluene	24·5	31
Ethyl Benzoate	0·00367	32
Fluorobenzene	0·15	33
Chlorobenzene	0·033	33
Bromobenzene	0·030	33
Iodobenzene	0·18	33
Cinnamic Acid	0·111	34
Ethyl Phenylacetate	3·66	35
Benzyl Chloride	0·302	35
t-Butyl Benzene	15·7	36

Any figure applying to an individual position in a substituted benzene, if above unity, represents the activation of that position by the substituent, and if below unity, measures the deactivation of the position. These values, quantitatively speaking, reflect combinations of inductive and mesomeric effects of substituents.

Nitration is facilitated by electron-releasing substituents, such as alkyl groups, but retarded by electron-attracting substituents (e.g., $-NO_2$, $-CO_2Et$.). Similar statements may be made for other types of electrophilic substitution reactions when I and M effects are in opposite directions (i.e., halogens, -OH, $-NR_2$ and -SR groups).

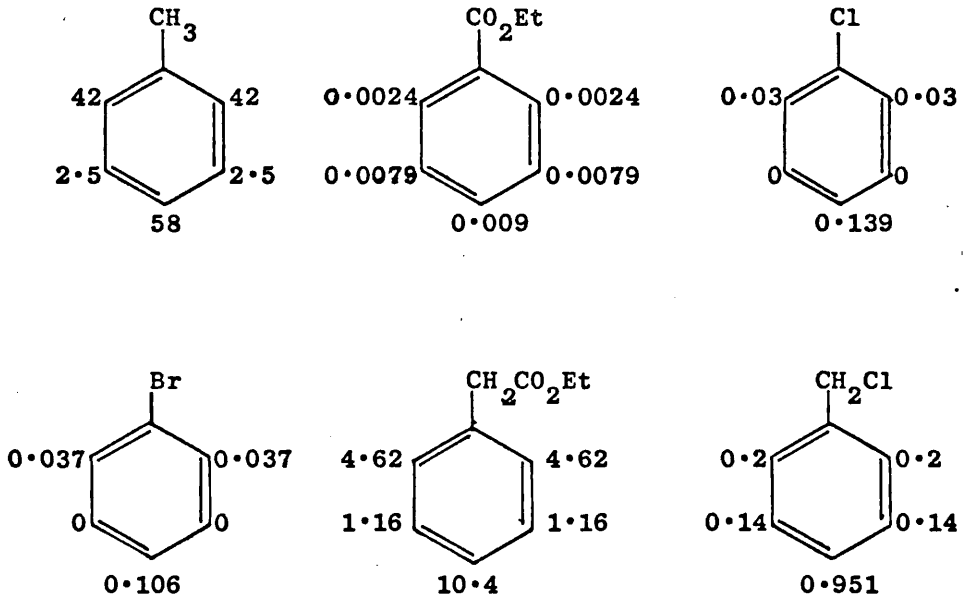
An important related question is that of orientation, for an aromatic ring may be generally attacked in two or more different and non-equivalent positions. As can be seen from Table 2, an electrophile, for example, nitronium ion, will attack all available positions of an

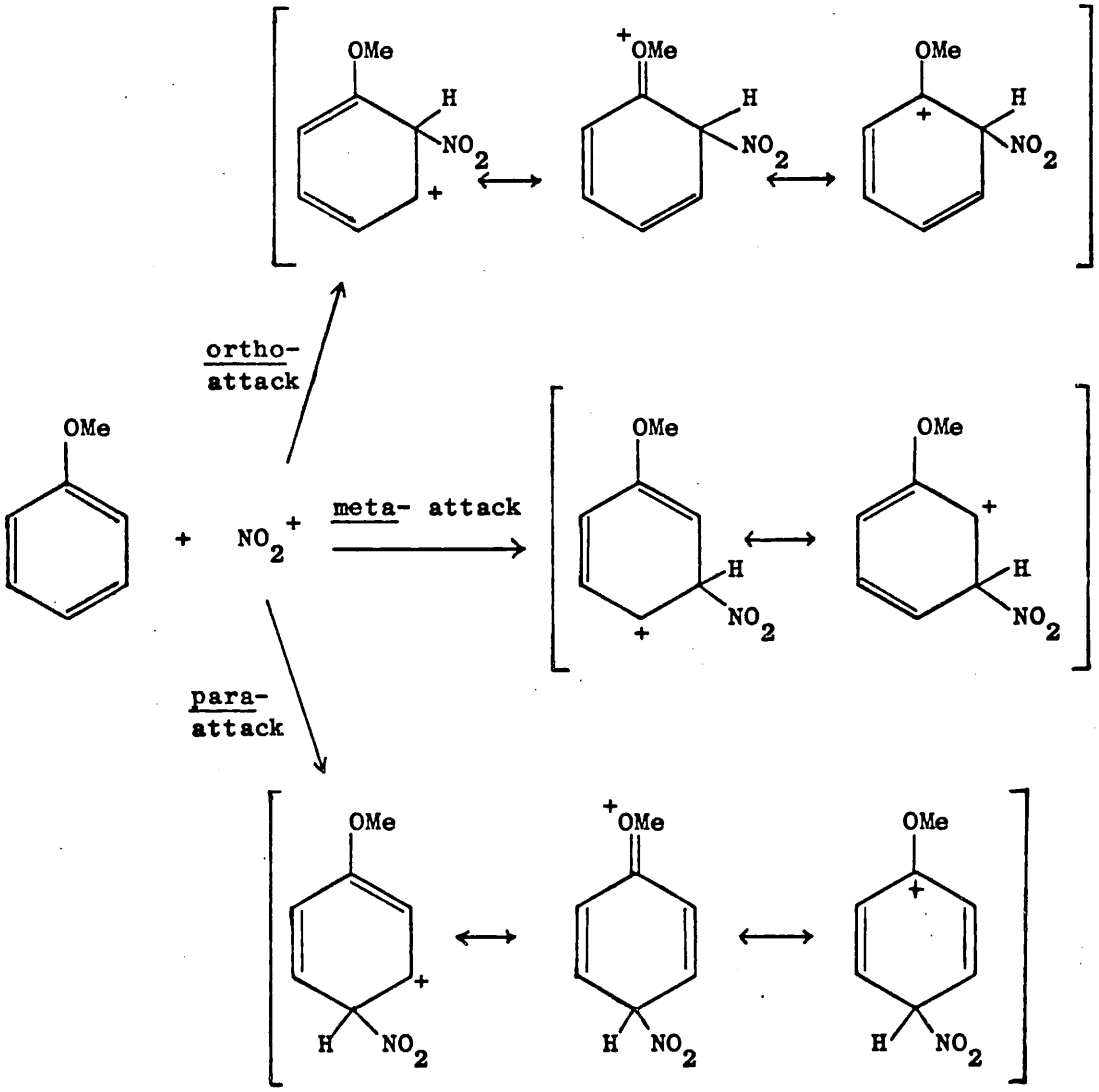
aromatic ring, but reactions at 'favoured' sites are more rapid.

The activated complex in aromatic nitration, resulting from attack at each of the available positions, is intermediate in character between substrate and the intermediate cation. For example, consider the nitration of anisole. Representative structures for each of the possible cation intermediates are shown in Scheme 4.

The complex having the lowest energy is that associated with the 'favoured' position for attack. In the intermediate for meta- attack, the positive charge carried in by NO_2^+ ion must remain on the benzene ring until

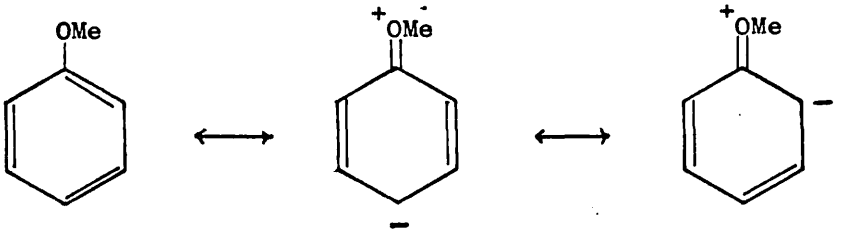
Table 2. Rates of attack in nitration on individual nuclear positions in benzene rings (rate for one individual position in benzene taken as unity)[23].





Scheme 4.

the proton departs, completing the substitution reaction. With ortho- and para- attack, π-electron density drifts from the electron-rich oxygen atom into the ring, dispersing the positive charge, and lowering the energy of both the intermediate and the transition state leading to it. It may also be concluded that in the nitration of anisole, attack should take place more readily at the ortho- and para- positions than at the meta- position, as suggested by structures VIII and IX.



VIII IX

This explains the formation of o-nitro- and p-nitroanisoles from the nitration of anisole.

The product of nitration of nitrobenzene is m-dinitrobenzene. The explanation for this is essentially the same. Groups which do not have unshared electron pairs, such as the nitro- group, often direct incoming electrophiles predominantly to the meta- positions, as this group withdraws electron density both inductively and mesomerically from the ring; this is reflected in structures V, VI, and VII (p. 17). An electrophile is directed mainly to the meta- position, where it will preferentially attack where electron density has been depleted least.

Orientation has so far been discussed in terms of the manner in which substituents affect, either by induction or mesomeric relay, the electron density in the substrate and in the activated complex. Electron density has been implied as being the same at both the ortho-

and para- positions. In actuality, this is never observed.

The para- carbon is in a more favourable position for attack than the ortho- carbon to the substituent, for the substituent acts as a shield(steric effect). This effect, which should lower the ortho- : para- ratio, is detectable even for small substituents and becomes quite important in the event that the substituent is bulky. Table 3 gives the ratios for the nitration of some alkylbenzenes.

Table 3. Ortho-:para- product ratio of nitration of alkylbenzenes.[31,35,37,38]

Aromatic Compound	ortho-:para- Ratio
$PhCH_3$	1.57
$PhCH_2CH_3$	0.93
$PhCH(CH_3)_2$	0.48
$PhC(CH_3)_3$	0.22

The intensity of the inductive effect decreases sharply with distance from the 'primary pole'. Thus, irrespective of mesomeric effects, the electron density at positions ortho- to the substituent are more heavily influenced by the I effect of the substituent than the para- positions.

And from this, one would expect the ortho-:para- ratio in the nitration of such compounds as benzaldehyde, benzoyl chloride and nitrobenzene to be low, since these compounds, from their inductive and mesomeric effects, are meta- directing in electrophilic substitution. But the ratios are found to be quite large; approximately 2 and 20 for benzaldehyde and nitrobenzene[38,39,40,41] respectively. Comparing the canonical

structures for nitrobenzene, VI and VII (p. 17), which depict the depletion of electron density, it appears that the so-called 'para-quinoid' structure, VII, has a significantly lower energy; thus, ortho- substitution should predominate over para-. This accounts for the large ortho-:para- ratios with certain compounds.

These examples suggest that inductive and mesomeric effects may be used to determine orientation and reactivity of aromatic compounds in electrophilic substitution.

1.1.11 LINEAR FREE ENERGY RELATIONSHIPS.

There exists a number of quantitative relationships between structure and reactivity. Of these, the most familiar is the Hammett equation,[42,43] which is widely applied to aromatic systems in the form set out in equation (18).

$$\log(K/Ko) = \sigma\rho \qquad (18)$$

(where K and Ko are rate or equilibrium constants of the substituted and unsubstituted compound respectively.)

The ratio of the equilibrium constants as set out in the left-hand side of equation (18), is proportional to the difference in the free energies of reactions of substituted and unsubstituted compounds. For this reason, this type of equation is often referred to as a 'linear free energy relationship.'

The first parameter, σ, is characteristic only of the substituent and its orientation with respect to the reaction site, and represents the ability of the substituent to attract or repel electrons by combination of its inductive and mesomeric effects.

The second parameter, ρ, characteristic of the reaction series at hand, is a measure of the sensitivity of this type of reaction series to ring substitution.

The ionisation of benzoic acid was arbitarily chosen by Hammett as the standard reaction (for which ρ is fixed at unity) and σ was defined on the basis of this standard. Values of σ for substituents in meta- and para- positions relative to the reaction centre were then calculated.

In meta- and para- substituted benzene derivatives, substituents are relatively rigid and lie far enough from the reaction centre to assume that steric interaction is negligible. Ortho- substituents are widely thought not to be amenable to the Hammett treatment due to probable steric influence although Charton[44,45] reached the unexpected conclusion that ortho-substituent effects are independent of steric interactions except for bulky substituents such as -I, -Ph and -t-Bu. However, the Hammett treatment is successful for ortho-substituted compounds when the reaction centre (Y) in o-$X \cdot C_6H_4 \cdot Y$ is physically separated from the ring, as in the ionisation constants of o-$X \cdot C_6H_4 \cdot OCH_2 \cdot CO_2H$.[45]

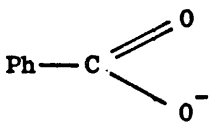
A positive value of σ for a given substituent indicates strong electron attraction of the substituent, a negative value indicating electron donation by the substituent.

The derived σ values prove reasonably successful whether the substrates are attacked by electrophilic, nucleophilic, or free-radical reagents, the important point being that the mechanism is constant within a given reaction series.

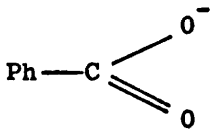
However, there are many reactions which do not fit this usage. These are mostly where attack is directed on the ring and where the substituent is one which can enter into direct resonance interaction with the reaction site.

In the case of the ionisation constant for p-nitrobenzoic acid

the carboxylate anion is already resonance stabilized (structures X and XI). Conjugation between a p-nitro group in the benzene ring and the carboxylate fragment does not occur. Accordingly, the nitro group in the para- position of benzoic acid does not increase the



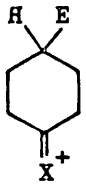
X



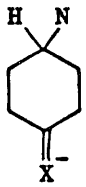
XI

ionisation constant as much as in the nitrophenol.

For these cases, two new sets of σ values have been devised; σ^+ values proposed by Brown[46] for cases in which an electron-donating group interacts with a developing positive charge in the transition state (aromatic electrophilic substitutions) and, by analogy, σ^- values[47] when electron-withdrawing groups interact with a developing negative charge; these points are illustrated by structures XII and XIII.

XII 

XII



XIII

XIII

(E = electrophile, N = nucleophile)

The Hammett equation is not the only linear free energy relationship. Some, like the Hammett equation, correlate structural changes in reactants, others, such as the Grunwald-Winstein relationship[48], also correlates changes in solvent. Linear free energy relationships may have mechanistic implications. If log (K/Ko) changes regularly and linearly with the various appropriate σ values, it is likely that the same mechanism is operating throughout the series.

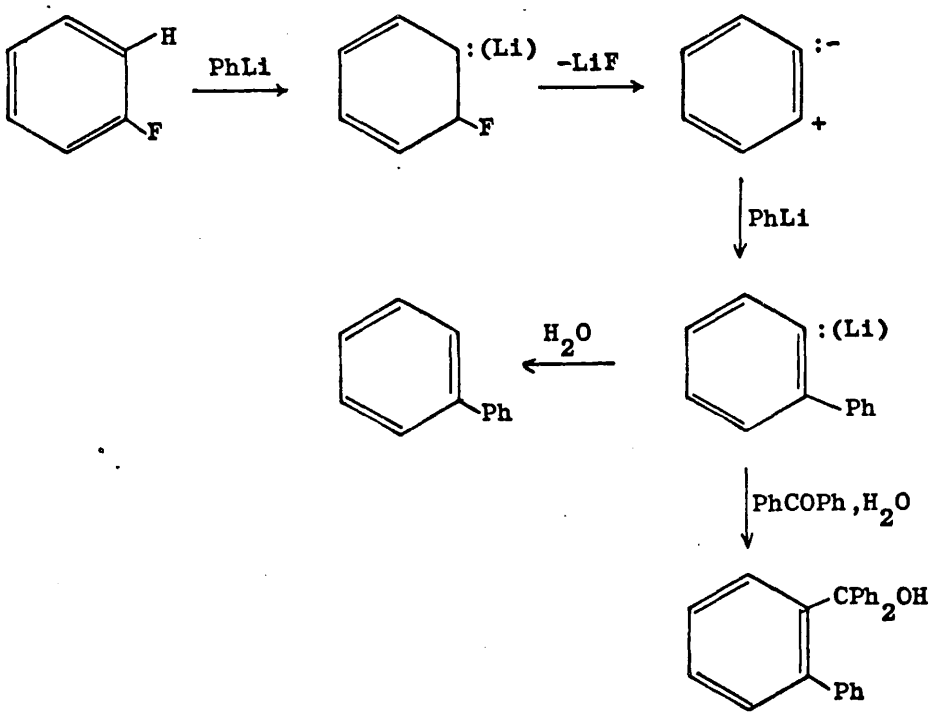
Information can also be obtained from the magnitude and sign of ρ. For example, a large negative value of ρ indicates a large electron demand at the reaction centre, from which it is concluded that a highly electron deficient centre, perhaps an incipient carbonium ion, is involved. In such a situation, σ^+ may prove to be more suitable than σ. Conversely, a positive value of ρ is associated with a developing negative charge in the transition state, and σ^- may more closely reflect the substituent effect.

The $\sigma\rho$ relationship even applies to free-radical processes, because free-radicals can have some polar character, though ρ values are usually small ($<1{\cdot}5$) whether positive or negative.

1.2. MODES OF REACTIONS OF ARYL HALIDES

1.2.1. THE BENZYNE (OR ELIMINATION-ADDITION) MECHANISM

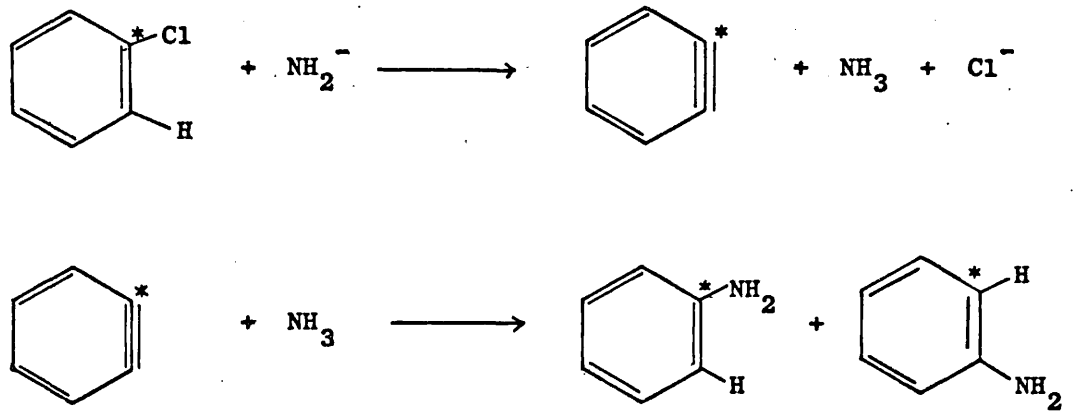
Some aromatic nucleophilic substitution reactions are clearly different in character from those which occur as cited in equations (15), (16) and (17). The idea that aromatic compounds, in certain circumstances, might undergo nucleophilic substitution by initial elimination of HX from neighbouring carbon atoms to form an aryne, followed by a nucleophilic addition to regenerate an aromatic compound, was first advanced, with experimental support, by Wittig.[49] His discovery was that the products from the reaction of phenyllithium with fluorobenzenes were dependent on the subsequent treatment of the reaction mixture. This is outlined in Scheme 5.



Scheme 5.

When water was added, the product was biphenyl; when benzophenone was added, the product was o-biphenylyldiphenylcarbinol. Wittig originally considered the unusual intermediate to be permanently polarised.

Bergstrom et al.[50] showed that halogenobenzenes (except fluorobenzene) reacted with potassium amide in liquid ammonia to form aniline. Roberts and his co-workers[51, 52a] then elegantly demonstrated the reaction of isotopically labelled chlorobenzene with potassium amide in liquid ammonia, revealing a product consisting of aniline labelled equally in the 1- and 2- positions, and explained these results in terms of a benzyne-type intermediate (illustrated in Scheme 6).

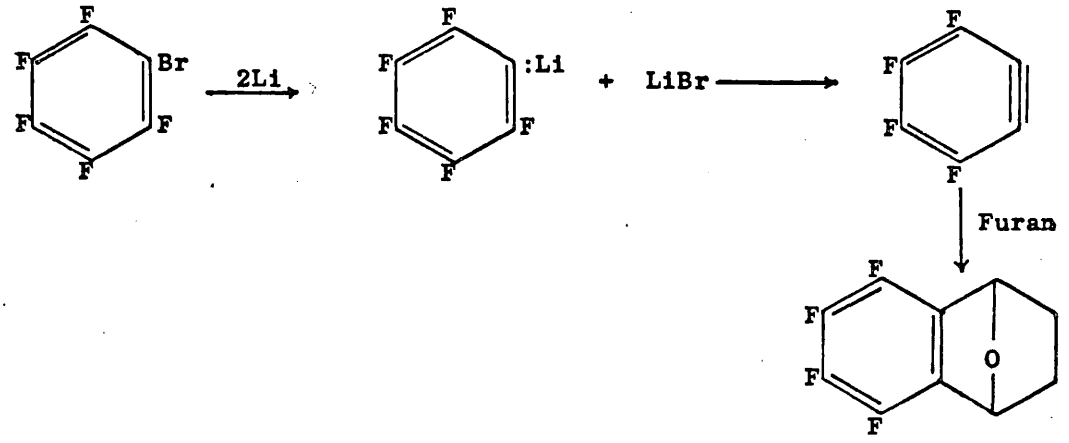


Scheme 6.

Halogenobenzenes lacking in ortho-hydrogen atoms (e.g., 2-bromo-3-methylanisole) were shown to be unreactive towards sodium amide in liquid ammonia.[53]

The formation of tetrafluorobenzyne has been indicated by the work of Coe, Stephens and Tatlow.[54] When bromopentafluorobenzene was treated with lithium amalgam, bromine was first eliminated with formation of pentafluorophenyllithium. Above 0°, some fluoride ion was also eliminated, and the tetrafluorobenzyne formed was trapped

by reaction with furan to give 5,8-epoxy-1,2,3,4-tetrafluoro-5,8-dihydronaphthalene (Scheme 7). Wittig and Pöhmer[55] demonstrated the corresponding reaction of o-bromofluorobenzene with lithium in furan.



Scheme 7.

Bradshaw and Lambert[56] had observed a fragmentation of 1—(o-bromophenyl)-2-p-toluenesulphonhydrazide with sodium methoxide in methanol. The cleavage of 1-phenyl-2-sulphonhydrazides by base, yielding benzene, nitrogen and sulphinate ion had been reported very much earlier.[57,58]

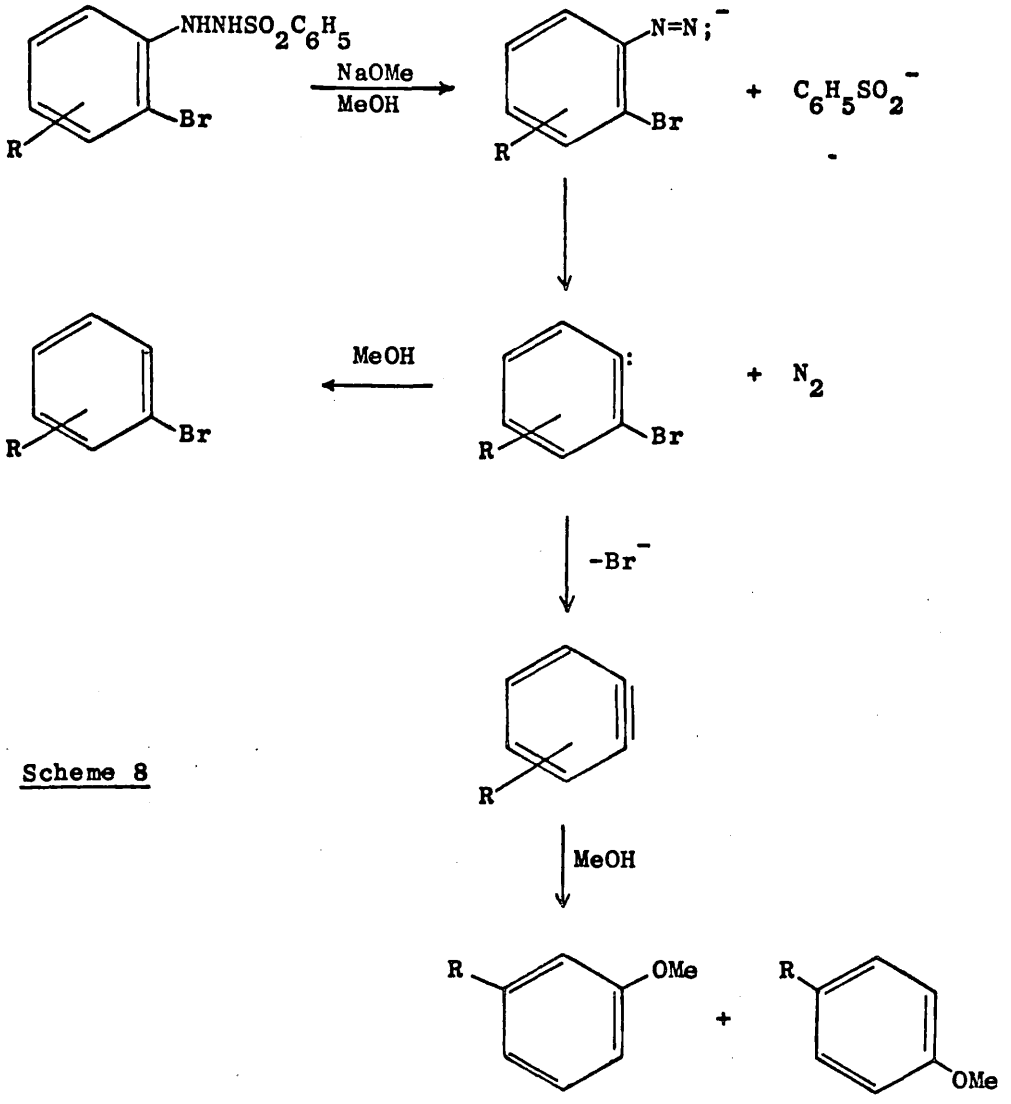
1.2.1.1. ALTERNATE o-HALOGENOPHENYL CARBANION REACTIONS.

o-Halogenophenyl anions are recognised to be intermediates in aryne formation.[51,52] Two prominent modes of reaction of halogenophenyl anions in protic solvents are loss of halide to form arynes, and proton capture from solvent molecules to form aryl halides. The relative rates of these reactions depend on the halogens present,[51,52] on the solvent, and on other substituents in the ring.[59] The order of reactivity of the monohalogenobenzenes with potassium amide in liquid ammonia to form arynes has been found to be unusual,[50] Br>I>Cl>>F and has been suggested as arising from a change in the rate-determining step.[51] When the leaving group is

bromine or iodine, proton removal is rate-determining, and the rate order is (F>Cl>)Br>I. When chlorine or fluorine is the leaving group, C-X bond cleavage is rate-determining and the order of this step is (I>Br>)Cl>F. Confirmation of this order was found in a direct competitive study of m-dihalogenobenzenes in which the two halogens were different.[60]

Roberts and his co-workers[51,52] produced a method of estimating the relative rates of proton capture and halide loss; in the case of o-chlorophenyl anions, the ratio could be reckoned from the yield of chloride ion and the change of deuterium content during an interrupted reaction of partially o-deuterated-chlorobenzene with sodium amide in liquid ammonia. This was adapted by Bunnett and Zoltewicz,[61] and the substituent effects on the ratio of proton capture to chloride ion loss from o-chlorophenyl anions in 60%NH_3-40% diethyl ether medium were determined. All substituents investigated increased the rate of proton capture relative to that of chloride ion loss. The substituents investigated include two (-Cl and -CF_3) which are normally electron attracting and two (-CH_3 and -OCH_3) which are normally electron releasing. The observation that substituents increase the rate of proton capture is not necessarily correct; it could be that both modes of reaction are retarded, aryne formation more than proton capture.

Bunnett and Happer[59] followed this by a quantitative study of the reaction set out in Scheme 8. Decomposition of 1-(o-bromophenyl)-2-p-toluenesulphonhydrazide caused by sodium methoxide in methanol produced bromobenzene, bromide ion and anisole. More than 96% of the bromine introduced was accounted for, and the reaction was thought to occur via o-bromophenyl anions.



Scheme 8

The ratio of the two anisoles formed varied according to the activating groups present, but in no cases was the total yield of anisole greater than 9%.

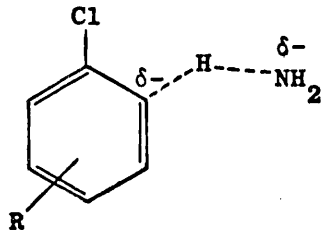
The ratio of yields of aryl bromide and bromide ions directly expresses the ratio of the first-order rate constants for proton capture and for bromide ion loss. For all the aryl substituents which were studied, this ratio increased, matching Bunnett and Zoltewicz's observations.[61]

By comparison of the two sets of data,[59,61] Bunnett and Happer showed that the small rate-enhancing effect of the methyl was the same

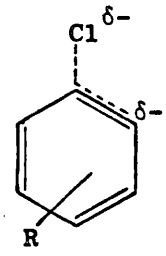
in both series; the methoxy group has a larger effect. The largest effects in both series were found with chlorine and the trifluoromethyl group. Similarity in the substituent effects implies that both ratios are determined by similar factors.

1.2.1.2. SUBSTITUENT EFFECTS IN BENZYNE REACTIONS.

Attempts were made by Bunnett and his co-workers[59,61] to explain these substituent effects in terms of the free energies of the transition states from proton capture (structure XIV) and halide ion loss (structure XV).



XIV



XV

The effects of electron-attracting substituents were interpreted[61] in terms of polar interactions of the substituent with the partially ionic transition states for proton capture and halide ion loss. From the fact that proton capture transition states (XIV) are more favourably affected by such substituents (as it is known that such substituents stabilise a phenyl anion in the order o>>m>p[62]), they were judged to have more negative charge on the carbon atom. Hence, XIV was considered to lie close to phenyl anion on the reaction co-ordinate, and XV to lie close to aryne.

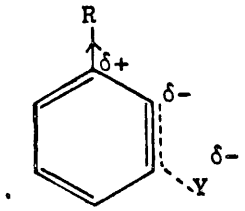
This argument was slightly altered[59] for the sodium methoxide in methanol system, since transition state XIV would be expected to lie closer to aryl anion because methanol is more acidic

than ammonia.

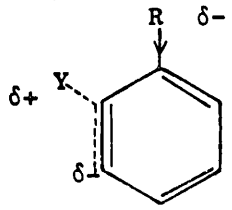
The effect of electron-releasing substituents on the ratio of the relative rates of proton capture and of halide ion loss was tentatively ascribed[61] to the destabilization of the arynes formed. This dependence reflected the degree of intermediacy of arynes in the base-catalysed reactions of the aryl halides.

Roberts et al.[52a] pointed out that ortho-substituted compounds can only form a 2,3-benzyne, and a para-substituted compound only a 3,4-benzyne, whereas a meta-substituted compound can form either or both. The direction of the elimination step depends upon which hydrogen ortho- to the halogen is more acidic, and the orientation of the benzyne formed appears essentially to be due to the inductive effect. A similar control seems to act in the subsequent nucleophilic addition.

In terms of the transition state theory, electron-withdrawing substituents favour reaction at the more distant position since then the partially shared aryne bond electrons are closer to the electron deficient carbon at the point of attachment (structure XVI),



XVI



XVII

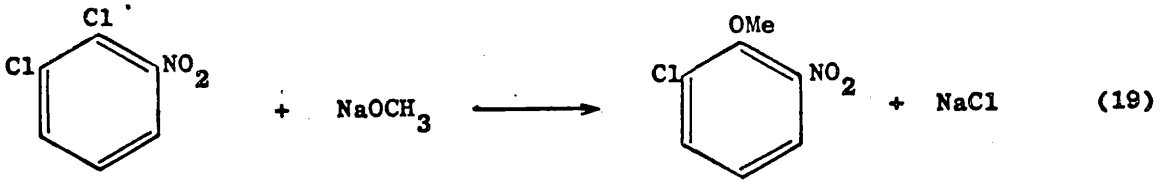
Conversely, with electron-releasing substituents, reaction is preferred at the nearer position (structure XVII), since the partially shared electrons are further from the electron-rich carbon at the point of attachment. These principles are illustrated in the reaction of the three isomers of dichlorobenzene with alkali metal amides. In each case, the expected product was

the one chiefly formed.[63]

The consequence of elimination-addition reactions in aromatic nucleophilic substitution is the formation of two products. The most successful definition of the boundary between the conventional and the aryne mechanisms has involved the reactions of 1-substituted naphthalenes with strong bases in piperidine. Reactions of 1-chloro-, 1-bromo- and 1-iodonaphthalenes with sodium amide in piperidine[64] showed two products in the ratio of 1:2, the major product representing rearrangement.

Direct displacement of halogen causes a single unrearranged product; this was evident at high temperatures in the reaction of 1-bromonaphthalene with piperidine (in absence of sodium amide) and in reactions of 1-naphthylmethyl sulphone, 1-naphthalenesulphonic acid (sodium salt) and 1-naphthylphenyl ether with sodium amide in boiling piperidine. Thus, it became clear that a strong base was necessary to generate the 1,2-naphthalyne.

Clearly this mechanism cannot encompass all aromatic nucleophilic substitutions, since many instances of displacement of groups flanked by two ortho-substituents are known (equation (19)).[65]

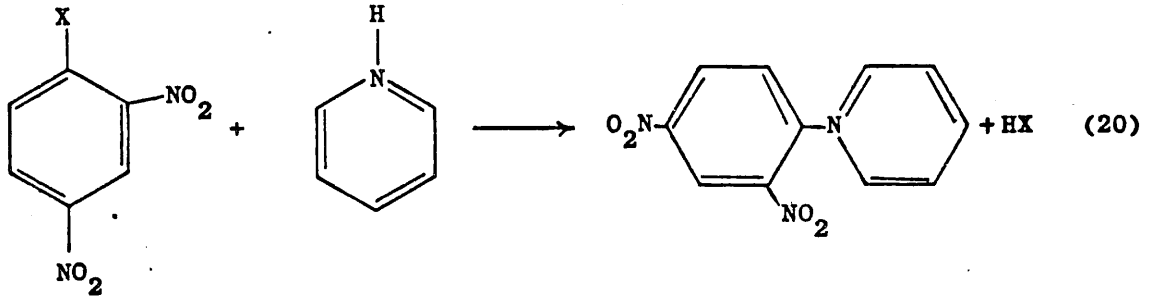


(19)

1.2.2. THE S_NAr MECHANISM

The vast majority of aromatic nucleophilic substitution reactions, exemplified in equations (15), (16) and (17), display kinetics and response to structural and environmental factors which indicate a bimolecular mechanism. Second-order kinetics are regularly observed, the reactions being first order with respect to the nucleophilic reagent and aromatic substrate. Substitution occurs more rapidly with stronger nucleophiles, whilst reactions are facilitated by substituents which withdraw electrons from the site of substitution.

This mechanism denoted S_NAr, (Scheme 2) consists of two steps; the attacking species forms a bond with the substrate giving an intermediate, and then the leaving group departs. There is ample evidence for this mechanism . In the following reaction (equation (20)) X, the leaving group, was varied. If the S_NAr mechanism was operating, then X would have a substantial effect on the rate of reaction if step 2, where the bond Ar-Y is broken, is rate determining.



(20)

In fact,[66] the rates differed only by a factor of 5, showing this not to be the rate-determining step.

Rates of bimolecular nucleophilic substitution depend not only on the nucleophilic power of the attacking reagent, the polar and

steric effects of substituents, but also on the nature of the expelled group. With suitable substituents, replacement of chlorine and other typical leaving groups becomes easy. Bunnett and Zahler,[67] on the basis of their very thorough study of the literature, suggest the following order of ease of expulsion, although this depends greatly on the nature of the nucleophile, $F > NO_2 > SOPh > Cl, Br, I > N_3 > OAr > OR > SR > SO_2R > NR_2$.

The influence of the leaving group seems to stem from the anionic stability of the expelled group, together with its ability to conjugate with the aromatic system. Among the halogens, fluorine is generally a much better leaving group than the other halogens. The most likely explanation is that the first step of the S_NAr mechanism is usually rate-determining, and this step is promoted by groups with a strong -I effect. This explains why fluoro- and nitro- are such good leaving groups when this mechanism operates.

1.2.2.1 EFFECTS OF SUBSTITUENTS.

Greater ease of replacement of halogen and other common leaving groups than of hydrogen means that in aromatic nucleophilic substitution reactions, there is often only one point at which replacement occurs and the effects of substituents can be simply and precisely related to their effect at that point.

Halogens form a complete series of special interest and importance. Fluorine is the most electronegative (largest -I effect) but is best able to conjugate its unshared pair of electrons in a deactivating + M effect; there is a smooth gradation through the halogen series. Accordingly, the relative weighting of the two effects could result in any order of activation for the halogens. From studies of methoxy and thiomethoxy group effects in S_NAr reactions, the factor controlling activating power in the *para*-position is conjugative electron-relase. The two factors (I and M)

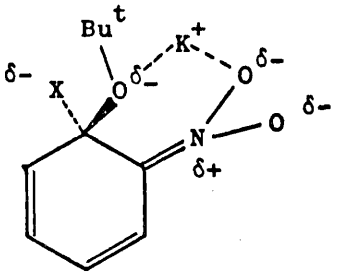
cancel out for fluorine and the inductive effect slightly outweighs the mesomeric effect for the rest, giving an experimental pattern of activation in the order, F < H < Cl < Br ~ I.

Irrespective of whether conjugative destabilization outweighs inductive stabilisation, it is generally accepted that the former operates more effectively from para- than ortho- sites, and the latter operates most efficiently at the ortho- position. Both mesomeric and inductive effects reinforce each other in aromatic nucleophilic substitution reactions, and lead to higher reactivity at the ortho- position, as illustrated with 2,4-dihalogenonitrobenzenes. Their reactions with a variety of nucleophiles,[68] whereby the 2-halogen is preferentially replaced, leads to conclusions that ortho- substitution is favoured. It must be pointed out that chlorine in the 2-position has a secondary steric effect in the transition state of the substitution of the 4-chlorine, since it prevents the full co-planarity of the nitro group with the ring.

Miller and his co-workers[69,70] have compared the ease of replacement of halogen by methoxide ion in methanol in the o- and p-halogenonitrobenzenes, and showed for all halogens that the o-nitro- group is slightly less activating than the p-nitro- group, although Bunnett and Morath[68] have shown that the o-nitro group is clearly more activating in the reaction of piperidine with o- and p-chloronitrobenzenes; the latter being explained by built-in solvation, possibly through hydrogen bonding.

The kinetics of the reaction of potassium methoxide with the fluoronitrobenzenes[71] gives an ortho-:para- activation ratio around unity. The addition of dicyclohexyl-18-crown-6 to the system has a negligible effect. For the same substrates with potassium t-butoxide in t-butyl alcohol, addition of the crown ether (in equimolar

quantities to the nucleophile), the rate of reaction of the o-nitro- substituted substrate is increased by a factor of 3, whereas that of the p-nitro- derivative is increased by nearly 2000. This high ortho-:para-ratio in t-butyl alcohol in the absence of addenda has been attributed mainly to specific stabilization of the transition state of the reaction of the o-nitro- substituted substrate by K^+ cation bridging between the nucleophile and the oxygen atoms of the $-NO_2$ group (structure XVIII).



XVIII

Clearly such an interaction is not allowed in the p-nitro- substituted compound.

When there is an important ortho- effect, one should look further than direct inductive and mesomeric effects for an explanation of the activation or deactivation. Hydrogen bonding or primary and secondary steric effects may lead to explaining the effects.

Transition states can be influenced conjugatively by a meta-substituent only by relay from the meta- ring atom, to which it is attached, to the neighbouring ortho- and para- positions. Thus, true conjugative stabilization or destabilization will be absent; however, moderate inductive stabilization will be observed.

Bevan and Bye,[72] and Miller,[73] compared the reactivity of fluorobenzene with m- and p-fluoronitrobenzene towards sodium methoxide in methanol. Bevan and Bye also measured rates for fluoro-3,5—dinitrobenzene and showed that a second nitro group meta-, had the same effect as the first, whereas Miller showed the grouping

in fluoro-2,4-dinitrobenzene to be less effective than would result from additive activation by ortho- and para-nitro- groups. The substituent rate factors obtained by Miller were for p-nitro-, $4{\cdot}73 \times 10^8$, and for a meta-nitro- group, $4{\cdot}7 \times 10^4$. Similar values were obtained by Bevan and Bye. These substituent rate factors clearly show that conjugative stabilization occurs with p-nitro compared with the meta-nitro derivative.

In the reaction of the dichlorobenzenes with methoxide ion, the activating order of chlorine appears to be o ~ m > p, whilst chlorine substituent effects in the reaction with chloronitrobenzene reveals the m-chlorine substituent to have the most pronounced effect.[74]

1.2.2.2. EFFECT OF SOLVENT SYSTEM.

The effects that changes of solvent have upon the rates of reactions occurring in them were early rationalised by the Hughes-Ingold theory of solvation. This explains solvent behaviour in terms of the formation or destruction of charge on passing from the ground state to the transition state, and understood solvent properties, implicitly, in terms of the dielectric constant. However, dielectric properties are not the only contributors in determining rates of reaction; thus, Miller and Parker[75] have shown that the rate of reaction of tetraethylammonium azide with p-fluoro- or p-iodonitrobenzene changes by a factor of 7×10^3 in going from dimethylformamide to methanol, although the dielectric constants are identical.

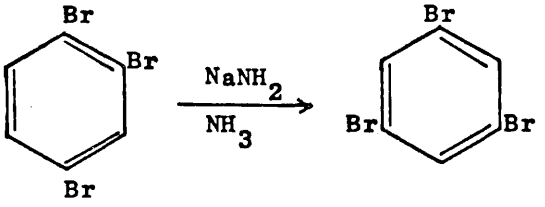
In aromatic nucleophilic substitution, the function of the solvent has been carefully studied by a number of workers. Suhr,[76] for example, measured the rate of reaction of some 4-substituted-nitrobenzene derivatives with piperidine in a number of solvents, and other workers have made detailed studies of the effects of changes

in the composition of solvent mixtures (e.g., dimethyl sulphoxide-water)[77,78] on the rates of S_NAr processes in such media.

While the main increase in reactivity is when the proportion of protic solvent is low and approaches zero, there is a quite noticeable enhancement in rate even with small concentrations of dimethyl sulphoxide (DMSO). Kingsbury[77] showed this to be essentially independent of the substrate. In the range 0-80% DMSO, the rate of reaction of methoxide ion with p-fluoronitrobenzene was increased about 2000-fold, and has been mainly attributed to a decrease of solvation in forming the transition state.

1.2.3. FURTHER REACTIONS OF HALOGENOPHENYL ANIONS - THE HALOGEN BARN DANCE.

In the course of a study of the action of sodium amide in liquid ammonia on several di- and trihalogenated benzenes, Wotiz and Huba[79] observed the unprecidented isomerisation of 1,2,4-tribromobenzene, equation (21).



(21)

1,2,4-Trichlorobenzene, under the same conditions, gave 3,4-dichloroaniline, via the benzyne intermediate, as expected. Wotiz and Huba had reported a 33% yield of the 1,3,5-tribromobenzene isomer. Bunnett and Moyer[80] obtained yields of 7-13% using $NaNH_2$ or KNH_2. However, potassium anilide in liquid ammonia gave much better yields (up to 60%). Rearrangement was never complete. This base-catalysed isomerisation was also accompanied by small amounts (≈5%) of the disproportionation products, di- and tetrabromobenzenes.

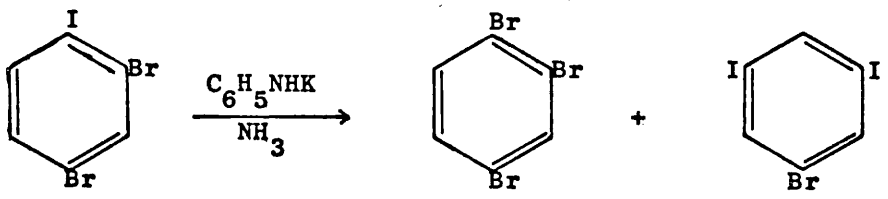
It was also reported[80] that 1-bromo-2,4-dichlorobenzene rearranged to 1-bromo-3,5-dichlorobenzene (33%) under similar conditions. However, 1,2,4-trichloro- and 1,2,4-triiodobenzene did not isomerise, nor was the reversion of 1,3,5-tribromobenzene to 1,2,4-tribromobenzene observable, even to a slight extent.[80]

The action of strong bases in liquid ammonia on halogenobenzenes is known to form arynes;[49,51] the addition of halide ions to arynes have been observed;[81] and addition of nucleophiles to 3-halogenobenzynes is known to be directed preferentially to the aryne carbon more remote from halogen.[82] A mechanism involving these

steps, therefore, is plausible.

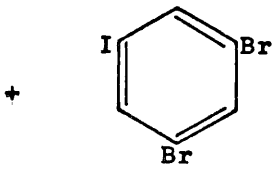
However, in this case, there is compelling evidence against the aryne mechanism. It predicts that reactions performed in the presence of a foreign halide ion, for example, in the presence of added KBr, should form products incorporating the foreign halogen, but no such products were obtained. Products and product ratios in the presence of added salts are the same as in its absence.

The fact that 1,2,4-tribromobenzene overshadows its 1,3,5-tribromo-isomer as a product from 1-iodo-2,4-dibromobenzene is incompatible with an aryne mechanism, since it would predict the formation of 1,3,5-tribromobenzene (equation 22), rather than 1,2,4-tribromobenzene.



(22)

12% 4%



28%

The failure of 1,3,5-tribromobenzene to revert to 1,2,4-tribromobenzene is also inconsistent with an aryne mechanism since bromine is readily lost under such conditions,[51] and subsequent addition to the carbanion would occur to yield a 1,2,4- isomer.

A sample of fully deuterated 1,2,4-tribromobenzene was exposed to potassium anilide in ammonia; 1,3,5-tribromobenzene was formed, and the 1,2,4-tribromobenzene that was recovered was free of deuterium.[80] Both facts showed that exchange probably occurred via aryl anion intermediates. This experiment demonstrated that o-bromophenyl anion intermediates are generated (and reprotonated) repeatedly in these systems. Their tendency to reprotonate rather than expel bromide ion has been discussed in section 1.2.1.1.

Experiments with 1-iodo-2,4-dibromobenzene illuminated the mechanism (equation (22)). Obviously halogen atoms are transferred between benzene rings; whatever the mechanism of disproportionation, it must be intermolecular in character.

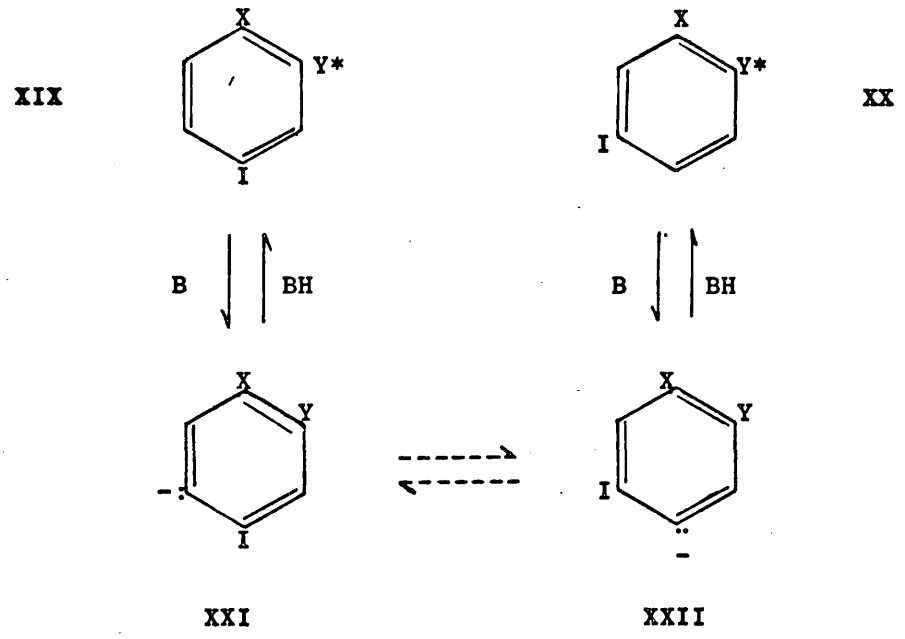
Although such halogen exchange between rings is evidently intermolecular, isomerisation and isotope-scrambling reactions might, nevertheless, be intramolecular in character. Conceivably, o-halogenophenyl anions might undergo 1,2-shifts of halogen.

An intriguing observation[80] was that 1,2,4-triiodobenzene afforded very little of its 1,3,5-isomer(< 5%) under conditions which were favourable for the isomerisation of 1,2,4-tribromobenzene, and the isomerisation and disproportionation of 1-iodo-2,4-dibromobenzene or of 1-iodo-2-bromo-4-chlorobenzene. A conceivable explanation is that aggregation of the three iodine atoms in a 1,2,3-arrangement, as an intermediate complex, is sterically so unfavourable that reaction of the initial anion and substrate is too slow.

A sample of 1,2,4-tribromobenzene with radiobromide in the 1- position was exposed to potassium anilide and ammonia. Both 1,2,4-tribromobenzene and 1,3,5-tribromobenzene were isolated from

the product mixture. In the recovered 1,2,4-isomer, the radiolabel was found to be equally distributed among the 1-, 2-, and 4-positions.[83] Statistical redistribution of the radiolabel also occurred with 1,2,4-triiodobenzene with the I^{131} label originally in the 2- position.[84]

Thus, the scrambling of iodine of 1,2,4-triiodobenzene-2-I^{131} might occur, in part, as in Scheme 9 (where X = Y = I).



Scheme 9.

The 1-labelled isomer (XX) could conceivably be formed by the 5-anion (XXI) and a subsequent 1,2-shift of the 4-iodine of XXI to the erstwhile carbanionic centre to form XXII, and finally protonation to form XX. Further transformation could convert this into the 4-labelled radioisomer of XIX.

There is no precedent for a 1,2-shift of a halogen atom to a carbanionic site. 1,2-Migration accompanying a sigmatropic

rearrangement has been described.[85]

This 1,2-shift hypothesis was tested using 1-chloro-2-fluoro-4-iodobenzene and 1-chloro-2-fluoro-5-iodobenzene. If isomerisation occurred by a 1,2-shift in o-iodophenyl anions, these substrates ought to interconvert via anions under the same conditions which brought about scrambling of the radiolabel. No such interconversion was found.

It was curious that some unrearranged substrate was always found in the product mixture, and that 1,3,5-tribromobenzene would not revert to 1,2,4-tribromobenzene. The incompleteness of isomerisation may be attributed to attaining a state of equilibrium; this is contradicted by the failure of 1,3,5-tribromobenzene to revert to the 1,2,4-isomer.

1,3,5-Tribromobenzene reverts to 1,2,4-tribromobenzene[86] if a small amount (<5%) of 1,2,4-tribromobenzene or tetrabromobenzene was added as a 'primer'. The ultimate ratio of the 1,2,4- and 1,3,5- isomers was essentially the same irrespective of which isomer was the initial reactant.

A state of equilibrium is obviously attained. However, the establishment of the equilibrium seems to require cocatalysis by 1,2,4,5-tetrabromobenzene or other suitable positive bromine donors.

The presence of dibromobenzenes amongst the reaction products indicates that the catalyst may be formed by disproportionation of the tribromobenzenes, and more easily from 1,2,4-tribromobenzene than the 1,3,5-isomer.

All materials used by Wotiz and Huba, and by Bunnett and Moyer were contaminated by traces of 1,2,3,5-tetrabromobenzene or other cocatalyst. An ultra-purified sample of 1,2,4-tribromobenzene was found to isomerise just as readily as ordinary samples, so it was concluded that tetrabromobenzenes did not need to be introduced

in order to facilitate the isomerisation of 1,2,4-tribromobenzene. The dilemma regarding the mechanism was resolved by observing all the products from the isomerisation of 1,2,4-tribromobenzene; 1,2,3,5-tetrabromobenzene had been generated in small amounts.

The need for a cocatalyst in order to achieve reversion of 1,3,5-tribromobenzene to 1,2,4-tribromobenzene requires a mechanism for its formation. Since neither the aryne mechanism nor the 1,2-shift mechanism allows any function for a tetrabromobenzene cocatalyst, both are disqualified.

A much better account of these observations is given by a mechanism in which the essential feature is the transfer of positive halogen from a halogenobenzene to an aryl anion, that is, a nucleophilic displacement by an aryl anion <u>on halogen</u> of an aryl halide, illustrated in equation (23).

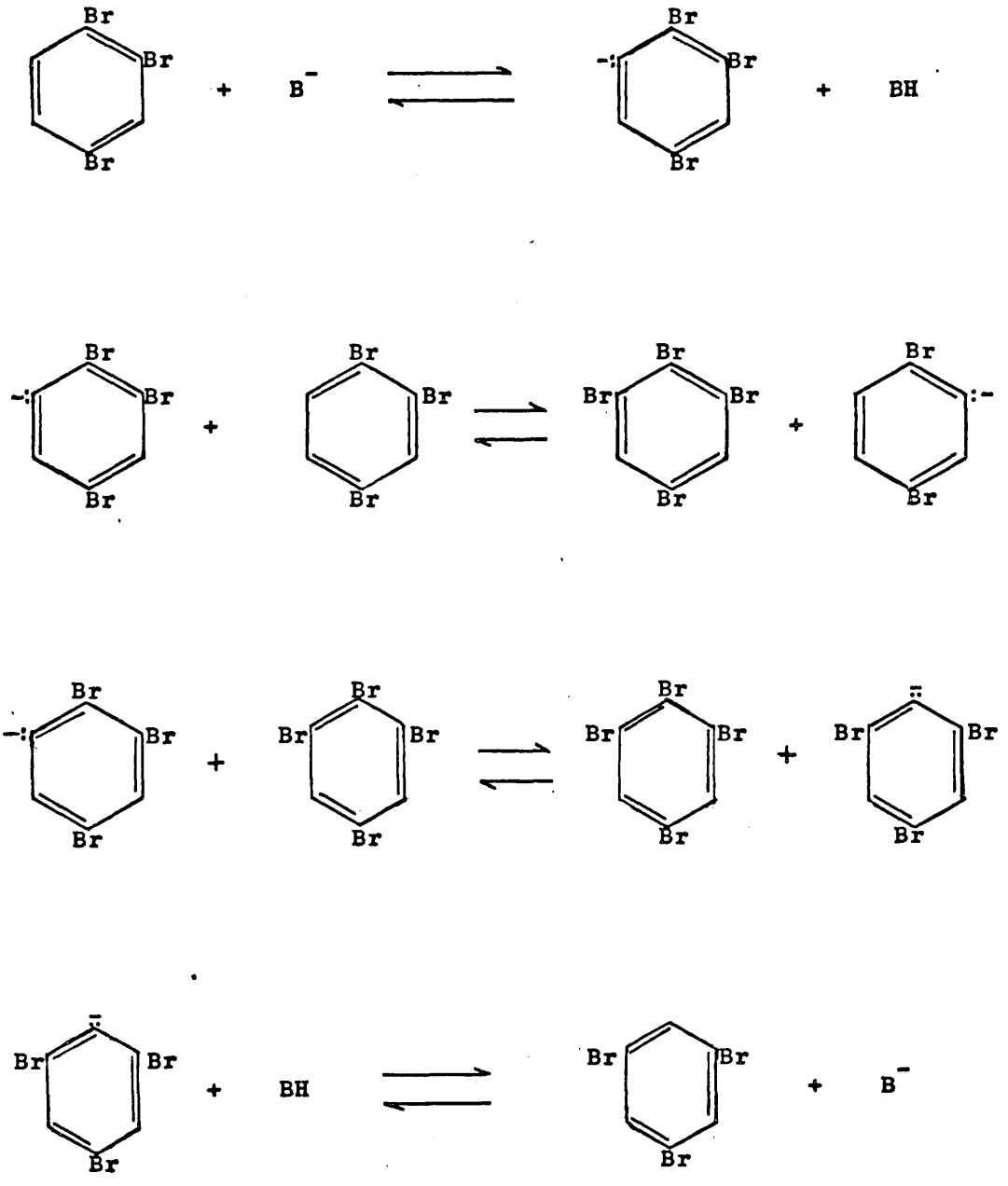
$$(Ar:)^- + Ar'-X \longrightarrow Ar-X + (Ar':)^- \qquad (23)$$

The reaction may be likened to proton transfer, in which a base reacts with a Brønsted acid to form a new base and a new acid. In neither case is it implied that the positive hydrogen or halogen has free existence during the transfer process. Nucleophilic displacements by carbanions on halogens are known in other connections, namely, the base-induced isomerisation and disproportionation reactions amongst bromine derivatives of thiophene[87,88] and other heterocycles[89] and in reactions of certain polyhalides by diphenylmethide ion in ammonia.[90]

The mechanism compatible with these facts is outlined in Scheme 10.

It should be noted that tetrabromobenzene is both consumed and generated in step 3. Steps 1 and 4 are straightforward acid-base reactions. The key step (step 3) finds analogy in the halogen-metal interconversion.[91]

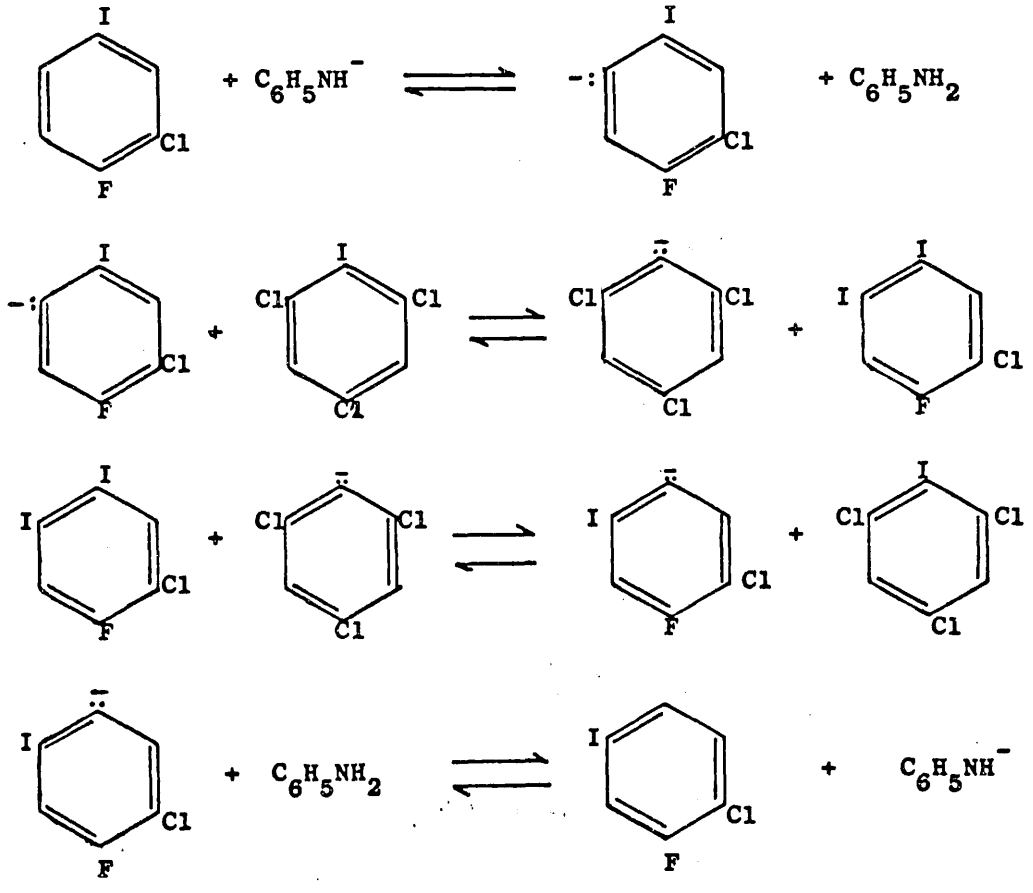
Bunnett and Scorrano have found[86] that potassium t-butoxide in dimethyl formamide (DMF) or hexamethylphosphoramide (HMPA) solution serves as an excellent isomerisation catalyst.



Scheme 10.

When catalysis is provided by potassium t-butoxide in DMF or potassium anilide in ammonia, mechanisms such as that shown in Scheme 10 are apparently more feasible only if the various phenyl anions are made energetically accessible by the presence of halogens ortho- to anionic sites, and if the halogen to be transferred is bromine or iodine. (Chlorine and fluorine are known to be rather unreactive in halogen-metal interconversions.[91])

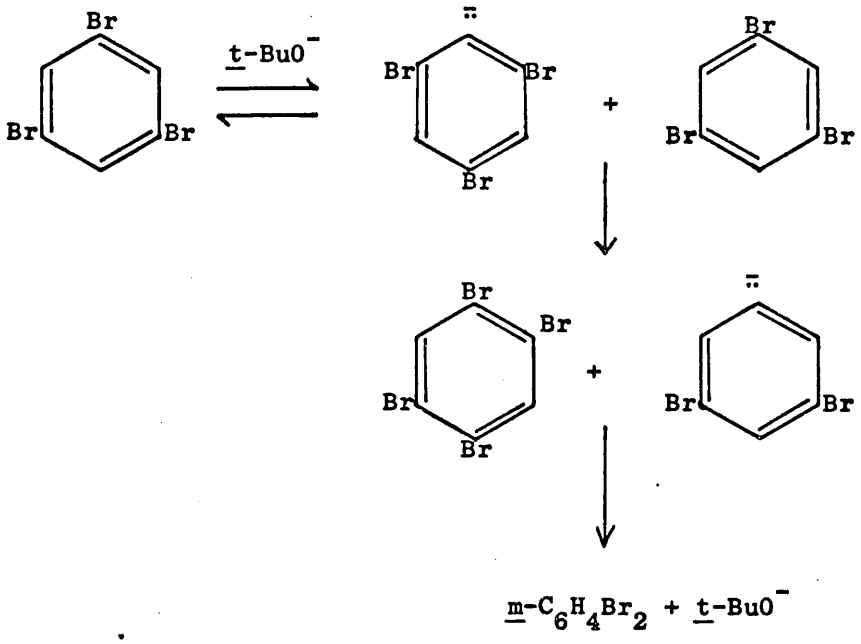
1-Chloro-2-fluoro-5-iodobenzene is known not to isomerise on treatment with potassium anilide in ammonia,[86] the only inherently labile halogen being iodine, which is not ortho- to another halogen. Isomerisation may be possible if a suitable cocatalyst may provide positive iodine. Indeed, it does isomerise in the presence of 1-iodo-2,4,6-trichlorobenzene; 1,3,5-trichlorobenzene and several fluorochlorodiiodobenzenes are also formed.[86] This isomerisation is reflected in the positive halogen transfer mechanism, Scheme 11.



Scheme 11.

Proton capture by 2,4,6-trichlorophenyl anion is clearly a prominent further step.

Reversion of 1,3,5-tribromobenzene to 1,2,4-tribromobenzene occurs in HMPA[86] without the need for cocatalysis. Substantial amounts of disproportionation, to di- and tetrabromobenzenes occurs, and the ratio of m- to p-dibromobenzene increases with time. Isomerisation without the need for addition of a good positive bromine donor as cocatalyst implies that an aryl anion without a halogen ortho- to its anionic centre plays a significant role as an intermediate (Scheme 12):



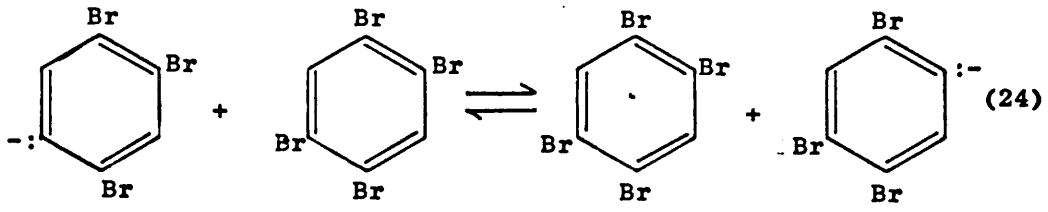
Scheme 12.

Thus, disproportionation of 1,3,5-tribromobenzene forms a tetrabromobenzene which cocatalyses the isomerisation.

By rules which seem to be obeyed in ammonia, ammonia/diethyl ether and DMF media, a species such as m-dibromophenyl anion should not be energetically accessible. The exceedingly high chemical potential of strongly basic anions in HMPA[92] is probably responsible

for the occurrence of reactions in this medium which do not occur in the other media investigated.

The scrambling of halogens in radiolabelled 1,2,4-tribromo- or 1,2,4-triiodobenzene has not been shown to need cocatalysis. Nevertheless, a scrambling mechanism involving cocatalysis by internally generated 1,2,4,5-tetrahalogenobenzene is attractive because of the chemical equivalence, except for radiolabels, of the four halogens of a 1,2,4,5-tetrahalogenobenzene (equation (24)), which explains the entirely random distribution of the label after reaction.

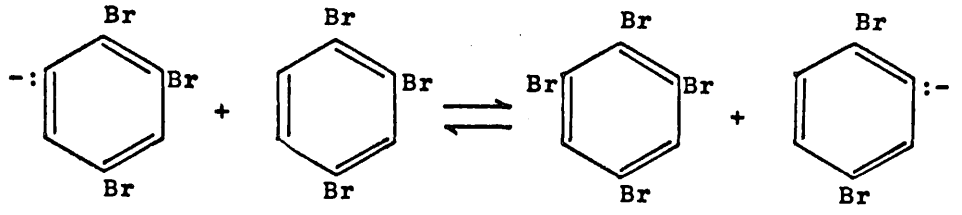


(24)

The type of mechanism represented in Schemes 10 and 11 may be characterised as a (2n + 1) - halogen version of the positive halogen transfer mechanism. The transition state for the key halogen transfer step involves attack of a n-polyhalogenophenyl anion on the halogen of a (n + 1) - polyhalogenobenzene; altogether it contains (2n + 1) - halogen atoms. When isomerisation, disproportionation, or scrambling of a trihalogenobenzene is at issue, the mechanism as represented in Schemes 10 and 11, may be designated a seven-halogen process.[80,86]

Migration of halogen may occur in some cases by a 2n - halogen analogue of the positive halogen transfer mechanism. A six-halogen version for isomerisation, disproportionation and scrambling in

trihalogenobenzenes was originally suggested, although it is now excluded by the cocatalysis observations. One of the key steps in the six-halogen version is presented in equation (25), because it is of relevance to the positive halogen transfer mechanism.



(25)

This depicts a positive halogen transfer, forming a tetrabromobenzene and a dibromophenyl anion. In the potassium anilide-ammonia and potassium t-butoxide-DMF systems, protonation of the dibromophenyl anion is more rapid than the subsequent attack of the dibromophenyl anion on the 2-bromine substituent of the tetrabromobenzene. Thus, this reaction appears to serve as a step in the disproportionation to di- and tetrabromobenzenes, but not as a step in the isomerisation, except that it forms a tetrabromobenzene cocatalyst.

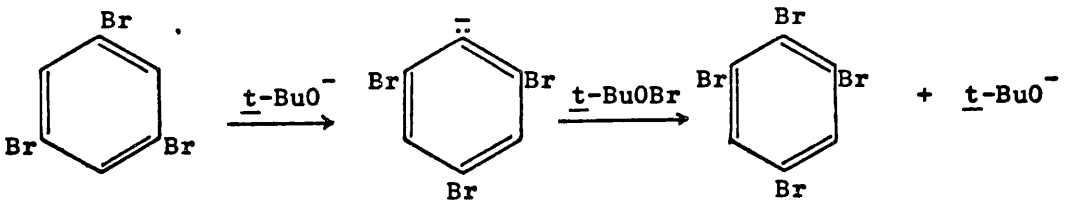
Instead of direct positive halogen transfer from aryl halide to aryl anion, it might be transferred first to the anilide ion, forming a N-halogenoaniline, which then passed the halogen on to the aryl anion. There are arguments against such a mechanism. A chain-carrying step would require encounter between two reactive intermediates (N-halogenoaniline and aryl anion), and a N-halogenoaniline in the presence of anilide ion would be likely to form hydrazobenzene and halide ion rather than wait for the aryl anion. Isomerisation and disproportionation are said to be catalysed by oxygen bases,[86] and as such, intermediates of the type R·O·Br

may intervene in positive halogen transfer reactions.

Radical mechanisms are incompatible with the fact that iodine is not captured from iodobenzene during isomerisation,[86] nor do they accommodate the need of some reactions for cocatalysis. Furthermore, radical mechanisms of such high efficiency as those processes observed in DMF or HMPA are improbable in such solvents which are good hydrogen atom donors to radicals.[93]

The positive halogen transfer mechanism, known as the base-catalysed 'Halogen Barn Dance', in the seven-halogen version, is the only mechanism which is compatible with all the evidence at hand.

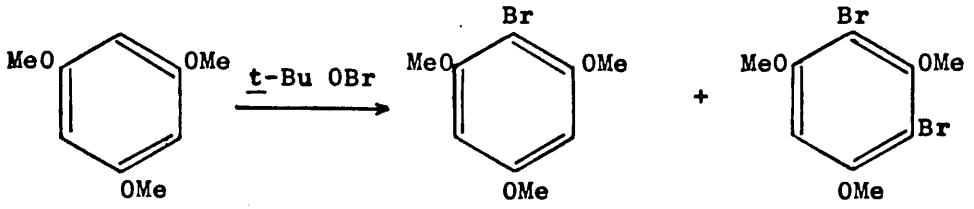
Such a mechanism has recently been implied to account for the bromination of 1,3,5-tribromobenzene in basic solution.[94] 1,3,5-Tribromobenzene is unreactive with t-butyl hyperbromite[95] in DMF or HMPA. During a 5 minute exposure, no detectable bromination occurred. However, 1,3,5-tribromobenzene is rapidly brominated by t-BuOBr in the presence of potassium t-butoxide; during 10 seconds in DMF, a mixture of tetrabromobenzenes was formed (which rapidly interconvert on exposure to t-BuO^-K^+ in DMF or HMPA[96]) in 47% yield, as well as a 16% yield of pentabromobenzene. Thus, bromination is base-catalysed and a carbanion mechanism is implied, Scheme 13.



Scheme 13.

1,3,5-Trimethoxybenzene is readily brominated by t-BuOBr; during a 5 minute reaction with a two-fold excess of t-BuOBr in HMPA,

59% of its 2-bromo- and 41% of its 2,4-dibromo- derivatives are formed, equation (26).



(26)

It must be noted that although such electrophilic bromination can be explained in terms of carbanions, the two systems chosen by Mach and Bunnett are slightly different, and more classical electrophilic substitution is much more possible under such conditions.

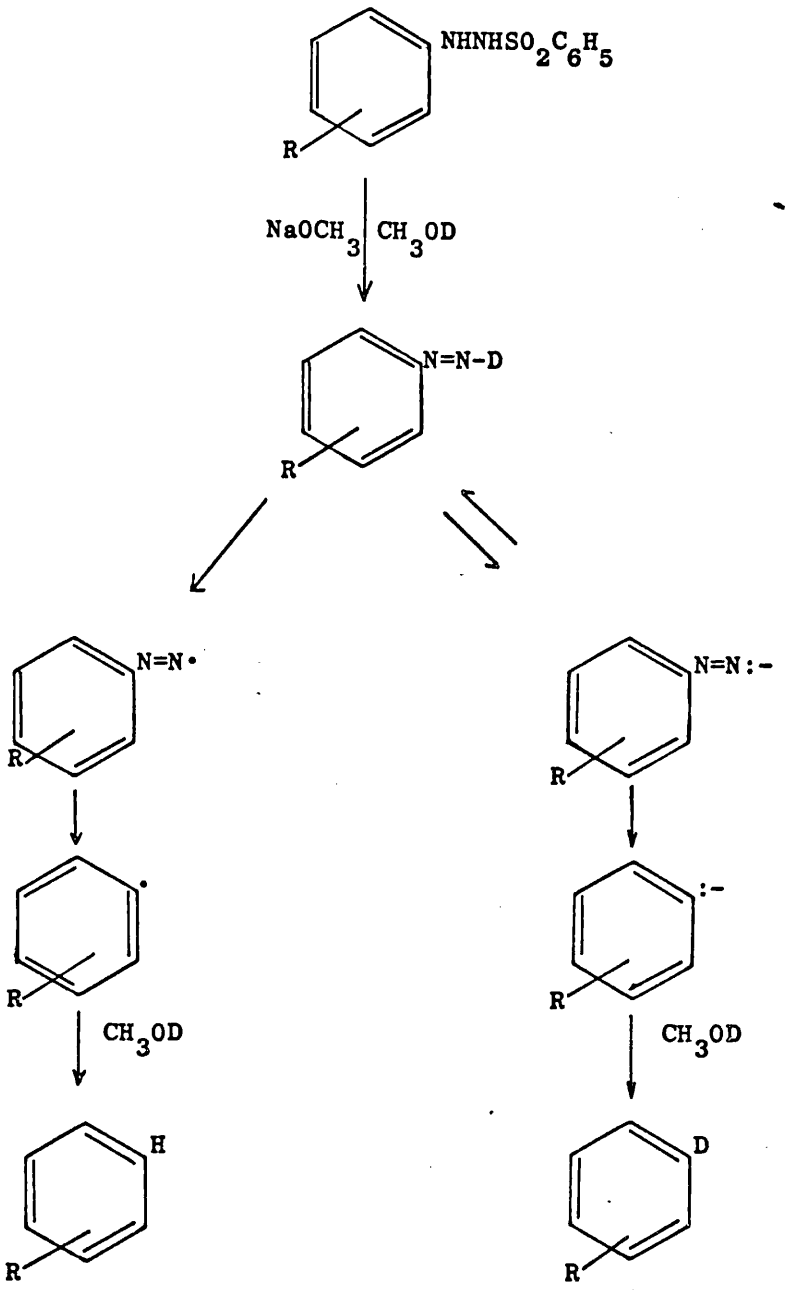
1.2.4. RADICAL ABSTRACTION OF HALOGEN FROM ARYL HALIDES.

Although radical abstraction of halogen atoms from alkyl halides of appropriate constitution is well known, the corresponding reactions of aryl halides does not appear to have been described extensively.

Happer[97] studied the action of methanolic sodium methoxide in 1-(2-iodo-4-chlorophenyl)-2-benzenesulphonhydrazide for the purposes of ascertaining the relative rates of proton capture (to form m-chloroiodobenzene) and iodine loss (to form an aryne and ultimately, chloroanisoles) by the intermediate halogenophenyl anion, as outlined in Scheme 14.

Because of a quantitative discrepancy between two nearly identical runs, the effect of sodium methoxide concentration on the product proportions was studied. The results obtained were largely unexpected. Happer discerned that the ratio of chloroanisole isomers (para-:meta-) depended on the concentration of sodium methoxide, and that in 2M sodium methoxide, 31% chlorobenzene was formed. He obtained evidence that the chlorobenzene resulted from the deiodination of the m-chloroiodobenzene under the conditions of the reaction (c.f. Scheme 8).

A thorough study of the deiodination[98,99,100] revealed that deiodination did not occur unless both sodium methoxide and a radical source (e.g. peroxydisulphate ion or phenyltriazomethane) were present. Even when both sodium methoxide and a radical source were present, deiodination was blocked by the presence of nitrobenzene. Thus, m-chloroiodobenzene underwent deiodination on treatment with 1-(o-chlorophenyl)-2-p-toluenesulphonhydrazide in 2M sodium methoxide, but not in the alcoholic base alone or with benzenesulphonamide in alcoholic base.



Scheme 14.

Cleavage of the 1-aryl-2-benzenesulphonhydrazides is believed to be initiated by base-induced elimination of the elements of benzenesulphonic acid, forming an aryldiimide which could decompose either by a radical route, or in the presence of a base, by a carbanion route, Scheme 14. The ultimate product in the presence of CH_3OD would be deuterium free by a radical route, while that from a

carbanionic route would be deuterated. It has been observed[98] that formation of a deuterated product is favoured by higher sodium methoxide concentration and by an ortho-chlorine substituent, attributed to a shift in the equilibrium between radical and carbanionic route, and because the chlorine substituent aids the formation of a more stable carbanion.[62] However, it was noted that p-nitrobenzenediazonium ion gives virtually deuterium free nitrobenzene under all conditions studied.

A mechanism compatible with the radical reaction observed is set out in equations (27)-(31).

$$R\cdot + CH_3OH \longrightarrow RH + \cdot CH_2OH \qquad (27)$$

$$CH_3O^- + \cdot CH_2OH \rightleftharpoons CH_3OH + \cdot CH_2O^- \qquad (28)$$

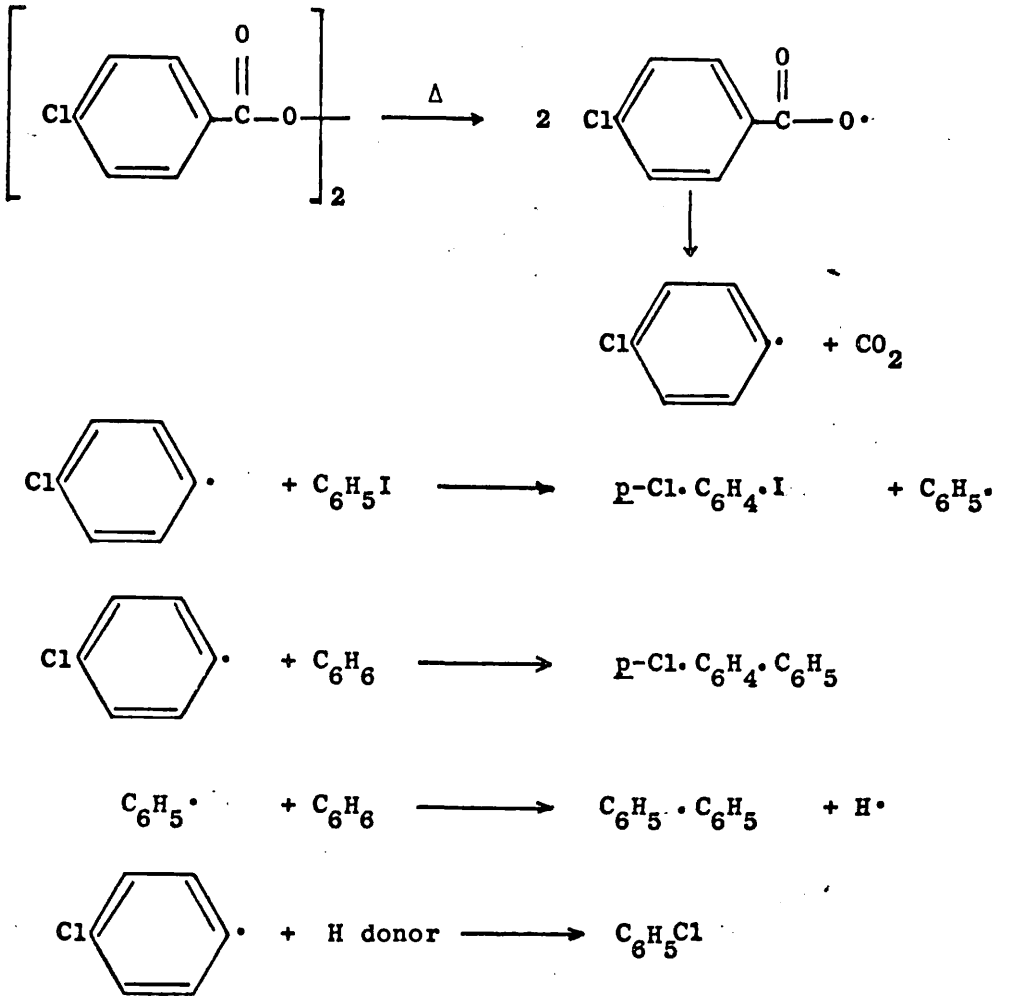
$$\cdot CH_2O^- + ArI \longrightarrow CH_2O + [ArI]^{\cdot -} \qquad (29)$$

$$[ArI]^{\cdot -} \longrightarrow Ar\cdot + I^- \qquad (30)$$

$$Ar\cdot + CH_3OH \longrightarrow ArH + \cdot CH_2OH \qquad (31)$$

Nitrobenzene blocks deiodination possibly by accepting electrons from $\cdot CH_2O^-$ more readily than m-chloroiodobenzene accepts them. The fact that m-chloroiodobenzene is more rapidly deiodinated than iodobenzene is also consistent with the mechanism, since the chlorine substituent increases the efficiency of electron transfer.[101]

Further evidence that radicals readily abstract iodine from aryl iodides was recognised by observing p-chloroiodobenzene as a prominent product from the decomposition of bis(p-chlorophenyl) peroxide in a benzene solution containing iodobenzene.[100] Other products detected, all in smaller yields, including 4-chlorobiphenyl, biphenyl and chlorobenzene, are accounted for by Scheme 15.



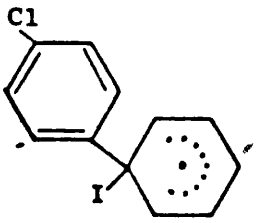
Scheme 15.

All the reactions proposed have ample precedent in modern literature except the iodine transfer from iodobenzene to the chlorophenyl radical.

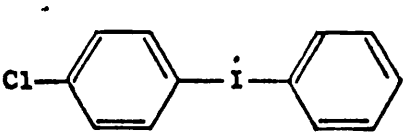
Decomposition of bis(p-chlorophenyl) peroxide in pure iodobenzene also afforded p-chloroiodobenzene as the principle product.[100] An independent demonstration of iodine exchange involved the decomposition of benzoyl peroxide in a benzene solution of m-chloroiodobenzene. The only product was iodobenzene, postulated as capture of an iodine atom from m-chloroiodobenzene by phenyl radicals from the decomposition of the peroxide. Attempts to show bromine transfer in analogous experiments failed.

The products are readily accounted for by postulation of

iodine atom transfer from ArI to Ar· radicals. Photolysis of the aryl iodide which might occur simultaneously with the pyrolysis of the benzoyl peroxide, was not possible since light was excluded from the reaction. Transiodination may have been initiated to form an aryliodocyclohexadienyl radical (structure XXIII), losing its iodine to a p-chlorophenyl radical either by direct radical attack on iodine or by spontaneous homolysis.



XXIII



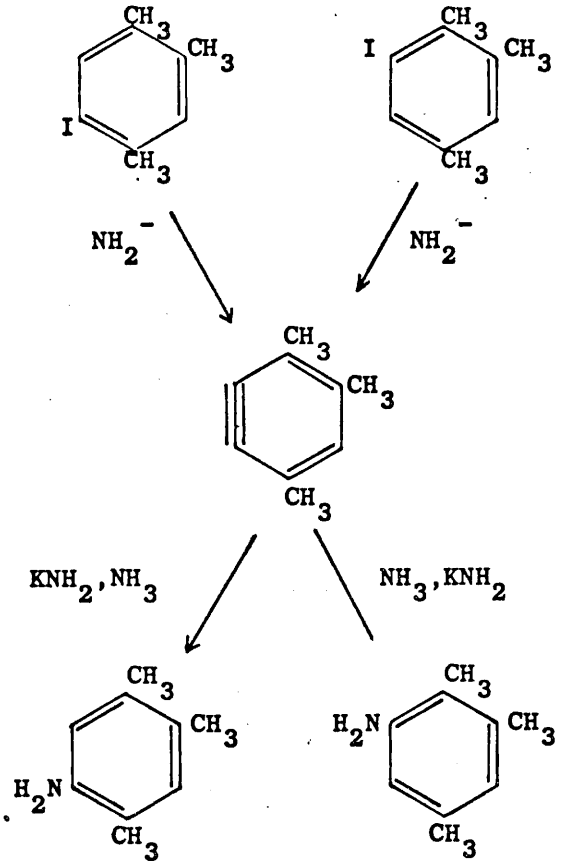
XXIV

This mode of reaction has been disregarded since it requires formation of as much p-chlorobiphenyl as p-chloroiodobenzene.

The transiodination reaction may, however, comprise two steps and involve a diaryliodine intermediate (structure XXIV). This intermediate may revert to the species from which it was formed (e.g., iodobenzene and p-chlorophenyl radical) or progress to a new product pair (p-chloroiodobenzene and phenyl radical). The reduction of diphenyliodonium salts gives supporting evidence.[102,103]

Bunnett and Wamser[100] made a rough estimate of the reactivity of p-chlorophenyl radicals in abstracting iodine relative to arylating benzene by taking into account the yields of p-chloroiodobenzene and p-chlorobiphenyl and the amounts of iodobenzene and benzene in the reaction mixtures. They estimated that the rate coefficient for iodine capture is fifty times greater than that for p-chlorophenylation of benzene; compared with the fact that iodobenzene is phenylated about 1·8 times faster than benzene.[104]

According to the aryne hypothesis, 5- and 6-iodopseudocumenes should react with potassium amide in liquid ammonia to form the same aryne and thus, the same proportion of aminopseudocumenes. This expectation is fulfilled by the chloro- and bromo- analogues. However, this is not the case of the iodo- compounds,[105] each giving preferentially the amine of the same orientation (Scheme 16).



Scheme 16.

A mixture of the aryne mechanism (to account for the considerable degree of cine substitution which does occur) and a mechanism of substitution without rearrangement is indicated.

A clue to the mechanism of substitution without rearrangement is provided by the reaction of iodopseudocumenes with KNH_2 in liquid ammonia in the presence of tetraphenylhydrazine , a radical scavenger. The amino compounds formed are in a ratio analogous to those from the chloro- and bromo- derivatives, that is, the ratio expected from the aryne mechanism. The fact that tetraphenylhydrazine suppresses substitution without rearrangement is evidence for a radical mechanism. A mechanism compatible with these observations is set forth in equations (32)-(35).

$$\text{electron donor} + \text{ArI} \longrightarrow [\text{ArI}]^{-\cdot} + \text{residue} \qquad (32)$$

$$[\text{ArI}]^{-\cdot} \longrightarrow \text{Ar}\cdot + \text{I}^- \qquad (33)$$

$$\text{Ar}\cdot + \text{NH}_2^- \longrightarrow [\text{ArNH}_2]^{-\cdot} \qquad (34)$$

$$[\text{ArNH}_2]^{-\cdot} \longrightarrow \text{ArNH}_2 + [\text{ArI}]^{-\cdot} \qquad (35)$$

This mechanism is substantiated by the fact that the non-rearranging substitution is promoted by the addition of potassium metal to the KNH_2/NH_3 system, since potassium metal in ammonia exists as K^+ ion and the solvated electron, e^-_{solv}, a superb electron donor.[106] Steps analogous to equations (32),(33) and (35) are well known from previous work.[98] The combination of an aryl radical with a nucleophile as in equation (34) has less precedent, but has been reported for reactions of p-nitrophenyl radical with cyanide ion and nitrite ion.[107] Equations (33), (34) and (35) constitute a propagation cycle. This mechanism closely resembles mechanisms which have been advanced on good evidence for substitutions at saturated carbon, some of which were earlier thought to be S_N2 reactions.[108]

It has been suggested that such reactions be symbolised $S_{RN}1$, which stands for substitution, radical-nucleophilic,

unimolecular. The mechanism is unimolecular in the same sense as S_N1, except that unimolecular bond fission occurs in a radical anion instead of a neutral molecule.

By promoting the $S_{RN}1$ mechanism through the addition of potassium metal, one can cause aryl halides to undergo aminodehalogenation without rearrangement despite the possible incursion of the aryne mechanism with its proclivity to cine substitution. Thus, it is possible to induce substitutions in structures where the aryne mechanism is possible, for example, a halogen flanked on both sides by ortho- substituents, can be caused to undergo aminodehalogenation with KNH_2/NH_3, and a phenoxy group of a diaryl ether can be replaced by an amino group.[105]

Unactivated aryl halides were long considered to be unreactive with nucleophiles. However, Rossi and Bunnett[109] have shown that bromobenzene reacts readily with acetone enolate ion, under u.v. irradiation in liquid ammonia to afford phenylacetone in high yield, together with some 1,1-diphenyl-2-propanone, as shown in equation (36).

$$C_6H_5Br + CH_2{:}C(CH_3)O^-K^+ \xrightarrow[NH_3]{h\nu} C_6H_5CH_2{\cdot}CO{\cdot}CH_3 + (C_6H_5)_2{\cdot}CO{\cdot}CH_3 \quad (36)$$

Under similar conditions halogenoarenes also bring about the arylation of other types of carbanions.[110,111] Aryl iodides and bromides undergo ready photostimulated reaction with thiophenoxide ion[112,113] (equation (37)) and with dialkyl phosphite ions,[114] shown in equation (38), to give, respectively, diaryl sulphides and dialkyl aryl phosphonate esters.

$$C_6H_5I + C_6H_5S^-K^+ \xrightarrow[DMSO]{h\nu} C_6H_5{\cdot}S{\cdot}C_6H_5 + KI \quad (37)$$

$$C_6H_5I + (EtO)_2\,PO^-K^+ \xrightarrow{h\nu} C_6H_5{\cdot}PO{\cdot}(OEt)_2 + KI \quad (38)$$

All these reactions are believed to occur by the $S_{RN}1$ mechanism.

That mechanism for the arylation of acetone enolate ion, which is essentially the same as that of equation (32)-(35), is outlined in equations (39)-(43).

$$ArX + \text{electron donor} \longrightarrow [ArX]^{\cdot -} + \text{residue} \qquad (39)$$

$$[ArX]^{\cdot -} \longrightarrow Ar\cdot + X^- \qquad (40)$$

$$Ar\cdot + CH_3COCH_2^- \longrightarrow Ar\text{-}CH_2\text{-}\overset{O^-}{\overset{|}{C}}\cdot\text{-}CH_3 \qquad (41)$$

$$ArCH_2\text{-}\overset{O^-}{\overset{|}{C}}\cdot\text{-}CH_3 + ArX \longrightarrow ArCH_2COCH_3 + [ArX]^{\cdot -} \qquad (42)$$

$$ArCH_2\text{-}\overset{O^-}{\overset{|}{C}}\cdot\text{-}CH_3 + e^-_{solv} \xrightarrow{NH_3} ArCH_2\text{-}\overset{O^-}{\overset{|}{C}}H\text{-}CH_3 \qquad (43)$$

Although the cycle involves radical and radical anion intermediates, and an electron-transfer step, its overall consequence is nucleophilic substitution.

The reaction of a number of substituted bromo- and iodobenzenes with an excess of acetone enolate ion under photochemical stimulation were studied. The synthesis was unsuccessful when strongly electron-releasing groups such as $-NEt_2$ and $-O^-$ are <u>para</u>- to the nucleofugic group. It also fails with <u>m</u>-nitrohalogenobenzenes and is only marginally successful with <u>m</u>-iodobenzotrifluoride. The synthesis is remarkably insensitive to steric hindrance by <u>ortho</u>-substituents.

The association of low reactivity in the arylation reaction and the formation of dehalogenation products in substantial amounts is of mechanistic interest. When the aryl radical is encumbered with large <u>ortho</u>- substituents, it is plausible that a second mode of

reaction with acetone enolate ion may come into play. This second mode is electron-transfer, as in equation (44), generating an aryl anion and an acetonyl radical. The aryl anion quickly takes a

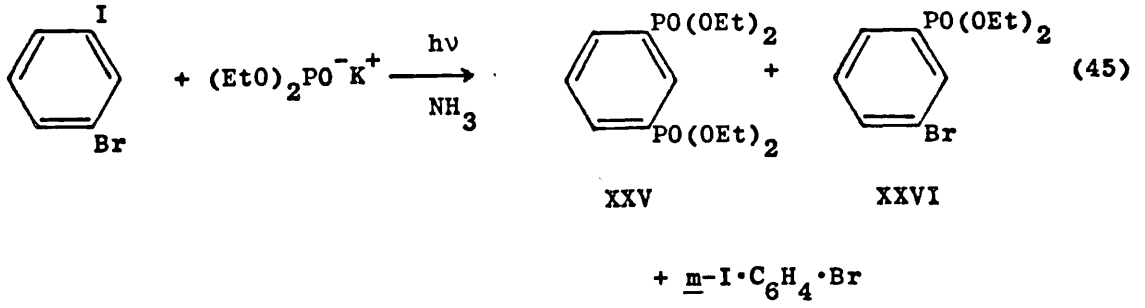
$$Ar\cdot + CH_3CH_2O^- \longrightarrow Ar:^- + CH_3COCH_2\cdot \qquad (44)$$

proton from the solvent to form the observed dehalogenation product. If the acetonyl radical then took part in one or more steps leading to termination products, the association of low reactivity with dehalogenation would find an explanation.

Probably the strongest evidence for the mechanism is its capacity to account for some extraordinary phenomena, which is achieved with some adaptation or extension of the original mechanism, but with no change in its essential features.

In liquid ammonia solution, iodobenzene undergoes ready photostimulated reaction with diethyl phosphite ion to form diethylphenyl phosphonate (equation (38)). One might suppose that with dihalogenobenzenes, one halogen would be substituted, and then the other; and that the uninvolved halogen would exert a substituent effect on the first substitution. However, the situation is somewhat more complex.

Consider the reaction of m-bromoiodobenzene with diethyl phosphite ion in liquid ammonia.[114,115,116,117] (equation (45)).



(45)

XXV XXVI

+ m-I·C$_6$H$_4$·Br

Upon interruption after 7 minutes irradiation, 60% of the

disubstituted product, structure XXV, 7% of the monophosphate ester, structure XXVI, and 28% of unreacted m-bromoiodobenzene were found. It is striking that so little XXVI was present in the company of so much XXV and unreacted starting material.

Such a condition might arise if substitution was stepwise and the conversion of XXVI to XXV was much faster than of the starting material to XXVI. However, the transformation of XXVI to XXV was found to be slower than of starting material to XXVI.[117] It follows that XXVI cannot be an intermediate on the main pathway of m-bromoiodobenzene to the disubstitution product.

The $S_{RN}1$ mechanism provides, however, a straightforward interpretation. Equations (46)-(51) show the propagation cycle for the case of iodobenzene substituted with a second halogen.

$$\left[XC_6H_4I\right]^{\cdot-} \longrightarrow XC_6H_4\cdot + I^- \tag{46}$$

$$XC_6H_4\cdot + Y^- \longrightarrow \left[XC_6H_4Y\right]^{\cdot-} \tag{47}$$

$$\left[XC_6H_4Y\right]^{\cdot-} + XC_6H_4I \longrightarrow \left[XC_6H_4I\right]^{\cdot-} + XC_6H_4Y \tag{48}$$

$$\left[XC_6H_4Y\right]^{\cdot-} \longrightarrow YC_6H_4\cdot + X^- \tag{49}$$

$$YC_6H_4\cdot + Y^- \longrightarrow \left[C_6H_4Y_2\right]^{\cdot-} \tag{50}$$

$$\left[C_6H_4Y_2\right]^{\cdot-} + XC_6H_4I \longrightarrow C_6H_4Y_2 + \left[XC_6H_4I\right]^{\cdot-} \tag{51}$$

Equations (46)-(51) provide two alternate propagation cycles. One comprises equations (46)-(48) and effects replacement of iodine, but not of halogen, X. The other comprises equations (46),(47), and (49)-(51), and results in replacement of both halogens. Which cycle prevails depends on the relative rates of the steps set out in equations (48) and (49). The significance of the set of equations (46)-(51), is that it provides for the conversion of XC_6H_4I to

disubstitution product without the intermediacy of monosubstitution product. Instead, it proposes the radical anion of the latter, $[XC_6H_4Y]^{\cdot-}$ to be an intermediate.

Liquid ammonia has been the solvent for nearly all aromatic $S_{RN}1$ reactions. Bunnett, Scamchorn and Traber[118] carried out studies in other solvents and found that DMSO appeared to be the best solvent, all reactions occurring in high yield. Halogenobenzenes, unsubstituted or provided even with electron-releasing substituents, have been shown to react with certain nucleophiles under stimulation by electrons or photons to form products of substitution, in a manner consistent with the $S_{RN}1$ mechanism. There has been very little evidence of thermally induced aromatic substitution by this mechanism other than the reaction of amide ion in ammonia with some iodopseudocumenes (Scheme 15).[105] More recently, however, iodo- and bromobenzene have been reported[119] as reacting with potassium pinacolone enolate in DMSO at 25° in the dark, to form the substitution product $Ph{\cdot}CH_2{\cdot}CO{\cdot}C(CH_3)_3$. The reaction was shown to be accelerated by light and inhibited by p-dinitrobenzene. The iodobenzene: bromobenzene reactivity ratio, about 6, was the same in the dark and the photostimulated reactions.

The rate law governing the reaction of iodobenzene with potassium pinacolone enolate in DMSO[119] showed a peculiar dependence on concentration (equation (52)) which had no simple mechanistic significance.

$$-x + a\ln(a/a - x) = k_e t \qquad (52)$$

These facts constitute evidence for a light-catalysed $S_{RN}1$ mechanism.

1.2.5. PROTIODEHALOGENATION OF ARYL HALIDES.

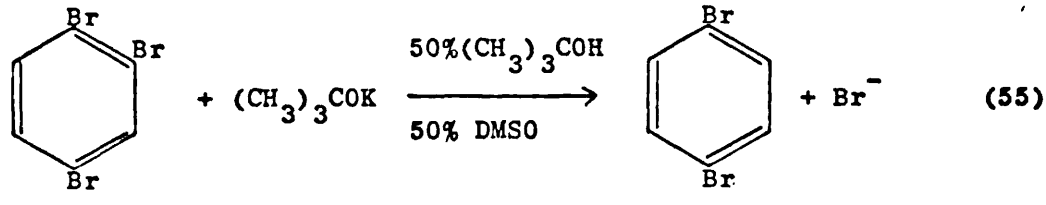
In 1938, van der Linden,[120] whilst studying the reaction of polychloro- and polybromobenzenes with sodium methoxide in alcoholic butanone, came upon some unusual products; these being pentabromobenzene and 1,2,4,5-tetrabromobenzene in yields which depend on the temperature at which the reaction was maintained as shown in equations (53) and (54).

$$C_6Br_6 \xrightarrow{\text{Room Temp.}} C_6Br_6 + C_6Br_5H \qquad (53)$$

$$C_6Br_6 \xrightarrow{\text{Reflux}} C_6Br_4H_2 \qquad (54)$$

The unexpected products are derived from hexabromobenzene by means of what has come to be termed protiodebromination.

In the course of a search for further base-solvent systems in which the base-catalysed halogen dance (Section 1.2.3.) might be caused to occur, Moyer[121] exposed 1,2,4-tribromobenzene to potassium t-butoxide in 50% t-butyl alcohol-50% DMSO. The unexpected product was p-dibromobenzene, in 70% yield, equation (55).

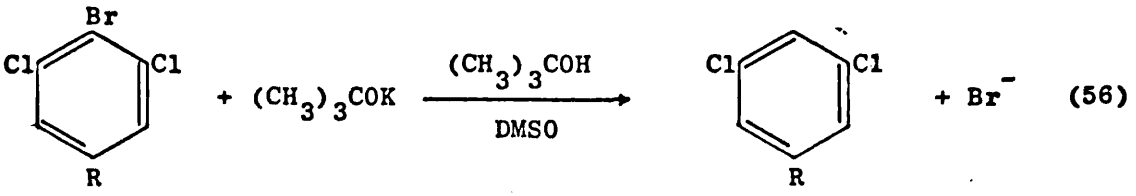


(55)

Further investigation[122] showed that the same reagent also effects deiodination more readily than debromination. Dechlorination was not observed, though sought.

In general, protiodehalogenation occurs at sites ortho- to other halogen atoms and is most easy for halogens flanked on both sides by ortho-halogens. 4-Substituted-2,6-dichlorobromobenzenes were even more reactive when the R group (equation (56)) in the

4-position was an electron-attracting substituent.[122]



(56)

Because of concurrent studies on deiodination reactions involving aryl radical intermediates,[99] Bunnett and Victor[122] sought to detect radicals in the dehalogenation of 1-bromo- and 1-iodo-2,6-dichlorobenzenes and 1,2,4-tribromobenzene in benzene-rich systems. Dehalogenation occurred as usual, but no biphenyl derivatives were detected.

Although these results discouraged consideration of a radical mechanism, the possibility that aryl halides somehow accepted an electron, expelled a halide ion and thereby formed an aryl radical, as in the radical-induced deiodination of aryl iodides in alkaline methanol[99] was nevertheless examined.[122] In 2M methanolic sodium methoxide with 1-phenyl-2-benzenesulphonhydrazide, 1-chloro-2-bromo-4-iodobenzene lost only iodine, forming o-chlorobromobenzene, but with potassium t-butoxide in 50:50 t-BuOH-DMSO, the same aryl halide afforded mainly bromide ion (55%) and p-chloroiodobenzene (37%), though iodide ion (39%) and o-bromochlorobenzene (22%) were also formed. This pattern of halogen mobility observed in the t-BuOH-DMSO system is not that characteristic of the electron-transfer mode of dehalogenation.

At the outset, the role of the DMSO was not clear, so other dipolar, aprotic solvents as 'cosolvents' were investigated by measuring the extent of debromination of 1-bromo-2,6-dichlorobenzene effected by $(CH_3)_3COK$ in various 50%$(CH_3)_3COH$ - 50% cosolvent media.

Cosolvents found to be effective (though less so than DMSO) were N,N-dimethylacetamide, N-methylpyrrolidone and tetramethyl sulphone. Ineffective cosolvents were diphenyl sulphoxide, dimethyl formamide and hexamethylphosphorotriamide.[122]

The feature that sets apart the effective and ineffective cosolvents is that the effective ones have a methylene group α— to a carbonyl, sulphonyl, or sulphinyl group, whilst all the ineffective ones lack this characteristic.

The following mechanism, detailed for DMSO (equations (57)-(60)) is compatible with all the observations.[122]

$$(CH_3)_3CO^- + CH_3SOCH_3 \rightleftharpoons (CH_3)_3COH + CH_3SOCH_2^- \qquad (57)$$

$$CH_3SOCH_2^- + ArX \longrightarrow Ar:^- + CH_3SOCH_2X \qquad (58)$$

$$Ar:^- + (CH_3)_3COH \longrightarrow ArH + (CH_3)_3CO^- \qquad (59)$$

$$\text{base} + CH_3SOCH_2X \longrightarrow X^- + \text{residue} \qquad (60)$$

Of the four steps, (57) is amply precedented.[123] (58) is a nucleophilic displacement on halogen, forming an aryl anion and a halogenomethyl sulphoxide. Nucleophilic displacements on halogen are implicated in the base-catalysed isomerisation and disproportionation of oligohalogenobenzenes[80] and in the scrambling of 1,2,4-triiodobenzenes[84] (section 1.2.3.) The last step, equation (60), is unclear but might involve S_N2 displacement of halogen by either $(CH_3)_3CO^-$ or $CH_3SOCH_2^-$ or α -elimination of HX. This latter step seems likely to occur but no organic products from this proposed step have been detected.

This proposed mechanism accounts for the beneficial effect of o-halogen substituents (stabilizing phenyl anions[62]), the dehalogenation susceptibility order of I > Br > Cl, the absence of radical

intermediates and the dependence of reactivity on cosolvent identity. The reactive cosolvents are 'semi-protic' in the sense that they can yield protons to strong bases to form carbanions which may react analogously to the dimsyl anion (equation (56)).

Collins and Suschitzky[124] confirmed van der Linden's earlier work, showing hexabromobenzene to produce 1,2,4,5-tetrabromobenzene together with a small amount of the 1,2,3,5-isomer. They also noted that similar products were formed when the reaction was carried out in a boiling mixture of potassium t-butoxide, t-butyl alcohol and butanone, and the appearance of 1,3,5-tribromobenzene when DMSO was used instead of butanone. They explained their observations by the mechanism first put forward by Bunnett and his co-workers[121,122] (equations (57)-(60)).

Bolton and Sandall undertook a study of nucleophilic displacements in polyhalogenoaromatic compounds. They noted that polyfluorobromobenzenes could lose both bromine and fluorine on treatment with sodium methoxide in butanone-methanol.[125] This result was unexpected, firstly because fluorine is much more easily displaced from aromatic carbon by methoxide ion,[67] and also because ketonic solvents accelerate such nucleophilic displacements of fluorine often markedly.[76]

Table 4 shows the yields of bromide ion, fluoride ion and organic product in the reaction of some derivatives of 3-bromo-1,2,4,5-tetrafluorobenzene with 1 mol. equivalent of sodium methoxide in butanone-methanol (3:1, v/v).[125] The product yields suggested the main reaction to be that of protiodebromination.

Fluorine displacement is appreciable only in reactions of bromopentafluorobenzene and of m-dibromotetrafluorobenzene.

Table 4. Product yields from the reaction of sodium methoxide in butanone-methanol with p-XC_6F_4Br at 298K (mol. % per mole base consumed.)

X	Br^- (%)	F^- (%)	Organic Product
Br	98	0	p-HC_6F_4Br
H	97	1	p-$H_2C_6F_4$
F	87	13	C_6F_5H, p-BrC_6F_4·OMe
OMe	96	1	p-HC_6F_4OMe
NH_2	ca.95	0	p-$HC_6F_4NH_2$
Ph	97	1	p-HC_6F_4Ph

The reactions of all the bromopolyfluoroaromatic compounds with solutions of sodium methoxide in butanone-methanol (3:1, v/v; 298K) followed the kinetic form (equation (61)),

$$d\left[Br^-\right]/dt = - n.d\left[OMe^-\right]/dt = k_2\left[ArBr\right]\left[OMe^-\right] \qquad (61)$$

The second-order rate coefficients associated with the debromination of the derivatives of 3-bromo-1,2,4,5-tetrafluorobenzene in butanone-methanol (3:1, v/v; 298K) are given in Table 5. The substituent effect is consistent with a nucleophilic attack upon an atom attached to the aromatic system but not well able to conjugate with it. The base-catalysed debromination may, therefore, involve anionic attack at exocyclic bromine, but the kinetic studies gave no hint to the identity of the anion.

Under the experimental conditions, it seemed that the probable reagent was the butanone anion.

Table 5. Second-order rate coefficients for debromination of $p\text{-}XC_6F_4Br$ by sodium methoxide in butanone-methanol (3:1, v/v; 298K).[125]

X	$10^2k/l.mol.^{-1}s.^{-1}$
H	0·100 ± 0·006
F	4·5 ± 0·02
Br	10·2 ± 0·4
OMe	0·075 ± 0·003
CF_3	ca 60 ± 5
Ph	0·087 ± 0·003
NH_2	0·021 ± 0·001

Bolton and Sandall followed this up by a study of the protiodeiodination of certain aryl iodides under similar conditions;[126] the second-order rate coefficients are given in Table 6. A similar kinetic form was found, equation (62),

$$d[I^-]/dt = k_2[ArI][NaOMe] \qquad (62)$$

in methanol, protiodeiodination of iodopentachlorobenzene showed the kinetic form, equation (63),

$$d[I^-]/dt = k_3[ArI][NaOMe][Butanone]. \qquad (63)$$

The deiodination agent was therefore thought to be the butanone anion or its kinetic equivalent.

In butanone-methanol (3:1, v/v), the deiodination of pentachloroiodobenzene at 298K was not slowed, nor was the corresponding reaction of 2,6-dichloroiodobenzene accelerated, by added pentachlorobenzene. Although equilibrium concentrations of pentachlorophenyl anion were expected to be present, these did not

Table 6. Second-order rate coefficients for base-catalysed deiodination of iodobenzene derivatives (3:1, v/v butanone-methanol; 323K)[126]

Phenyl substituents	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$
2,6-dichloro-	0·077 ± 0·004
2,6-dibromo-	0·31 ± 0·02
2,3,4-trichloro-	0·023 ± 0·003
2,4,5-trichloro-	0·029 ± 0·001
2,4,6-trichloro-	2·6 ± 0·05
2,4,6-tribromo-	7·6 ± 0·3
2,4,6-trifluoro-	7·6 ± 0·1
2,6-dibromo-4-fluoro-	2·8 ± 0·1
2,6-dichloro-4-bromo-	3·4 ± 0·1
2,6-dichloro-4-iodo-	2·9 ± 0·5
2,3,4,5-tetrachloro-	0·97 ± 0·03
2,3,4,6-tetrachloro-	220 ± 6
2,3,5,6-tetrachloro-	1540 ± 20
2,3,4,5,6-pentachloro-	20 000 ± 1600

interfere with the deiodination demonstrating the essential irreversibility of the iodine transfer reaction (equation (64)), analogous to equation (58) in the proposed mechanism.

$$ArI + CH_3C\bar{O}CHCH_3 \longrightarrow Ar^- + CH_3COCHIMe \qquad (64)$$

If the iodine transfer reaction was reversible, the presence of a second aryl anion ($C_6Cl_5^-$) would allow a competition with the formation of a second aryl iodide of much greater reactivity (in the case of 2,6-dichloroiodobenzene). The lack of any discernible acceleration under these conditions confirms the irreversibility of

the iodine transfer process.

It appears that ortho-halogen substituents are much more effective than those in meta- or para positions in aiding protiodehalogenation. The o-chlorine substituent increases the second-order rate coefficient by a factor of ca. 10^4; fluorine and bromine both seem to show a similar effect, perhaps slightly greater than that of chlorine in the ortho- position. In the meta- position chlorine has a much weaker effect (a rate factor of about 10^2) and halogen substituents in the para- position increase the rate of constant by factors of 20-40.

Although this trend is general, the additivity principle is not strictly obeyed as shown by comparing the relative rates of 2,4,6-trichloro- and 2,6-dichloro-iodobenzenes. A para- chlorine substituent here increases the rate by a factor of 34, but only by 13 times when comparing the more crowded 2,3,5,6-tetrachloro- and pentachloro-iodobenzenes. This effect may arise due to induced interaction between adjacent substituents, or from the crowding of the iodine substituent by flanking, buttressed halogen atoms and the subsequent weakening of the C-I bond.

The activating effect of halogen substituents upon protiodeiodination is similar to, and perhaps slightly greater than, that seen in protiodebromination reactions[125,126] Protiodeiodination appears to occur more readily than protiodebromination under the same conditions (second-order rate coefficients of bromo- and iodo-pentachlorobenzenes in butanone-methanol (3:1, v/v; 323K) are $0{\cdot}0176 \pm 0{\cdot}0004$ l.mol.$^{-1}$s.$^{-1}$ and $20 \pm 1{\cdot}6$ l.mol.$^{-1}$s.$^{-1}$ respectively. These observations suggest that the transition state in protiodeiodination involves some weakening of the C-I bond, and confirms the general mechanism which has been proposed for this reaction system.

1.2.6. SCOPE OF PRESENT WORK.

The reaction of polyhalogenoaromatic compounds with sodium methoxide in a variety of solvents has been reported to occur via a number of mechanisms, to give an aryl alkyl ether by methoxydehalogenation or a reduction product by protiodehalogenation.

The intention of the work is to investigate this reaction in a solvent-system (DMSO-methanol) biased towards protiodehalogenation. In order to elucidate these processes, the products from the reaction of some substituted iodobenzenes with sodium methoxide in DMSO-methanol are to be examined. A kinetic study of this process is to be investigated, and in doing so, it is hoped that confirmation of one of the proposed mechanisms may result. The mechanism of the elimination of halogen may also give an indication as to the effect of substituents in this system.

The mechanism of protiodeiodination in this solvent system had to be deduced. If, as expected by analogy with hexabromobenzene or the chloroiodobenzenes in ketonic solvents, the reaction proceeds by attack upon iodine, then the comparisons with benzyl and benzoic systems may be made; in particular, the effect of substituents, especially chlorine, is of interest. A comparison of the electronic effects of substituents upon attack on iodine and of carbon may be instructive. The comparison may also be made by observing the relative extents of methoxydehalogenation and protiodeiodination.

2. EXPERIMENTAL.

2.1. Preparation and purification of reagents.

Dimethyl sulphoxide.

AnalaR dimethyl sulphoxide (B.D.H. Chemicals Ltd.) was purified by distillation under reduced pressure, rejecting the forerun (5%) and tailings. This material was then further purified by fractional freezing to m.p. 18·5° (lit. m.p. 18·55°).[127]

Methanol.

Methanol, b.p. 64·6°/760 mm Hg (lit.b.p., 64·4-64·7°) was purified by previously reported methods[128] from A.R. material (B.D.H. Chemicals Ltd.).

Preparation and standardisation of sodium methoxide.

Pellets of sodium, cleaned by washing with light petroleum, were added to the purified methanol[129] and the solution was boiled for several hours. Concentrated (ca. 2M) solutions of sodium methoxide were formed. Small amounts of sodium carbonate also formed, which soon precipitated out of solution, and were filtered off. The methoxide ion concentration of the clear supernant liquid was measured by suitably diluting a known volume of methoxide ion solution with freshly-boiled distilled water, and titrating with standard sulphuric acid (0·1M) using phenolphthalein as indicator.

Stock solutions of both methanol and methanolic sodium methoxide in dimethyl sulphoxide were made by weighing a quantity of purified dimethyl sulphoxide in a well-stoppered container, deriving from this weight (d_4^{20}, 1·100g.cm.$^{-3}$), the volume of dimethyl sulphoxide, and then adding the necessary volume of purified methanol or methanolic sodium methoxide from a burette so that the final composition of the dimethyl sulphoxide- methanol solvent mixture was 9:1, v/v. The methoxide ion concentration of such mixtures of methanolic sodium methoxide and dimethyl sulphoxide was

checked by titration with standard acid as before.

2.2. Preparation of aryl iodides.

2.2.1 General procedure.

The amine (0·50 mole) was dissolved in 6M hydrochloric acid (250 ml.) and diazotised between 0^{o} and 5^{o} by the slow addition of sodium nitrite solution (0·52 mole). On completion of the diazotisation, when a sample of the reaction mixture gave a clear solution with water, the mixture was poured slowly into a well-stirred solution of potassium iodide (0·50 mole) in water (100 ml.)

During the vigorous decomposition, nitrogen was evolved, iodine was liberated, and a brown unstable precipitate was formed in the solution. The reaction mixture was allowed to stand for 15 minutes at room temperature, and was then warmed on a steam bath until gas evolution ceased.

The cooled solution was then shaken with ether and the organic layer was separated and washed with aqueous sodium hydroxide, sodium metabisulphite, and finally water. After drying the solution (Na_2SO_4), the solvent was removed using a rotary evaporator.

The compounds were firstly purified by steam distillation. Liquid aryl iodides were then fractionally distilled under reduced pressure; solid iodides were purified by column chromatography upon alumina using light petroleum, followed by recrystallisation where necessary to obtain water-white material.

The compounds prepared in this way are listed in Table 7.

2.2.2. Preparation of some polychloroiodoarenes.

The diazotisation of polychloroanilines was carried out in sulphuric acid and acetic acid.[134] The following method was used for the preparation of the polychloroiodobenzenes listed in Table 8.

Table 7. Chloro- and dichloroiodobenzenes.

Phenyl Substituents	M.p./B.p./°C	Lit.m.p./b.p/°C	Yield/%	Purity*/%
2-chloro-	96/9mm.	110/16mm.[130]	65	98
2,3-dichloro-	35-36	35-36[61]	50	99
2,4-dichloro	130/55mm.	259-61/760mm.[131]	74	97
2,5-dichloro-	21	21[132]	65	100
2,6-dichloro-	68-68·5	68[133]	68	100
3,4-dichloro-	30·5	30-31[133]	59	98
3,5-dichloro-	54	54[133]	60	97

* Purity checked by g.l.c.

General procedure.

The amine (0·50 mole) was stirred with sulphuric acid (250ml., d=1·84g.cm.$^{-3}$) and acetic acid (100 ml.) at 0°. The amine was most successfully diazotised by the addition of solid sodium nitrite (0·52 mole) to the stirred suspension at temperatures below 10°. When the bulk of the solid had dissolved, and diazotisation was complete (indicated by dilution of the reaction mixture with water giving a clear solution), the mixture was carefully poured onto ice and was then treated with a concentrated solution of potassium iodide (0·50 mole) in water (100 ml.)

The diazonium salts were allowed to decompose below 25°, to avoid exchange reactions causing the loss of chlorine. When the mixture had attained room temperature, the mixture was warmed gently on a water bath until the evolution of nitrogen had ceased.

The resulting cooled solution was then extracted with ether (250 ml.), and the organic layer separated. This was then washed with successive solutions of sodium hydroxide and sodium metabisulphite, and finally water. The solvent was then dried over anhydrous sodium sulphate, and finally removed using a rotary evaporator.

The compounds were firstly purified by steam distillation, followed by further purification by column chromatography upon alumina using light petroleum, and subsequent recrystallisation.

Table 8. Polychloroiodoarenes.

Phenyl Substituents	M.p./B.p./°C	Lit.m.p./b.p./°C	Yield/%	Purity*/%
2,3,4-trichloro-	66[a]	66-66·5[126]	59	99
2,4,5-trichloro-	106·5-107	107[135]	64	100
2,4,6-trichloro-	53-54	54[134]	67	100
2,3,4,5-tetrachloro-	84·5[b]	89-90[136]	56	98
2,3,4,6-tetrachloro-	71·5-71·8	78·5[135]	49	100
2,3,5,6-tetrachloro-	88·5-90·5	88-90[137]	61	97
2,3,4,5,6-pentachloro-	207	208·5[135]	65	99

a,b Commercially available parent amine as precursor.

* Purity checked by titration of iodide ion formed during protiodeiodination.

2.3. Miscellaneous preparations.

2.3.1. Preparation of 3,4,5-trichloroiodobenzene.

A solution of 2,6-dichloroaniline (0·1 mole) in acetic acid (60 ml.) was refluxed gently while a solution of iodine monochloride (0·12 mole) in acetic acid (20 ml.) was added dropwise. When all the reagent had been added, the mixture was boiled for 2 hours.

The mixture was then cooled and poured onto ice, when a precipitate formed, which was filtered off and recrystallised from alcohol. 2,6-Dichloro-4-iodoaniline formed in 70% yield; m.p., 95-96° (lit. m.p., 99·5°[126]).

2,6-Dichloro-4-iodoaniline (0·05 mole) was dissolved in 6M

hydrochloric acid (30 ml.), and the solution treated at 0° with a solution of sodium nitrite (0·052 mole) in water (5 ml.) until diazotisation was complete.

Crystalline copper sulphate (0·06 mole) and sodium chloride (0·07 mole) were dissolved in water (50 ml.). The resulting solution was then reduced using a solution of sodium bisulphite (0·02 mole) in water (20 ml.). This mixed solution, which rapidly became green, was cooled to 10-15°, where cuprous chloride separated. The supernatant liquor was decantered from the colourless CuCl, and the precipitate washed twice by decantation with water. The moist CuCl was then dissolved in 6M hydrochloric acid (25 ml.).

The cold diazotised solution was then passed, with shaking, into the cold CuCl solution, where the mixture became thick. This mixture was then warmed to room temperature, with occasional stirring, and finally warmed to 40° to complete the decomposition of the diazonium ion.

The resulting mixture was then steam distilled. The organic product from the distillate was obtained by extraction with ether (250 ml.). The ethereal layer was then dried and the ether removed using a rotary evaporator.

The solid product was then purified by column chromatography (light petroleum upon alumina), followed by recrystallisation from aqueous alcohol, yielding colourless needles of 3,4,5-trichloroiodobenzene, m.p. 45·5°; yield 42% (lit. m.p., 46-48°[138]).

This compound was characterised by n.m.r. (δ = 7·65 p.p.m.), mass spectrometry (m/e, 306(100), 308(100), 310(33), 312(4)) and elemental analysis (Calculated, C = 23·4%, H = 0·65%. Found, C = 23·7%, H = 0·65%).

2.3.2. Preparation of 2-chloro- and 2,3,5,6-tetrachloro-4-iodoanisole.

The preparation of the initial phenols was carried out using the method of Brazier and McCombie.[139]

p-Iodophenol was prepared from p-aminophenol by diazotisation in sulphuric acid. The crude substance obtained, m.p., 90-91° (lit. m.p., 94°;[139] yield 63%), was used without further purification.

A solution of p-iodophenol in carbon tetrachloride was treated with a steady stream of chlorine. The resulting iodo-dichloride, which precipitated, was filtered off and left to decompose, evolving HCl, giving 2-chloro-4-iodophenol. This compound underwent similar subsequent treatment with chlorine in carbon tetrachloride to yield successively 2,6-dichloro-, 2,3,6-trichloro- and 2,3,5,6-tetrachloro-4-iodophenol, which are listed in Table 9.

Table 9. Polychloro-4-iodophenol.[139]

Substituted 4-iodophenol	M.p./°C	Lit.m.p./°C	Yield/%
2-chloro-	52·5	54	51
2,6-dichloro-	91	91-92	47
2,3,6-trichloro-	51	51-52	45
2,3,5,6-tetrachloro-	70	72	54

Solutions of 2-chloro- and 2,3,5,6-tetrachloro-4-iodophenol in sodium hydroxide were treated with dimethyl sulphate (1·5 moles) to give the corresponding anisoles. 2-chloro-4-iodoanisole, recrystallised from aqueous alcohol, was obtained as colourless needles, m.p. 86° (m/e 268(100), 270(33) δ_{OMe} = 3·84 p.p.m.). Similarly, 2,3,5,6-tetrachloro-4-iodoanisole gave yellow crystals, m.p. 164° (m/e, 380(75), 382(100) 384(50), 386(11), δ_{OMe} = 3·94 p.p.m.).

2.3.3. Preparation of some derivatives of 2,6-dichloro-4-X-iodobenzenes.

2.3.3.1. Preparation of 2,6-dichloro-4-nitroiodobenzene.

Preparation of this compound was carried out by diazotisation of 2,6-dichloro-4-nitroaniline (as in section 2.2.2.) and subsequent treatment of the diazotised solution with potassium iodide. Purification, effected by steam distillation and crystallisation from alcohol, yielded needles of 2,6-dichloro-4-nitroiodobenzene, m.p. 152-53° in 60% yield (lit. m.p., 153°[140]).

2.3.3.2. Preparation of 2,6-dichloro-4-bromoiodobenzene.

2,6-Dichloro-4-bromoaniline analogously gave colourless plates of 2,6-dichloro-4-bromoiodobenzene, m.p. 69·8 - 70·5° (lit. m.p., 67·5 - 68·2[126]; yield, 68%).

2.3.3.3. Preparation of 1,3-dichloro-2,5-diiodobenzene.

Similarly, 2,6-dichloro-4-iodoaniline (section 2.3.1.) gave 1,3-dichloro-2,5-diiodobenzene, m.p. 79 - 80° (lit. m.p., 79·2 - 80·4°,[126] yield, 55%).

2.3.4. Preparation of 2,3,4-trichloro-6-methyliodobenzene.

This compound was prepared by firstly acetylating 5-chloro-o-toluidine (25g.) using a mixture of acetic anhydride (25 ml.) and acetic acid (50 ml.). After gently warming on a water bath for 20 minutes, the solution was poured into ice-water, and the resulting precipitate filtered off. Recrystallisation from aqueous alcohol yielded 5-chloro-o-acetotoluidide, m.p. 139° (lit. m.p., 139-40°;[142] yield, 97%).

5-Chloro-o-acetotoluidide (40g, 0·22 mole) was dissolved in nitromethane (200 ml.), and the solution warmed to 80°. A steady stream of chlorine was passed through the warm solution for 6 hours. On cooling, a solid crystallised out of solution, and was filtered off.

This product was then hydrolysed by boiling with 6$\underline{M}$ hydrochloric acid (300 ml.) until a test portion of the solution remained clear on dilution with water. The resulting mixture was then neutralised with sodium hydroxide and the brown product was filtered off. Mass spectrometry indicated the compound to be a trichlorotoluidine.

This amine (21g, 0·1 mole) was diazotised below 10° in sulphuric acid (40 ml., d=1·84g.cm.$^{-3}$) and acetic acid (20 ml.) using sodium nitrite (8·3g, 0·12 mole) in water (12 ml.), and the diazotised solution then poured slowly onto ice, followed by addition of a concentrated solution of potassium iodide. (16·6g, 0·10 mole) in water. The solution was allowed to warm to room temperature, and finally warmed to 40° until nitrogen ceased to be evolved.

The organic products were extracted from the cooled solution by shaking with ether (250 ml.); the ethereal layer being washed with solutions of sodium metabisulphite and sodium hydroxide, and finally water. The ethereal layer was then dried (Na_2SO_4) and the ether removed using a rotary evaporator, leaving a red solid.

This product was then purified by steam distillation, followed by column chromatography (using light petroleum upon alumina), and gave two products (g.l.c.) which were isomeric by mass spectroscopy and n.m.r., the first fraction having m.p. 70-72° (yield, 27%) and the second, m.p. 78-80° (yield, 19%).

The first material was characterised by reducing the compound in dimethyl sulphoxide using sodium borohydride, and nitrating the product with fuming nitric acid.[142] The nitro-compound, recrystallised from alcohol, m.p. 78-80°, was shown by

mass spectrometry to be a trichloronitrotoluene; the m.p. corresponded to 3,4,5-trichloro-2-nitrotoluene (lit. m.p. 80-81°[142]). Correspondingly, elemental analysis of the first fraction (Calculated, C=26·2%, H=1·24%. Found, C=26·2%, H=1·2%) showed the material to be an iodotrichlorotoluene. Thus, the first fraction is clearly 2,3,4-trichloro-6-methyliodobenzene. The second material could not be characterised unambiguously.

2.3.5. Preparation of 2-iodo-4,5,6-trichloro-m-xylene.

2,6-Dimethylaniline (12·1g, 0·10 mole) gave 2,6-dimethyliodobenzene, b.p. 122-124°/21 mm. (lit. b.p., 228-230°/760 mm.[143]) in 65% yield.

Chlorination of 2,6-dimethyliodobenzene was then attempted using the method described for the chlorination of p-iodophenol (section 2.3.2.). Chlorine was passed through a cold solution of 2,6-dimethyliodobenzene (11·69, 0·05 mole) in carbon tetrachloride (100 ml.). The solid which separated, gave no warming, hydrogen chloride and a liquid, which was distilled under reduced pressure (b.p., 154°/33 mm.). This 2,6-dimethyl-4-chloroiodobenzene was 98% pure (by g.l.c. and mass spectroscopy). The yield was 57%.

Attempts at further chlorination by this method were unsuccessful. 2,6-Dimethyl-4-chloroiodobenzene(7·5g, 0·028 mole) was dissolved in nitromethane (50 ml.) and an excess of sulphuryl chloride added, and the resulting solution was gently refluxed for three hours. The nitromethane was then distilled off using a water bath, and the remaining mixture poured into water, and the resulting solid filtered off. The white product was recrystallised from a mixture of chloroform and ethanol (1:1). Analysis of the product by g.l.c. showed that the solid was composed of two products. Mass spectrometry indicated that the two compounds were 2-iodo-4,5,6-trichloro-m-xylene and tetrachloro-m-xylene.

Tetrachloro-m-xylene was prepared by the method of Datta and Fernandes,[144] m.p. 223-5° (lit. m.p., 210°). G.l.c. analysis showed this compound to have the same retention time as that of the impurity in 2-iodo-4,5,6-trichloro-m-xylene.

Vacuum sublimation increased the purity of 2-iodo-4,5,6-trichloro-m-xylene to 64% (by g.l.c.) giving material m.p., 203-5°.

2.3.6. Preparation of some derivatives of (α,α,α-trifluoromethyl)iodobenzene.

2.3.6.1. Preparation of o-, m- and p-(α,α,α-trifluoromethyl)iodobenzene.

In all three cases, the desired derivatives were prepared by diazotisation of the corresponding amines by the general method (section 2.2.1.). The compounds prepared in this way are listed in Table 10.

Table 10. o-, m- and p-(α,α,α-trifluoromethyl)iodobenzene.

(α,α,α-Trifluoromethyl)iodobenzene	B.p./°C	Lit.b.p./°C	Yield/%	Purity*/%
ortho-	199	197·5-8/750mm.[145]	58	79
meta-	74/18mm.	82-82·5/25mm.[146]	52	97
para-	190	185·5-6/745mm.[145]	56	98

*Purity checked by g.l.c.

2.3.6.2. Preparation of 2-(α,α,α-trifluoromethyl)-4-nitroiodobenzene.

The method described by Petit and Tatlow[147] was used to prepare this compound. Yellow needles of 2-(α,α,α-trifluoromethyl)-4-nitroiodobenzene were obtained, m.p. 80° (lit. m.p., 82°) in 48% yield.

2.3.6.3. Preparation of 2-(α,α,α-trifluoromethyl)-4-bromoiodobenzene.

This compound was prepared by the method of McBee et al.,[148] giving 2-(α,α,α-trifluoromethyl)-4-bromoiodobenzene, m.p. 77° (lit. m.p., 77-8°) in 52% yield.

2.3.6.4. Preparation of 2-(α,α,α-trifluoromethyl)-4-nitroanisole.

This preparation involved taking commercially available 2-chloro-5-nitro-(α,α,α-trifluoromethyl)benzene (2g.) and dissolving it in a mixture of DMSO-methanol (9:1, v/v), and then adding a solution of sodium methoxide in methanol (5 ml.). The resulting solution was boiled until a yellow solid precipitated out of solution. The solid was filtered off, washed thoroughly with water, and recrystallised from alcohol, giving 2-(α,α,α-trifluoromethyl)-4-nitroanisole, 79° (lit. m.p., 79-79·5°[149]).

2.3.7. Preparation of some derivatives of nitroiodobenzene.

2-Nitro-, 4-nitro- and 2,4-dinitroiodobenzenes were prepared from commercially available amines by the diazotisation procedure described by Hodgson and Walker,[150] followed by treatment with potassium iodide solution. These compounds are listed in Table 11.

Table 11. Derivatives of nitroiodobenzene.

Iodobenzene	M.p./°C	Lit. m.p./°C	Yield/%	Purity*/%
2-nitro-	49-49·5	49·5[151]	68	100
4-nitro-	172·5-3	173[152]	74	100
2,4-dinitro-	89	88·5-90[153]	72	100

*Purity checked by g.l.c.

2.3.8. Preparation of pentabromoiodobenzene.

Pentabromoaniline was prepared from p-nitroaniline by the method of Kornblum, Kelley and Cooper.[154] The amine, m.p., 262° (lit. m.p., 262°), was characterised by elemental analysis (Calculated: C=14·8%, N=2·9%, H=0·41%. Found: C=14·6%, N=2·9%, H=0·4%), and then diazotised using the method of Hodgson and

Mahadevan,[134] and treated with a suspension of potassium iodide in water.

The resulting mixture was treated with a solution of sodium metabisulphite, to remove elemental iodine and the solid material was then taken up in chloroform. Evaporation of the dried ($MgSO4$) solvent, followed by recrystallisation of the crude material from dimethyl formamide, gave pentabromoiodobenzene, m.p., 312-313° (lit. m.p., 315-316°[155]).

2.3.9. Preparation of some polychloroanisoles.

The commercially available polychlorophenol in aqueous sodium hydroxide (2M) was treated with dimethyl sulphate (1·5 mole) at 50°-70°. The anisole was isolated by pouring the resulting suspension into water, filtering off the solid and recrystallisation if required.

2.3.10. Polychlorobenzenes.

All materials used were commercial samples which were recrystallised before use.

2.4. Kinetic studies.

Technique for following the reactions.

A known amount (10-100 mmole) of the aryl halide was placed in a 50 ml. volumetric flask and dissolved in DMSO-methanol (9:1, v/v). The flask was then immersed in a water bath, thermostated to 50°, and left to equilibrate for one hour.

The reaction was initiated by adding a known volume of the sodium methoxide solution to the aryl halide solution, and quickly making the total volume of solution up to 50 ml., by addition of any DMSO-methanol (9:1, v/v) needed. The zero time was taken as the half-point of addition of methoxide ion.

Aliquots (5 ml.) were withdrawn after suitable time intervals and quenched by pouring them into an excess of dilute nitric acid. The liberated halide ion was then analysed titrimetrically against silver ion, (Orion 94-17A chloride ion electrode;90-01 Calomel reference electrode). Where a differential potientiometric analysis was required, an Eil automatic titrator 7070-400 and a digital burette dispenser were used. From these titres, a rate constant could be calculated. The reactions were usually followed over two half lifes, taking six to eight points.

Experimental results were consistent to ± 10% and to within ± 5% within each kinetic study.

2.5 Analysis of products.

For the determination of the organic products from these reactions, the aryl halide was dissolved in DMSO-methanol (9:1,v/v), and placed in the thermostated water bath (50^{o}), and after a suitable period for the solution to reach the required temperature, the reaction was initiated with the methoxide ion solution. After an appropriate time, the solution was quenched in an excess of dilute nitric acid, and the organic products were extracted with ether. The ethereal layer was washed thoroughly with water to remove traces of DMSO, dried over anhydrous sodium sulphate and the ether removed using the rotary evaporator.

The subsequent residue, containing the organic products, was analysed by g.l.c., n.m.r. and mass spectrometry as necessary.

These reactions, to obtain product analyses, were carried out in strict adherence to the method used for the kinetic study to minimise any discrepancy that may occur due to experimental error.

Where addition of scavengers (for free radicals) or other compounds which may have helped to elucidate the mechanism, these

compounds were added to the aryl halide solution before initiation with methoxide ion. The reaction mixtures were then treated in the usual manner (see Appendix).

2.6 Analytical Techniques.

2.6.1 Gas-liquid chromatography.

G.l.c. investigations were carried out on a Pye Unicam series 204 gas chromatograph, using an OV-1 column (5ft x 1/8in.) nitrogen gas as carrier and a F.i. detector. The carrier gas glow rate, column temperature, detector sensitivity and size of sample injection were varied to give retention times of between 10 and 20 minutes. Identification of reaction products was achieved by comparison of retention times with those of authentic samples under identical conditions.

2.6.2. Nuclear magnetic resonance spectroscopy.

All ^{1}H n.m.r. spectra were recorded on a Perkin-Elmer R12B at 60 MHz or a Jeol FX90 instrument at 90 MHz, using TMS (tetramethylsilane) as an internal standard and deuterochloroform as solvent.

2.6.3 Mass spectroscopy.

Mass spectra were taken on a VG-Micromass 12B instrument, at 70 eV and 2-4 kV accelerating potential.

A VG-Micromass 7070 instrument linked with a Pye 104 gas chromatograph using an OV-17 column and employing oven temperature programming was used for g.c.m.s. studies. We are grateful to University College, London, and Professor J. H. Ridd for providing these facilities.

3. DISCUSSION.

The introduction of this thesis pointed out a number of different mechanisms by which halogens may be removed from aryl halides. The interchange of bromine or of iodine between polyhalogenoarenes in solutions of potassium amide in liquid ammonia has been thoroughly investigated,[79,80,83,84] whilst the protiodeiodination of polyhalogenoiodoarenes has previously been studied kinetically in solutions of butanone and methanol in the presence of sodium methoxide.[126] Similar reduction of polybromobenzenes[124,125] and of 1,3-dichloro-2-bromobenzenes[122] have also been reported.

3.1. PROTIODEIODINATION - A NUCLEOPHILIC PROCESS?

Nucleophilic displacement of halogens by attack upon aromatic carbon is a common feature in the reactions of polyfluoroaromatic compounds in classical nucleophilic aromatic substitution reactions. Aryl bromides, however, give reduction products in alkaline solutions of ketones in methanol, and not methyl ethers.[124] The loss of both bromine and fluorine from polyfluorobromobenzenes on treatment with sodium methoxide in butanone-methanol (3:1, v/v; 298K)[125] was unexpected, since fluorine is much more readily displaced from aromatic carbon by methoxide,[67] and also because ketonic solvents accelerate such displacements.[76] Relative yields from this reaction suggested the course of the reaction to be, equation (65),

$$(RH) + MeO^- + ArBr \longrightarrow ArH + Br^- + ROMe \qquad (65)$$

The reactions of all the polyfluorobromoaromatic compounds studied under these conditions followed the kinetic form (equation (66)),

$$-d\left[OMe^-\right]/dt = k_2\left[ArBr\right]\left[OMe^-\right]. \qquad (66)$$

Bromine displacement, when it was the only mode of reaction, followed the expected relationship, given in equation (61).

Substituent effects were in agreement with nucleophilic attack upon an atom attached to the aromatic ring, not at the carbon atom. The derived linear free energy plot gave $\rho = 4{\cdot}3 \pm 0{\cdot}6$ from substituent constants, σ; other parameters (e.g., σ^-) gave no better fit, nor was there a correlation with the free energy of displacement of fluorine in C_6F_5X by methoxide ion in methanol at 323K.[125]

The attack by base upon polyfluoroaromatic compounds has been shown to involve second-order kinetics in a number of solvents, including methanol.[167] On passing from methanol to butanone-methanol mixtures, the rate of a 'classical' two-stage nucleophilic displacement reaction would be expected to increase considerably; Parker has shown acetone to be a much 'faster' solvent than methanol for such processes.[156]

Nucleophilic attack upon carbon does not occur readily in hexabromo- and hexachlorobenzenes, and the alternative displacement at halogen is only found in polybromoarenes.[120] This protiodebromination reaction might prevail because nucleophilic displacement at carbon is slow when chloride and bromide ions are being expelled. This hypothesis might be tested by a study of the reaction of polybromopolyfluorobenzenes with methanolic sodium methoxide in butanone. The halogen substituents in these compounds facilitate both debromination (nucleophilic attack upon bromine) and defluorination (nucleophilic attack on carbon).

Fluorine displacement from p-dibromotetrafluorobenzene by methoxide ion did not occur appreciably under these conditions. Even with bromopentafluorobenzene, where the bromine substituent

activates this nucleophilic process, anisole formation accounted for only one quarter of the reaction product.[125]

Bromine displacement occurred at similar rates in both compounds, and seems to be consistent with a mechanism of base-catalysed protiodebromination, in which the rate-determining step is attack upon the exocyclic bromine substituent, rather than attack at the ring carbon atom, equations (67)-(70),

$$CH_3O^- + CH_3CH_2COCH_3 \rightleftharpoons CH_3OH + [CH_3CHCOCH_3]^- \quad (67)$$

$$[CH_3CHCOCH_3]^- + ArBr \longrightarrow Ar^- + CH_3CHBrCOCH_3 \quad (68)$$

$$Ar^- + CH_3OH \longrightarrow ArH + CH_3O^- \quad (69)$$

$$Base + CH_3CHBrCOCH_3 \longrightarrow Br^- + residue \quad (70)$$

The base-catalysed protiodebromination of polyfluorobromobenzene derivatives seems consistent with the protiodebromination sequence shown (equations (67)-(70)).[125]

Bolton and Sandall[126] followed this up by the study of polyhalogenoaryl iodides by the same reagent mixture, and a kinetic study of the process. It appeared that protiodeiodination occurred more readily when the aryl iodide was heated with solutions of sodium methoxide in butanone-methanol (3:1, v/v). Under these conditions, the rate equation was shown to be that given in equation (62).

A corresponding study of the reaction in methanol was also carried out, and the protiodeiodination of iodopentachlorobenzene showed the kinetic form, given in equation (63). The third order rate constant showed only slight alteration with the butanone concentration, consistent with a gross solvent effect; first-order dependence upon the concentrations of aryl iodide and base were found.

Under conditions of the reaction, one would expect equilibrium amounts of butanone anion being formed, in keeping with the equilibrium constant (equation (71)),

$$K = \frac{[CH_3OH][CH_3\bar{C}HCOCH_3]}{[CH_3O^-][CH_3CH_2COCH_3]} \qquad (71)$$

Accordingly, the rate equation for the protiodeiodination reaction (equation (62)) becomes, equation (72),

$$d[I^-]/dt = \frac{k_{true}\, K\, [CH_3\bar{C}HCOCH_3][CH_3OH][ArI]}{[CH_3CH_2COCH_3]} \qquad (72)$$

When K, the equilibrium constant linking the concentrations of butanone anion and methoxide ion (equation (71)), is large, the equilibrium concentration of butanone anion is proportional to $[CH_3CH_2COCH_3]/[CH_3OH]$. When K is small, the equilibrium concentration of butanone anion is nearly that of the added base.

In the reactions of the polyfluorobromobenzenes under these conditions,[125] changing the solvent composition affects the nucleophilic displacement of both fluorine and bromine, although debromination is evidently much more sensitive.[125] This is consistent with a difference in the solvent effect upon the two reactions, and also with $K \gg 1$, in keeping with the value ($K = 1000$) derived from the estimated acidity constants of methanol and butanone.[157]

It was assumed that the deiodinating agent was the butanone anion, or its kinetic equivalent. Such loss of iodine, under these conditions, is always much slower than the reduction of elemental iodine,[126] and so only the transference of halogen from

halogenoarene to butanone anion seemed kinetically significant, and the subsequent formation of iodide ion and the formation of the carbanionic reagent are not rate-determining processes under these conditions.

The order of ease of displacement of halogens in these conditions has been found to be in the order, I > Br > Cl,F.[125,126] Such an order implies some bond weakening of C-X in the transition stage, this again confirming another aspect of the mechanism. Substituent effects were also consistent with the proposed mechanism.

Other workers reached similar conclusions in their consideration of the products of reaction of polybromobenzenes under similar conditions, and suggested the intermediacy of α-halogenoketones. It is this latter step, equation (73), which is the unknown entity in the proposed mechanism.[122,124]

$$CH_3CHXCOCH_3 + \text{Base} \longrightarrow X^- + \text{residue} \qquad (73)$$

The intermediates linking the aryl iodide and iodide ion product have not been successfully identified. No-one has yet isolated any α-halogenoketones (or allied compounds) in the reaction products. This is probably due to fast attack of α-halogencketones by nucleophiles present in the reaction medium leading to a variety of products, some possibly water soluble, making isolation of these products difficult.

In attempts at following the displaced iodine, it was hoped to show the intermediacy of compounds which would clearly indicate the mechanism of this displacement. Pentachloroiodobenzene gave no iodide ion with methanolic solutions of either 1,3,5-trihydroxybenzene, or of 3,5-dimethylphenol in alkaline media (sodium methoxide), and no 4-iodo-3,5-dimethylphenol could be detected by mass spectrometry. No

simple intermediates could be isolated as a means of detecting the mode of reaction of the displaced iodine.

The interchange of bromine or of iodine (the Halogen Barn dance, Section 1.2.3.) in solutions of polyhalogenobenzenes and amide ions in liquid ammonia results in isomerisation, and to some extent, disproportionation. This exchange undoubtedly occurs via aryl anion intermediates. The reaction products from 1-iodo-2,4-dibromobenzene with amide ion in liquid ammonia[80] were consistent with a mechanism involving halogen atom transfer, the consequence of which is an aryl anion effecting nucleophilic attack on bromine (or on iodine) displacing another aryl anion, transferring a positive bromine fragment from one carbon to another. o-Halogen promotes both the loss of aromatic hydrogen to form o-halogenophenyl anions, and the displacement of electropositive iodine. The presence of other halogen substituents partly determines which of these processes occurs and hence the extents to which the halogen barn dance is supplanted by protiodeiodination when certain cosolvents are present.[96]

3.2. RADICAL-INDUCED DEHALOGENATION.

More recently a radical mechanism has been proposed to account for some of the reactions of aryl halides.[98,99,100] The capability of aryl halides to accept electrons from suitable donors and the tendency of the resulting radical anions to eject halide ions forming aryl radicals are prominent features in both the radical-induced deiodination in alkaline methanol and substitution by the $S_{RN}1$ mechanism.

The fact that iodopseudocumenes undergo reaction with amide ions in liquid ammonia[105] to give non-rearranged substitution products and not a mixture of two isomers as predicted by an aryne mechanism,

can be explained by the $S_{RN}1$ mechanism. This mechanism can also be successfully applied to explain the reaction of unactivated aryl halides with acetone enolate ion on irradiation in liquid ammonia[109] to afford phenylacetone, and other related reactions.[110,112,114]

Bunnett suggested[109] that in an encumbered aryl iodide which gives a sterically hindered intermediate, abstraction of hydrogen competes with nucleophilic attack; the less rapidly attacked aryl halides gave appreciable amounts of reduction products (ArH), (equation (44), p.64).

In attempts to determine the rate of photostimulated reaction of iodobenzene with enolate icns, Scamehorn and Bunnett[119] found that a substantial fraction of the reaction occurred before irradiation had commenced. Iodo- and bromobenzenes react with potassium pinacolone enolate in DMSO at 25° in the dark to yield the substitution product, $PhCH_2COC(CH_3)_3$. The reaction, which is light-catalysed, is thought to behave in a fashion consistent with the $S_{RN}1$ mechanism. Stimulation of these reactions by photons may involve the photolysis of C-X bonds, or photostimulation of the electron-transfer from the nucleophile to substrate.

These reactions showed an unusual kinetic form which the authors[119] could not correlate with the proposed reaction mechanism.

There has been little other evidence[158] of thermally induced aromatic substitution by this mechanism.

The $S_{RN}1$ mechanism has been successfully applied to explain the formation of a disubstitution product without the intermediacy of the monosubstitution product in reactions involving m-bromoiodobenzene and potassium diethyl phosphite in liquid ammonia on irradiation.[115,116,117]

Happer[97] studied the effect of change of sodium methoxide concentration on product proportions in the reaction of methanolic sodium methoxide on 1-(2-iodo-4-chlorophenyl)-2-benzenesulphonhydrazide, and found that the p-:m- chloroanisole ratio was indeed dependent on the sodium methoxide concentration, for example, in 2M sodium methoxide, 31% of chlorobenzene was formed. A thorough study of this reaction[98,99,100] showed that the chlorobenzene was formed by loss of iodine from m-chloroiodobenzene, and that deiodination did not take place unless both sodium methoxide and a radical source was present. Deiodination in the presence of CH_3OD afforded chlorobenzene virtually deuterium free, indicating the intermediacy of m-chlorophenyl radicals.

Similar reactions involving the replacement of diazonium groups from o-halogenobenzenediazonium ions[98] has also been shown to be strongly dependent on the base concentration. This is shown particularly by the products formed in CH_3OD solution. When only one equivalent of sodium methoxide is provided per mole of o-chlorobenzenediazonium ions, the chlorobenzene is nearly deuterium free, but when 2M sodium methoxide is used, the product is mainly o-deuterochlorobenzene. These results imply that a radical mechanism predominates at low sodium methoxide concentrations, but is almost wholly supplanted by an ionic mechanism in 2M sodium methoxide.

The formation of deuterated dediazoniation products in CH_3OD has been taken as evidence for a mechanism involving aryl anion intermediates.[98] In further support of this interpretation are the facts that in 2M methoxide ion, the proportions of Br^- ion and bromobenzene from o-bromobenzenediazonium ion are as expected from

o-bromophenyl anion, and that the yield of chlorobenzene from m-Cl·$ArN_2^+ \cdot BF_4^-$ [98] under conditions that give a high degree of deuteration, is not adversely affected by the presence of abundant oxygen (since oxygen has been shown to have a remarkable rate-enhancing effect on the thermally induced reactions of halogenobenzenes with pinacolone enolate ion in DMSO[119], which occurs via the $S_{RN}1$ mechanism). Indeed, it appears that there is a delicate balance between the radical and carbanionic mechanisms, the carbanionic route being feasible where a high concentration of methoxide ion exists.

In cases where the $S_{RN}1$ mechanism was thought to operate, Bunnett and his co-workers[109,119], added nitrobenzene to the reaction mixtures in an attempt to show the free-radical nature of the reactions under study. In all cases where the $S_{RN}1$ mechanism was shown to be operating, addition of nitrobenzene to those reaction mixtures inhibited dehalogenation of aryl halides. The reaction is thought to be inhibited because nitrobenzene accepts an electron far more readily than the aryl halide. The reaction of 5- and 6-iodopseudocumenes with potassium amide in liquid ammonia[105] gives non-rearranged products. Addition of tetraphenylhydrazine, a free-radical scavenger, to the reaction medium promotes formation of rearranged products, that is, reaction occurring via an aryne intermediate, suppressing the free-radical mechanism. Free-radical inhibitors are successful in restraining $S_{RN}1$ mechanisms, although an exceptional case is the unexplained acceleration of the 'dark' reaction of iodo- and bromobenzenes with potassium pinacolone enolate in DMSO at 25°, by addition of nitrobenzene and oxygen.[119]

In the present system, addition of nitrobenzene to 2,4,6-trichloroiodobenzene in DMSO-methanol (9:1, v/v; 323K) and to

pentachloroiodobenzene in butanone-methanol (3:1, v/v; 323K)[126] did not prevent, nor reduce the rate at which protiodeiodination occurred.

3.3. THE ARYNE POSSIBILITY.

Whilst the mechanism of base-catalysed protiodehalogenation of aryl halides by alkoxides in alcohol-ketone solvent systems (equations (67)-(70)) certainly exists in situations where both aromatic sites adjacent to the displaced halogen are occupied by substituents other than hydrogen, an aryne mechanism must not be ruled out. It is difficult to identify such a mechanism, although it is quite feasible for it to occur in compounds which have protons ortho- to halogen.

In the case of the less activated polychloroiodoarenes, namely, 3,4- and 3,5-dichloro- and 3,4,5-trichloroiodobenzenes, loss of a proton, followed by loss of either chlorine or iodine to give an aryne—type intermediate, may explain the substantial amounts of anisoles which we found (table 19, p.124).

Certainly it is difficult to envisage such a mechanism operating when protiodehalogenation is the main course of reaction under these conditions. The aryne mechanism has been ignored in reactions involving pinacolone enolate ions in DMSO,[119] although solutions of enolate ions in DMSO are strongly basic, and potassium t-butoxide in DMSO at 25° can generate benzyne from bromobenzene (albeit slowly)[159]; addition of an excess of potassium t-butoxide does not accelerate the reactions with aryl halides,[119] which would have been expected if aryne formation was necessary to the reaction.

The fact that p-iodotoluene reacts with pinacolone enolate ions under these conditions to afford only the p-methyl derivative,

and none of the m-methyl product[119] is evidence against an aryne mechanism. 2-Iodomesitylene, which is unable to be converted to an aryne intermediate, reacts under the same conditions, by the $S_{RN}1$ mechanism, to yield the product, 1-mesityl-3,3-dimethyl-2-butanone[119], as expected, together with a small amount of mesitylene (deiodination product).

It was also noted that bromobenzene, under these $S_{RN}1$ conditions, reacted more slowly than iodobenzene, whereas the converse is true for reactions proceeding through an aryne mechanism.[60] By extension, since protiodeiodination occurs more readily than protiodebromination, this is evidence against an aryne mechanism.

3.4. THE SOLVENT SYSTEM.

Most of the work carried out on the $S_{RN}1$ mechanism has been done using a single solvent. Liquid ammonia seemed to be most convenient. DMSO is also thought to be a good solvent for such reactions because of its low reactivity as a hydrogen donor[118,160] towards aryl radicals.

In the base-catalysed dehalogenation of polyhalogenobenzenes by alkoxide ions in alcohol-ketone solvent systems, a carbanionic route to dehalogenation seems more favourable. Similarly, DMSO has often been described as a 'faster' solvent in promoting protiodehalogenation.[96,121,124] Thus, hexabromobenzene is reduced to 1,3,5-tribromobenzene on treatment with potassium t-butoxide in solutions of t-butyl alcohol—DMSO (50:50, v/v).[124]

In order to confirm that the protiodehalogenation mechanism is operating, the solvent system was changed, from that of previously reported systems,[96,124,126] in an attempt to demonstrate the generality of the mechanism. Thus, a solvent mixture of DMSO-methanol,

9:1, v/v, was chosen after testing other ratios of DMSO-methanol. The 9:1 ratio gave a higher value for the rate constant for iodine loss from 2,4,6-trichloroiodobenzene under conditions of the reaction, than did other ratios of DMSO-methanol. As this ratio, 'salting out' did not occur. In most of the reactions studied, protiodeiodination was the main course of reaction.

Reactions which evidently occur by the $S_{RN}1$ mechanism are known to be light-catalysed, and are effected in the presence of a highly basic nucleophile. The solvent must have low reactivity towards aryl radicals, and must also have low acidity so that protonation of the nucleophile does not ensue. The substrate does not require activating substituents, for the $S_{RN}1$ mechanism has been observed in situations where groups which are deactivating in classical nucleophilic substitution processes are present.

It should be noted at this point that Bolton and Sandall[161] quenched the liberation of iodide ion in $S_{RN}1$ reactions of iodobenzene by the addition of methanol (0·4M). No increased amounts of anisole were detected (further compelling evidence against an aryne mechanism). Methanol, having α-hydrogen atoms, is a good hydrogen atom donor to aryl radicals, and the methoxide ions present in basic methanol are far better.[162] Although such reactions of aryl radicals with solvent lead usually to termination, the by-product from such reactions of methoxide ion, formaldehyde radical anions ($\cdot CH_2O^-$), may lead back into the propagation cycle[163] (see equations (27)-(31)).

This suggests an important role for methanol in these conditions, and it is this which dictates which mechanism may be operating.

All of the reactions described occur under conditions similar to those used to effect nucleophilic substitution by the S_NAr and/or aryne mechanism. Clearly side reactions of one or more of these unusual types may attend, or even eclipse, the intended substitution, since all reactions are studied under apparently quite similar conditions.

3.5. FURTHER ATTEMPTS AT ELUCIDATING THE MECHANISM.

Since $S_{RN}1$ reactions are known to be light-catalysed, an attempt was made to accelerate the deiodination of o-chloroiodobenzene in DMSO-methanol (9:1, v/v; 298K) by irradiation with light. This proved to be unsuccessful, and is in marked contrast to $S_{RN}1$ reactions, where a slow 'dark' reaction may be markedly accelerated by light.

Benzene-rich mixtures of polychloroiodoarenes gave no polychlorobiaryls on treatment with base in solutions of DMSO-methanol (9:1, v/v) or butanone-methanol (3:1, v/v); no aryl radicals were therefore detected. The $S_{RN}1$ mechanism provides for the arylated species derived from the carbanion in protiodeiodination reactions, affording small amounts of biaryls. Accordingly, it was thought unlikely that aryl radicals are present in this reaction system, as no biaryls could be detected by mass spectroscopy or g.l.c.

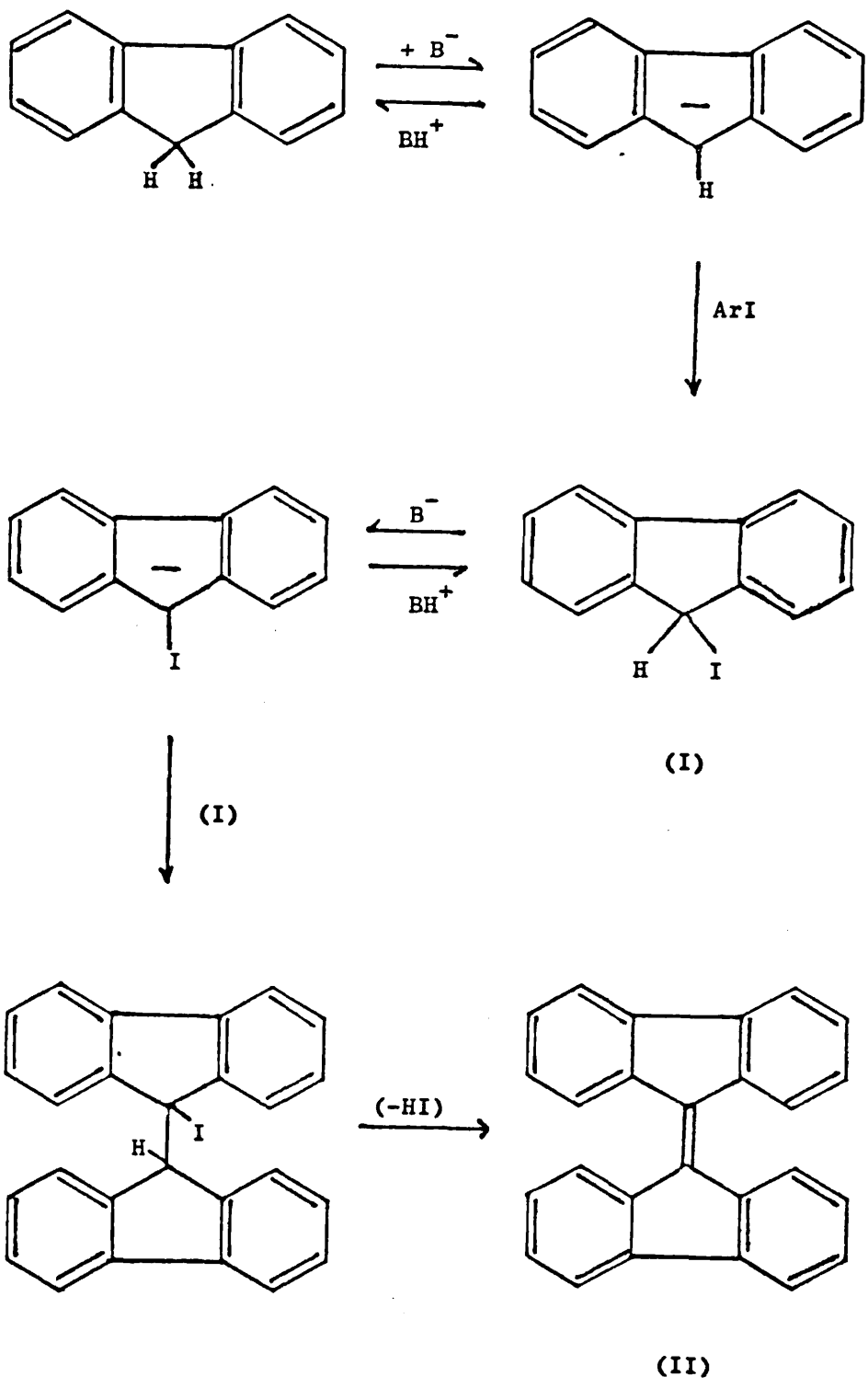
The deiodination of iodopentachlorobenzene in butanone-methanol (3:1, v/v; 298K) with sodium methoxide is not slowed by the addition of pentachlorobenzene.[126] Equilibrium concentrations of pentachlorophenyl anions are expected to be present under these conditions, but do not appear to interfere with the deiodination. The corresponding reaction with 2,6-dichloroiodobenzene is not accelerated by the addition of pentachlorobenzene.

In an attempt to divert the displaced iodine, a second carbanion was added to the reaction medium in an attempt to justify the proposed mechanism. Thus, fluorene, which readily forms a carbanion in DMSO-methanol mixtures, competes with the dimsyl anion to remove iodine from the aryl iodide even in mixtures rich in DMSO. The fluorene fragment then appeared as 9,9'-bifluorenylidene, and was isolated in ca. 50% yield, when either pentachloro- or 2,4,6-trichloroiodobenzene was treated with an equivalent quantity of fluorene and sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

No 9-arylfluorene was detected by mass spectrascopy, and so it appears that the mechanism is different to that of reacting aryl iodide and fluorene in liquid ammonia.[110] 9,9'-Bifluorenylidene is not formed in the absence of aryl iodide, and is known to be a common side-product from reactions of 9-halogenofluorenes with alkali[164,165] under conditions in which equilibrium amounts of 9-halogenofluorene anions are formed. Scheme 17 suggests a likely route to 9,9'-bifluorenylidene.

The essential feature of this mechanism, the formation of 9-iodofluorene by the electrophilic attack of the aryl iodide upon the fluorene anion, identifies the intermediate in the protiodeiodination reaction.

α-Halogenoketones and -sulphoxides are postulated intermediates in the protiodehalogenation mechanism which is believed to prevail here (equations (57)-(60)). While the dehalogenation of these intermediates is held to be a fast step of the sequence, the much lesser reactivity, towards nucleophiles, of α-bromosulphoxides than of α-bromoketones[166] implies conditions in which this step, and not the formation of these intermediates, is



Scheme 17

rate-determining.

The diethyl malonate carbanion is much less reactive than the dimethyl sulphoxide carbanion towards aryl iodides, and no reaction occurs if sufficient ester is present to account for the methoxide ion added. It is, however, quite a potent nucleophile towards alkyl halides[161] and its presence should cause α-iodosulphoxides to lose iodide ion quickly.

The addition of diethyl malonate to reacting solutions of pentachloroiodobenzene or of 2,4,6-trichloroiodobenzene in methoxide ion in DMSO-methanol (9:1, v/v) caused the rate of protiodeiodination to fall to zero to within the limits of observation (±1%). This suggested that no more than 2% of the reaction product was present as the α-iodosulphoxide. Since a build-up of the intermediate did not occur, for there was no subsequent formation of iodide ion when the ester had been added, the rate-determining step in protiodeiodination could not involve attack upon the iodosulphoxide, even in conditions where protiodeiodination was seen to be fast.

All the evidence available from the study of the protiodeiodination of aryl iodides in DMSO-methanol (9:1, v/v; 323K) by sodium methoxide seems to point to the proposed mechanism (equations (57)-(60)). The formation of 9,9'-bifluorenylidene on addition of fluorene to the reaction medium is clearly indicative of the transfer of positive iodine to a carbanion, confirming one aspect of the mechanism. No evidence has been obtained for the protiodeiodination to occur by a radical mechanism, and we therefore conclude that the mechanism operating under these conditions is that postulated.

3.6. KINETIC STUDIES.

3.6.1. THE LESS ACTIVATED ARYL IODIDES. ($k \not> 10^{-3}$ l.mol.$^{-1}$s.$^{-1}$)

In the reaction of the polychlorophenyl iodides with sodium methoxide in DMSO-methanol (9:1, v/v; 323K), protiodeiodination occurred exclusively. The rate constants for the protiodeiodination of these iodides are listed in Table 12.

Only in two cases were products other than those of protiodeiodination observed. N.m.r. studies revealed 2% anisole formation from the methoxydechlorination of 2,3-dichloroiodobenzene.

Table 12. Second order rate coefficients for the reaction of some aryl iodides with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

	Aryl iodide	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$
I	2-Chloro-	6×10^{-4}
II	2,3-Dichloro-	3·14
III	2,4-Dichloro-	0·90
IV	2,5-Dichloro-	3·5
V	2,6-Dichloro-	160

The analysis of the products from o-chloroiodobenzene on reaction with sodium methoxide in DMSO-methanol (9:1, v/v) revealed chlorobenzene to be the main observed (g.l.c.) product (> 95%). The problem associated with the product analysis of o-chloroiodobenzene is that of its low rate constant. In order for the analysis to be carried out, it was necessary to boil o-chloroiodobenzene with a solution of an excess of methoxide ion, for the reaction to proceed

far enough. As a result, ca. 30% of some less-volatile and unidentified products were formed (n.m.r.), probably thiomethoxy and other higher molecular weight compounds.

The substituent effects of chlorine in this process may be derived based on the rate constant for the protiodeiodination of o-chloroiodobenzene.

The substituent rate factor for an ortho-chlorine (k_V/k_I, ca. 3×10^5) is greater than that for a meta-chlorine (k_{II}/k_I and k_{IV}/k_I, ca. 6×10^3), whilst a para-chlorine substituent (k_{III}/k_I, $1{\cdot}5 \times 10^3$) has an even slightly smaller activating effect towards the protiodeiodination reaction.

If these derived rate factors are used to calculate, for example, a rate for the protiodeiodination of 2,3,4-trichloroiodobenzene, then the calculated second order rate constant is approximately 5·4 $l.mol.^{-1}s..^{-1}$ Since the observed rate constant is 0·031 $l.mol.^{-1}s.^{-1}$ strict additivity does not prevail. Similarly, the calculated rate constant for 2,4,6-trichloroiodobenzene is 243 $l.mol.^{-1}s.^{-1}$ against the observed k_2, 0·314 $l.mol.^{-1}s..^{-1}$ Although additional chlorine atoms evidently activate the aryl iodide system towards protiodeiodination, the additivity of these chlorine substituent rate factors is not obeyed.

3.6.1.1. THE TRIFLUOROMETHYL SUBSTITUENT.

As the rate of protiodeiodination of o-chloroiodobenzene is known, it is possible to calculate the rate of protiodeiodination of iodobenzene itself. This derived second order rate constant is of the order of 2×10^{-12} $l.mol.^{-1}s.^{-1}$, which would be virtually impossible to detect under the conditions of these reactions.

If this value is assumed to be reasonable, then the rate data (Table 13) from the iodobenzotrifluoride isomers provide substituent rate factors for the trifluoromethyl group, which also activates aryl iodides to protiodeiodination.

Table 13. Second order rate coefficients for the reaction of (α,α,α-trifluoromethyl)iodobenzene with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

$C_6H_4(CF_3)X$	$10^5k_2/l.mol.^{-1}s.^{-1}$
o-Iodo-	14
m-Iodo-	ca. 0·6
p-Iodo-	ca. 4

Thus, an ortho-CF_3 group (s.r.f., $1{\cdot}5 \times 10^8$) has a slightly greater effect than a para-CF_3 (s.r.f., 2×10^7), whilst the meta-CF_3 group (s.r.f., 3×10^5) has a somewhat lower effect. The substituent effects of the trifluoromethyl group in activating the protiodeiodination reaction are greater than that of the chlorine atom.

The order of activation of the trifluoromethyl group, o > p > m, and of chlorine, o > m > p, reflects the relative modes by which activation occurs in the two groups. The -I, + M electronic effect of chlorine, involves in the main, a more efficient contribution from the inductive effect, whereas the $-CF_3$ group, having a -I, -M electronic effect, owes more to a different mesomeric contribution in activating the aryl iodide system to protiodeiodination.

These substituent effects are much greater than any seen in

the more usual bimolecular aromatic nucleophilic substitution reactions. Some substituent rate factors for some S_NAr reactions are listed in Table 14.

Table 14. Substituent rate factors for some S_NAr reactions.

Substituent	log s.r.f.	s.r.f.	Reference
o-Cl	0·5705	3·72	167[a]
	1·8129	65	125[b]
m-Cl	0·8573	7·2	167[c]
	2·0899	123	125[b]
p-Cl	1·1461	14	167[d]
	1·4150	26	125[b]
o-CF_3	1·8808	76	167[e]
	3·7993	$6·3x10^3$	125[b]
m-CF_3	4·0000	10^4	125[b]
p-CF_3	2·9101	813	167[d]
	4·1461	$1·4x10^4$	125[b]

a, Reaction of 1-chloro-2-X-4,6-dinitrobenzene with MeO^-/MeOH(273K)

b, Reaction of C_6F_5X with MeO^-/MeOH(323K)

c, Reaction of 1-chloro-2,4-dinitro-5-X-benzenes with MeO^-/MeOH(273K)

d, Reaction of 1-chloro-2-nitro-4-X-benzenes with MeO^-/MeOH(323K)

e, Reaction of 1-chloro-2-X-4-nitrobenzene with MeO^-/MeOH(373K)

3.6.2. THE MORE ACTIVATED ARYL IODIDES ($k > 10^{-3}$ l. $mol.^{-1}s.^{-1}$)

The more fully substituted polychloroiodoarenes react with sodium methoxide in DMSO-methanol (9:1, v/v; 323K) to afford exclusively the protiodeiodination product. Methoxydehalogenation was not discernible in any of these compounds.

The rate constants for the protiodeiodination of these aryl iodides are given in Table 15.

Table 15. Second order rate constants for the reduction of some aryl iodides (sodium methoxide in DMSO-methanol (9:1, v/v; 323K)).

	Iodobenzene substituents	k_2/l. $mol.^{-1}s.^{-1}$
VI	2,3,4-Trichloro-	0·030
VII	2,4,5-Trichloro-	0·088
VIII	2,4,6-Trichloro-	0·314
IX	2,3,4,5-Tetrachloro-	0·246
X	2,3,4,6-Tetrachloro-	0·470
XI	2,3,5,6-Tetrachloro-	1·200
XII	2,3,4,5,6-Pentachloro-	ca. 1·500

It is possible to derive further substituent rate factors from these observed rate constants. As with the less activated aryl iodides under the same reaction conditions, the chlorine substituent activates in all positions in the order, o-Cl > m-Cl > p-Cl, although the more fully substituted polychloroiodoarenes show much weaker substituent effects.

An ortho-chlorine substituent has the largest activating effect (k_{VIII}/k_{III}, 348), whilst the substituent rate factor for

the meta-chlorine substituent (k_{VII}/k_{III}, 97) is lower. The para-chlorine substituent in these species appears to be lower still (k_{VII}/k_{IV}, 25).

Within this series of polychloroiodoarenes, the substituent rate factors seem to vary considerably. For example, the rate factor for a meta-chlorine substituent ranges between 97 (k_{VII}/k_{III}) and 1·49 (k_X/k_{VIII}). Similarly, a para-chlorine substituent rate factor appears to vary somewhat, being 25 when comparing 2,4,6-trichloro- with 2,6-dichloroiodobenzene, and only 1·25 when comparing 2,3,5,6-tetrachloro- and pentachloroiodobenzene.

Although these rate factors seem quite large, they are in stark contrast to the effect of chlorine in the less activated systems (section 3.6.1.), where a para-chlorine substituent, although having the least activating effect, shows a substituent rate factor of $1{\cdot}5 \times 10.^3$

Chlorine substituents evidently activate the system towards protiodeiodination, but there is quite an obvious suppression of these effects, which appears to depend on the degree of substitution already present, as one proceeds through the series to the fully substituted pentachloroiodobenzene.

As in section 3.6.1, additivity is not obeyed. From substituent rate factors obtained with the dichloroiodobenzenes, the calculated rate constant for the protiodeiodination of pentachloroiodobenzene is in the order of 5×10^{16} $l.mol.^{-1}s.^{-1}$ whereas the observed rate constant is merely 1·5 $l.mol.^{-1}s.^{-1}$ Even using the much lower substituent rate factors found from the results in Table 15, the calculated second order rate constant for pentachloroiodobenzene is ca. 10^3, which is still far greater than that observed.

However, the rate constant for the reaction of 2,3,5,6-tetrachloro-4-methoxyiodobenzene is 10^{-5} $l.mol.^{-1}s.^{-1}$; thus, a p-methoxy substituent appears to lower the rate by a factor of $10^{-5}/1{\cdot}2$. A p-chlorine increases the rate of reaction of 2,3,5,6-tetrachloroiodobenzene by a factor of $1{\cdot}5/1{\cdot}2$ only. The magnitude of the deactivating effect is inconsistent with the magnitude of substituent effects being observed in this series. The σ values ($\sigma_{p\text{-MeO}}$, 0·268; $\sigma_{p\text{-Cl}}$, -0·24), which are a measure of a group's electronic effect, do not suggest such a difference. Although the electronic effects of the two groups are in opposite directions, they are of similar magnitude, and as such, may be expected to exert similar substituent effects in the protiodeiodination reaction.

These points imply that there may have been some change in the rate-determining stage of the protiodeiodination reaction. In the proposed mechanism (equations (57)-(60)), the rate-determining stage is thought to be the attack of the aryl iodide by a carbanion derived from the solvent (equation (58)). The reaction of the α-halogenosulphoxide with base (equation (60)) may, however, become rate-determining when successive activation of the aryl iodide speeds equation (58) sufficiently.

In an effort to ascertain whether this is likely, phenacyl bromide (an α-halogenoketone) was treated under the same conditions as the protiodeiodination reactions. On exposure to sodium methoxide in DMSO-methanol (9:1, v/v; 323K), 96% of the bromide ion was released after one minute. Halogenoketones are known to react faster (a factor of *ca.* 10^4) at 25° than the corresponding halogenosulphoxide.[166]

Mass spectrometry studies failed to find any α-halogenoketones or -sulphoxides even in conditions in which there was a deficiency of base. Experiments carried out involving the addition of diethyl malonate was indicative of the absence of a build-up of material which could give iodide ion with alkoxide ion, which tends to refute the idea that the rate-determining stage changes on further halogenation of aryl iodides. Such a change could not account for the overall depression of chlorine substituent effects or the considerable suppression of rate by a p-methoxy substituent.

This substantial suppression of substituent effects in the polychloroiodobenzene system may be a result of an encounter-controlled reaction. The reagent which attacks the aryl iodide in the DMSO-methanol solvent system appears to be the dimsyl anion, because alkoxide ion in alcoholic solutions alone causes no protiodeiodination, nor indeed protiodehalogenation from other halogenoarenes, and also because in the analogous process, in butanone-containing mixtures, the butanone anion was indicated.[124,126]

The relative acidities of methanol (pK_a, 18[168]) and DMSO (pKa, 33 - 37 [169]) suggests that the true second-order rate constant (associated with attack by the dimsyl anion) is greater than the observed rate constant (which is expressed in terms of the methoxide ion concentration), by a factor ca.10^{15} when the relative concentrations of DMSO and methanol are taken into account. Hence, the rate law governing the protiodeiodination reaction becomes, equation (74),

$$d[I^-]/dt = k_{obs.}[MeO^-][ArI] = k_{true}[CH_3SOCH_2^-][ArI]. \qquad (74)$$

The reaction of the α-halogenosulphoxide with base (equation (60)) has a much lower rate constant associated with it because the methoxide ion concentration is substantially the

stoichiometric figure.

This means the rate constants listed in Tables 12, 13 and 15 must be raised by a factor of ca. 10^{15}, and this in turn, suggests that the rate of reaction of the aryl iodide exceeds that predicted (k, ca. 10^{10})[170] if every collision between the two species was successful (that is, an encounter-controlled rate).

Although there is no evidence of an upper limit to the observed rates (although $k_{obs.} = 2$ is certainly feasible), the great difference in observed substituent effects seen in the range of k_2 from 10^{-2} - 10^{-6} $l.mol.^{-1}s.^{-1}$ and $k_2 > 10^{-2}$ $l.mol.^{-1}s.^{-1}$ is consistent with the change of selectivity to be expected when substitution no longer affects the reaction rate, that is, when the speed of meeting controls the rate or, alternatively, when the rate-determining stage involves the nucleophilic attack of the alkyl iodide, ICH_2SOCH_3.

In an attempt to demonstrate the existence of an encounter-controlled process, a sample of pentabromoiodobenzene was subjected to sodium methoxide in DMSO-methanol (9:1, v/v; 323K). In studies carried out by Bolton and Sandall[126] on some polybromoiodobenzene derivatives, it was observed that bromine was slightly more activating (by a factor ca.4) towards protiodeiodination, than is the corresponding chlorine substituent. If an encounter-controlled reaction was operating, then an observed rate constant only slightly greater ($k_2 \not> 2$ $l.mol.^{-1}s.^{-1}$) than that found for pentachloroiodobenzene would be observed. Since pentabromoiodobenzene gives a second order rate constant, ca. 1·8 $l.mol.^{-1}s.,^{-1}$ it would appear that an encounter-controlled reaction may be operating.

In butanone-methanol, at apparent rates of reaction similar

to those found in DMSO-methanol, a para-chlorine substituent has a much greater accelerating effect (ca. 13[126]) than in the latter solvent system (k_{XI}/k_{XII} (Table 15) = 1·25). This suggests that the levelling effect is not apparent in the ketone-rich mixture; and this, in turn, is consistent with the much greater acidity of the ketone, so that the distinction between the apparent rate constant (equation (62)) and the true figure (equation (75)) involves a factor of ca. 10^3.

$$-d[ArI]/dt = k_{obs.}[ArI][MeO^-] = k_{true}[ArI][CH_3\bar{C}HCOCH_3]$$
$$= k_{true}K\frac{[ArI][MeO^-][CH_3CH_2COCH_3]}{[MeOH]} \qquad (75)$$

This, of course, is insufficient to raise the true rate constant to a value near that associated with encounter-control, and so allows substituent effects still to be fully exerted.

3.6.3. THE REACTIONS OF SOME POLYCHLOROBENZENES.

It is possible, as in the reaction of polyfluoropolybromobenzene derivatives with alkaline mixtures of butanone-methanol,[125] that protiodehalogenation and methoxydehalogenation may occur concurrently in the reactions of polychlorophenyl iodides with sodium methoxide in DMSO-methanol (9:1, v/v; 323K). In order for the extent of these competing processes to be assessed, the reaction of some polychlorobenzene derivatives with sodium methoxide in DMSO-methanol (9:1, v/v; 323K) was studied. The second order rate coefficients for the dehalogenation are listed in Table 16, together with an analysis of the products from this reaction.

It has been shown in the previous sections (3.6.1. and 3.6.2.) that under these conditions, aryl iodides undergo reduction

Table 16 Second order rate coefficients and product analysis of the reaction of some polychlorobenzene derivatives with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Polychlorobenzene	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$	Product	Yield/%
1,2,3-Trichlorobenzene	0·05	2,3-dichloroanisole	55
		2,6-dichloroanisole	45
1,3,5-Trichlorobenzene	0·25	3,5-dichloroanisole	100
1,2,3,4-Tetrachlorobenzene	2·70	2,3,4-trichloroanisole	5
		2,3,6-trichloroanisole	95
1,2,3,5-Tetrachlorobenzene	6	2,3,5-trichloroanisole	90
		2,4,6-trichloroanisole	10
1,2,4,5-Tetrachlorobenzene	2·78	2,4,5-trichloroanisole	100
Pentachlorobenzene	140	2,3,4,5-tetrachloroanisole	45
		2,3,4,6-tetrachloroanisole	trace
		2,3,5,6-tetrachloroanisole	55
Hexachlorobenzene	2100	2,3,4,5,6-pentachloroanisole	100

to give the corresponding hydrocarbon. Protiodebromination occurs under similar conditions.[124] Dechlorination by such a route has not been observed, although it is reported that 1,2,3,5-tetrachlorobenzene isomerises with potassium t-butoxide in hexamethylphosphorotriamide, as well as disproportionating to tri- and pentachlorobenzenes.[96]

Protiodechlorination has not been observed in the reactions involving these polychlorobenzenes with sodium methoxide in DMSO-methanol (9:1, v/v; 323K). The products from the reaction are those of methoxydechlorination, and are consistent with the orientation predicted from partial rate factors obtained from classical aromatic nucleophilic substitution processes.

The substituent rate factors obtained from the kinetic data are consistent with a nucleophilic process, the order of activation being $f_{m\text{-Cl}}(47) > f_{o\text{-Cl}}(35) > f_{p\text{-Cl}}(12)$. These values parallel those found in the methoxydefluorination of polyfluorochlorobenzenes[125] by methoxide ion in methanol (323K) by the following relationship, equation (76),

$$\log_{10} f_A = 0{\cdot}8 \log_{10} f_B \qquad (76)$$

in which reactions in DMSO-methanol have the lower sensitivity to substituent effects. From this relationship, since the reaction constant, ρ, for the reaction involving pentafluorohalogenobenzenes is known (ca.6),[125] the value of ρ for the reaction of polychlorobenzenes with sodium methoxide in DMSO-methanol appears to be ca. 4·8. This lower figure nevertheless indicates considerable interaction between substituents and the reaction centre in the transition state.

These studies with polychlorobenzenes offer a means to examine the possibility of methoxydechlorination and methoxydeiodination prevailing alongside protiodeiodination in reactions involving the polychlorophenyl iodides. Since the rate factor for iodine substituents from the reactions of pentafluorohalogenobenzenes with methoxide ion in methanol (323K) are known,[125] the relationship in equation (76) can be used to suggest that substituent rate factors for iodine substituents in methoxydechlorination in DMSO-methanol should in all three benzene orientations be ca. 16. From this, it was then possible to deduce rate constants for the methoxydechlorination of all the polychloroiodoarenes, from which may be decided whether methoxydehalogenation competes with protiodeiodination in reactions of the polychloroiodobenzenes.

By using the rate constants and rate factors obtained from Table 16, the rate constant for the methoxydechlorination of chlorobenzene may be calculated, giving a range of values, k_2 = ca. $3 \pm 0{\cdot}5 \times 10^{-8}$ l.mol.$^{-1}$s.$^{-1}$ A combination of the rate factor for an ortho-iodine substituent with this value, suggests that the second order rate constant for the methoxydechlorination of o-chloroiodobenzene is ca. 5×10^{-7} l.mol.$^{-1}$s.,$^{-1}$ which corresponds to the observed range of rate constants ($k_{obs.}$ = ca. 6×10^{-7} l.mol.$^{-1}$s.$^{-1}$) obtained from a study of the reaction of o-chloroiodobenzene under these conditions.

Table 17 lists the second order rate coefficients calculated for the methoxydehalogenation of the polychlorophenyl iodides studied. We find in some instances, that protiodeiodination prevails at rates similar to, or even less than, that of

methoxydechlorination of the appropriate chloride.

Table 17. Calculated second order rate constants for the methoxydehalogenation of polychloroiodobenzenes on reaction with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Iodobenzene	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$
2-Chloro-	0·0006
2,3-Dichloro-	0·041
2,4-Dichloro-	0·045
2,5-Dichloro-	0·019
2,6-Dichloro-	0·048
2,3,4-Trichloro-	2·1
2,4,5-Trichloro-	1·1
2,4,6-Trichloro-	5·6
2,3,4,5-Tetrachloro-	43
2,3,4,6-Tetrachloro-	85
2,3,5,6-Tetrachloro-	34
2,3,4,5,6-Pentachloro-	1030

Pentachloroiodobenzene (Table 15), for example, provides the protiodeiodination product at rates between those of methoxydechlorination of penta- and hexachlorobenzenes (Table 16), although chlorine displacement might be expected; similarly, 2,3,4,6-tetrachloroiodobenzene loses iodine to give 1,2,3,5-tetrachlorobenzene at a rate which is only one third that of the methoxydechlorination of pentachlorobenzene.

Methoxydeiodination is also a mode of reaction possible in the reaction of aryl iodides with sodium methoxide in

DMSO-methanol (9:1, v/v; 323K). Its extent could be roughly estimated by assuming that iodine is displaced at one-fifth of the rate of an identically situated chlorine atom, as in other S_NAr processes.[167] Such calculations suggest that methoxydeiodination would not be expected to contribute significantly (> 1%).

By comparison of the observed rate constants for the protiodeiodination of aryl iodides (Tables 12 and 15) with those calculated for the methoxydehalogenation of such compounds (Table 17), one would expect, in a number of cases, that methoxydehalogenation would be a competing process in the protiodeiodination reactions. For example, the calculated total second order rate constant for the methoxydehalogenation of pentachloroiodobenzene is 1·03 $l.mol.^{-1}s.^{-1}$ and should therefore account for some 70% of the observed reaction products.

Product analysis reveals pentachlorobenzene to be the only product. This is confirmed by the fact that n.m.r. reveals that the tetrachloroanisoles formed from an excess of methoxide ions has the same ratio as that found from the methoxydechlorination of pentachlorobenzene. No other anisoles were seen by n.m.r.. Pentachlorobenzene provided by the protiodeiodination of pentachloroiodobenzene is implied to be the only course of reaction; there is the possibility of methoxydechlorination of the starting material to afford 2,3,5,6-tetrachloro-4-iodoanisole, which is known to undergo protiodeiodination at a rate, k_2 = ca. 10^{-5} $l.mol.^{-1}s.^{-1}$, and would therefore not be expected to contribute to the isomer ratio of anisoles formed in the presence of excess methoxide ions. Hence, protiodeiodination appears to be the only process involved

with pentachloriodobenzene.

Since 55% of this methoxydechlorination occurs at the carbon atom *para*- to hydrogen in pentachlorobenzene, and as 2,3,4,6-tetrachloroiodobenzene and pentachlorobenzene differ only in the replacement of chlorine by iodine at one site *ortho*- to this position, it follows that such a replacement must weaken the susceptibility of the position towards methoxydechlorination. Indeed, the effect of an *ortho*- iodine group cannot be much greater than that of hydrogen in this system, judging from the rate of reaction of 1,2,3,5-tetrachlorobenzene.

In other less fully substituted compounds, methoxydechlorination would not be expected to exceed more than 10% of the product in protiodeiodination reactions, except in the case of *o*-chloriodobenzene. As the observed and calculated rate constants for the reaction of *o*-chloroiodobenzene are in good agreement, one would expect iodoanisole to account for *ca*. 75% of the product, the other product being chloroanisole (from methoxydeiodination). However, differential titrimetric analysis of the course of the reaction suggests that only iodine is lost (in preference to chlorine) from *o*-chloroiodobenzene; product analysis (g.l.c.) confirms the observed product to be chlorobenzene, obtained from the protiodeiodination reaction. This is in direct contrast to what is expected of this system.

3.6.4. THE REACTIONS INVOLVING NON-*ORTHO*-SUBSTITUTED ARYL IODIDES.

The polychlorophenyl iodides studied so far have had one common characteristic, that is, they have all contained an *ortho*-chlorine substituent. Protiodeiodination has occurred extensively in all these iodoarenes, to the exclusion of methoxydehalogenation,

which had been predicted to occur to quite large degrees in some of the derivatives.

In principle, both iodine and chlorine may be lost from such compounds, under conditions of the reaction, by direct attack of methoxide, and also by the reaction of a carbanion. While the mechanism of protiodeiodination (equations (57)-(60))certainly prevails in systems in which both aromatic sites adjacent to iodine are substituted by chlorine, it is possible that another mode of reaction could apply to compounds which do not contain ortho-substituents.

Proton-loss from a site ortho- to one or two halogen substituents (as in, for example, 3,4,5-trichloroiodobenzene) may, under conditions of the reaction, give an aromatic anion whose reactions may involve loss of iodine, or of chlorine, to provide a benzyne-type system.

A study of the reaction involving iodoarenes without an ortho- halogen substituent may help to elucidate further the mechanism involved in these reaction conditions. Accordingly, 3,4-dichloro-, 3,5-dichloro, and 3,4,5-trichloroiodobenzenes were prepared, and the reactions involving these substrates were studied.

Table 18 gives the second order rate constants associated with these reactions, while Table 19 lists the products obtained from such reactions.

It becomes immediately noticeable that the extent to which protiodeiodination occurs is suppressed considerably. The major product associated with these compounds is that of methoxydechlorination. The presence of chloroanisoles having one

Table 18. Second order rate coefficients for the reaction of some non-ortho-substituted aryl iodides with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Iodobenzene	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$
3,4-Dichloro-	0·05
3,5-Dichloro-	0·22
3,4,5-Trichloro-	24

chlorine atom less than the initial substrate probably arises from the protiodeiodination of the chloroiodoanisole formed in the first instance, by methoxydechlorination, since product analysis mixtures usually involved an excess of methoxide. It is highly unlikely that methoxydechlorination of the reduction product occurs, since we can predict a value for the rate of attack of chloro- and dichlorobenzenes under these conditions; it would not, therefore, be expected to contribute to the reaction product analysis.

As in section 3.6.3, from a knowledge of the substituent rate factors for chlorine observed in the polychlorobenzene series, and again assuming iodine to have an effect of one-fifth that of an identically placed chlorine atom, it is possible to deduce rate constants for the methoxydeiodination (k_{deI}) and methoxydechlorination (k_{deCl}) expected from these compounds. These derived rate constants are listed in Table 20.

Although these calculations do not allow any function for the protiodeiodination reaction, they do indicate approximately the amount of the various anisoles that may be expected. For

Table 19. Product analysis of the reaction of some non-ortho-substituted derivatives with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Aryl iodide	Product*	Yield/%
3,4-Dichloro-	Chloroiodoanisoles	ca. 80
	3,4-Dichloroanisole	11
	1,2-Dichlorobenzene	8
	Chloroanisole	trace
3,5-Dichloro-	3-Chloro-5-iodoanisole	52
	3,5-Dichloroanisole	21
	1,3-Dichlorobenzene	11
	3-Chloroanisole	18
3,4,5-Trichloro-	2,3-Dichloro-5-iodoanisole	ca. 80
	1,2,3-Trichlorobenzene	11
	3,4,5-Trichloroanisole	8
	1,2-Dichloroanisole	trace

* Product analysed by g.l.c.

example, from 3,5-dichloroiodobenzene, 19% of 3,5-dichloroanisole (from methoxydeiodination) might be anticipated in the product mixture. The experimental observation is that this anisole accounts for 21% of the products. Similarly, in 3,4,5-trichloroiodobenzene, the agreement between the calculated and observed product of methoxydeiodination is very good.

The major product, that of methoxydechlorination, is again in fair agreement with the predicted amounts, although the observed

Table 20. Calculated second order rate constants for the methoxydehalogenation of some non-ortho-substituted aryl iodides on reaction with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Aryl iodide	$10^3 k_{deI}$/l.mol.$^{-1}$s.$^{-1}$	$10^3 k_{deCl}$/l.mol.$^{-1}$s.$^{-1}$
3,4-Dichloro-	0·003	0·03
3,5-Dichloro-	0·011	0·046
3,4,5-Trichloro-	0·16	2·03

yields of chloroiodoanisoles are much lower than expected (obviously arising because of the part played by the protiodeiodination reaction).

The protiodeiodination reaction appears to account for only ca. 10% of the products from these non-ortho-substituted compounds. This apparently suggests that an ortho- chlorine substituent is essential for promoting the protiodeiodination of aryl iodides.

A further, more detailed study of the analysis of the products from 3,4-dichloroiodobenzene was made by boiling the reaction mixture, containing an excess of methoxide ion, for four hours and subjecting the product mixture to analysis by g.c.m.s.. 1,2-Dichlorobenzene and 3,4-dichloroanisole were produced in an approximately similar ratio to that obtained under the more normal kinetic conditions. In addition, a number of products were produced, which appeared to represent sulphur-containing compounds, such as thiomethoxychloroanisole and chloromethoxyphenylmethyl sulphoxide.

Although extensive methoxydechlorination is observed in these compounds, differential argentimetric analysis was not an accurate method for determining relative extents of iodine and

chlorine loss from these systems. In principle, aqueous solutions containing both iodide and chloride ions may be successfully analysed potentiometrically. On occasions, the addition of barium nitrate enables a clearer differentiation to be obtained, although the role of the barium salt is not apparently clear.

The analysis of mixtures of iodide ion and chloride ion in aqueous solutions containing small amounts of organic material, as occurs in the quenched samples obtained from the kinetic studies, does not appear to allow accurate determinations of these mixtures. The differential titrimetric analyses of these reaction mixtures did not suggest the loss of both chloride and iodide ion. This inability to distinguish the two halides may be due to the effect on the sensitivity of the silver electrode of the presence of organic material.

The suppression of the protiodeiodination reaction in the non-ortho-substituted aryl iodides, is not in itself indicative of a change in mechanism, possibly to a benzyne-type process. This alternative mode of reaction is obviously possible although Bunnett and his co-workers[59,61] have suggested that o-halogenophenyl anions with electron-attracting substituents are more likely to undergo proton capture back to aryl halide than halide ion loss to form an aryne.

In an effort to rule out the possibility of an aryne mechanism, attempts were made to prepare 2,3,4-trichloro-6-methyliodobenzene and 2,6-dimethyl-3,4,5-trichloroiodobenzene. Such compounds are not amenable to loss of iodine via an aryne mechanism.

The immediate problem associated with these compounds was that of purity. Pure samples of either compound could not be obtained. The mono-methyl derivative was thought to contain ca. 25%

of another isomer (g.l.c.), which could not be characterised unequivocally, while the dimethyl derivative was shown (g.l.c.) to contain ca. 35% tetrachloro-m-xylene as impurity. However, a tentative appraisal of the reaction of such compounds was possible. The reaction of the two compounds with sodium methoxide in DMSO-methanol (9:1, v/v; 323K) was carried out. Rate constants for the reactions are given in Table 21.

Table 21. Second order rate constants for the reaction of some methyl-substituted polychlorophenyl iodides with sodium methoxide in DMSO-methanol (9:1, v/v; 323K)

Aryl iodide	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$
2,3,4-Trichloro-6-methyl-	ca. 20
2,6-Dimethyl-3,4,5-trichloro-	ca. 0·2

An analysis of the products from these reactions was found to be rather difficult, since a number of products were obtained due to reactions of both the intended substrate and impurities. However, in the case of the dimethyl derivative, n.m.r. analysis of the product mixture revealed a singlet peak in the region associated with aromatic protons. It was concluded that protiodeiodination occurred most extensively, and that the methyl groups merely inhibit the protiodeiodination reaction electronically. It is doubtful that a benzyne-type process is operating under these conditions.

Since the compounds used here are somewhat impure, much more detailed work on these compounds must be made before totally refuting the possibility of an aryne-type mechanism.

3.6.5. THE PROTIODEIODINATION OF SOME DERIVATIVES OF 2,6-DICHLORO-4-X-IODOBENZENE.

Some derivatives of 2,6-dichloroiodobenzene were prepared, each having a substituent in the position *para*- to iodine. These compounds were allowed to react with sodium methoxide in DMSO-methanol (9:1, v/v; 323K); rate data associated with these reactions are listed in Table 22, together with an analysis of the products.

Table 22. Second order rate constants and product analysis for the reaction of 2,6-dichloro-4-X-iodobenzenes with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

4-X-Substituent	k_2/l.mol.$^{-1}$s.$^{-1}$	Product*
4-Bromo-	0·23	3,5-Dichlorobromobenzene
4-Iodo-	0·18	3,5-Dichlorodobenzene
4-Nitro-	*ca.* 0·2	2,6-Dichloro-4-nitroanisole

*Products analysed by g.l.c.

In the case of the 4-bromo- and 4-iodo- derivatives, protiodeiodination is the only observed course of the reaction. The 4-nitro-substituted compound reacted entirely to give 2,6-dichloro-4-nitroanisole. Kinetic studies of the 4-nitro-substituted derivative was extremely difficult as the compound appeared to have a detrimental effect on the sensitivity of the silver electrode towards iodide ions, and so the rate constant quoted is most inaccurate.

No conclusions can be drawn from these kinetic studies. Although with halogen - substituted iodobenzenes, protiodeiodination is the only observed mode of reaction, substituent effects are

different to those expected from the present studies. Iodine has a substituent effect only slightly greater than hydrogen in the same position by comparing the rates of reaction of 2,6-dichloroiodobenzene and 1,3-dichloro-2,5-diiodobenzene. Bromine does not exhibit the same effect in the 2,6-dichloro-4-X-system as it does in the protiodeiodination in butanone-methanol[126] or in the reaction of pentabromoiodobenzene in DMSO-methanol, where a bromine substituent has a slightly greater activating effect than an identically situation chlorine atom.

The apparent lowering of the rate-limit may be a result of a further acid-base equilibrium with the inherent polyhalogenobenzene, similar to that shown in equation (77).

$$C_6X_{6-n}H_n + MeO^- \rightleftharpoons C_6X_{6-n}H^-_{n-1} + MeOH \qquad (77)$$

Such a reaction may account for the lowering of the rate of protiodeiodination of 2,4,5-trichloroiodobenzene on addition of fluorene.

3.6.6. OTHER ACTIVATING SUBSTITUENTS IN PROTIODEIODINATION REACTIONS.

The three possible isomers of (α,α,α-trifluoromethyl)-iodobenzene have been shown to undergo protiodeiodination with sodium methoxide in DMSO-methanol (9:1, v/v; 323K). The rate constants, previously stated in Table 13, show the trifluoromethyl system to be a substantially superior activating group than chlorine. Attempts to prepare derivatives of such compounds were largely unsuccessful, but Table 23 lists the product analysis and rate data associated with those compounds which were successfully prepared.

The 4-bromo-substituted derivative undergoes extensive protiodeiodination. Minor products appear to arise from methoxydehalogenation. The 4-nitro-derivative, under these

Table 23. Second order rate constants and product analysis for the reaction of some substituted o-(α,α,α-trifluoromethyl)iodobenzene with sodium methoxide in DMSO-methanol (9:1, v/v; 323K).

Substituent	$10^3 k_2$/l.mol.$^{-1}$s.$^{-1}$	Product*	Yield/%
4-Bromo-	5·7	m-bromobenzotrifluoride	> 80
		3-bromo-b-methoxybenzotrifluoride	10
		2-iodo-5-methoxybenzotrifluoride	< 10
4-Nitro-	ca. 33	2-methoxy-5-nitrobenzotrifluoride	100

*Products determined by g.l.c. and n.m.r.

conditions, again gave exclusively the product of methoxydeiodination.

The protiodeiodination of iodobenzene containing nitro groups were also studied. The analysis of the reaction mixture from 2-nitroiodobenzene showed nitrobenzene, arising from protiodeiodination, as the only product. However, reactions involving 4-nitro- and 2,4-dinitrobenzenes indicate the sole product of the reaction to be that of methoxydeiodination. Evidently systems containing nitro groups are somewhat more complex.

4. APPENDIX.

SUMMARY OF OBSERVED RATE COEFFICIENTS/l.mol.$^{-1}$s.$^{-1}$

2-Chloroiodobenzene.

ArI	0·199 M	NaOMe	0·288 M	k_2	4·5 ± 0·5 x 10^{-7}
	0·215 M		0·288 M		6·55 ± 0·4 x 10^{-7}
	0·226 M		0·576 M		6·2 ± 1·5 x 10^{-7}
	0·072 M		0·230 M		6·6 ± 0·3 x 10^{-7}

2,3-Dichloroiodobenzene.

ArI	0·0126 M	NaOMe	0·0288 M	k_2	3·41 ± 0·6 x 10^{-3}
	0·0128 M		0·0144 M		3·23 ± 0·1 x 10^{-3}
	0·0010 M		0·0144 M		2·8 ± 0·3 x 10^{-3}

2,4-Dichloroiodobenzene.

ArI	0·021 M	NaOMe	0·072 M	k_2	8·84 ± 0·3 x 10^{-4}
	0·029 M		0·0288 M		9·9 ± 0·5 x 10^{-4}
	0·0265 M		0·0288 M		8·34 ± 0·5 x 10^{-4}

2,5-Dichloroiodobenzene.

ArI	0·0100 M	NaOMe	0·0576 M	k_2	3·06 ± 0·1 x 10^{-3}
	0·0128 M		0·0144 M		3·86 ± 0·1 x 10^{-3}
	0·0126 M		0·0144 M		3·62 ± 0·1 x 10^{-3}

2,6-Dichloroiodobenzene.

ArI	0·0141 M	NaOMe	0·0144 M	k_2	0·186 ± 0·012
	0·008 M		0·0288 M		0·168 ± 0·030
	0·0124 M		0·0144 M		0·133 ± 0·010

2,3,4-Trichloroiodobenzene.

ArI	0·010 M	NaOMe	0·0115 M	k_2	3·00 ± 0·15 x 10^{-2}
	0·017 M		0·0173 M		2·71 ± 0·14 x 10^{-2}
	0·011 M		0·0576 M		3·26 ± 0·09 x 10^{-2}

2,4,5-Trichloroiodobenzene.

ArI	0·0134 M	NaOMe	0·0144 M	k_2	$8·81 \pm 0·48 \times 10^{-2}$
	0·0098 M		0·0115 M		$10·32 \pm 1·2 \times 10^{-2}$
	0·0078 M		0·0288 M		$9·00 \pm 0·9 \times 10^{-2}$

2,4,6-Trichloroiodobenzene.

ArI	0·011 M	NaOMe	0·023 M	k_2	0·390 ± 0·070
	0·005 M		0·0028 M		0·314 ± 0·016
	0·010 M		0·0144 M		0·295 ± 0·016

2,3,4,5-Tetrachloroiodobenzene.

ArI	0·009 M	NaOMe	0·0115 M	k_2	0·246 ± 0·010
	0·010 M		0·0115 M		0·257 ± 0·022
	0·0085 M		0·0058 M		0·246 ± 0·013

2,3,5,6-Tetrachloroiodobenzene.

ArI	0·0078 M	NaOMe	0·0115 M	k_2	1·46 ± 0·08
	0·0074 M		0·0115 M		0·95 ± 0·08

2,3,4,6-Tetrachloroiodobenzene.

ArI	0·004 M	NaOMe	0·0115 M	k_2	0·446 ± 0·027
	0·004 M		0·0058 M		0·492 ± 0·033
	0·006 M		0·0288 M		0·465 ± 0·020

2,3,4,5,6-Pentachloroiodobenzene.

ArI	0·0082 M	NaOMe	0·0115 M	k_2	1·36 ± 0·04
	0·0035 M		0·004 M		1·65 ± 0·09

3,4-Dichloroiodobenzene.

ArI	0·0111 M	NaOMe	0·015 M	k_2	$5·46 \pm 0·33 \times 10^{-5}$
	0·0135 M		0·0288 M		$7·08 \pm 0·38 \times 10^{-5}$
	0·015 M		0·0288 M		$3·63 \pm 0·6 \times 10^{-5}$

3,5-Dichloroiodobenzene.

ArI	0·0106 M	NaOMe	0·058 M	k_2	$2·08 \pm 0·02 \times 10^{-4}$
	0·009 M		0·058 M		$2·26 \pm 0·05 \times 10^{-4}$
	0·0122 M		0·0173 M		$2·57 \pm 0·26 \times 10^{-4}$

3,4,5-Trichloroiodobenzene.

ArI	0·0075 M	NaOMe	0·0144 M	k_2	$2·51 \pm 0·24 \times 10^{-2}$
	0·0108 M		0·0144 M		$2·42 \pm 0·21 \times 10^{-2}$
	0·0113 M		0·0144 M		$2·08 \pm 0·10 \times 10^{-2}$

1,2,3-Trichlorobenzene.

ArCl	0·012 M	NaOMe	0·058 M	k_2	$4·59 \pm 0·36 \times 10^{-5}$
	0·0114 M		0·058 M		$4·97 \pm 0·90 \times 10^{-5}$
	0·012 M		0·115 M		$5·98 \pm 0·76$ z 10^{-5}

1,3,5-Trichlorobenzene.

ArCl	0·009 M	NaOMe	0·046 M	k_2	$1·81 \pm 0·09 \times 10^{-4}$
	0·0133 M		0·0288 M		$2·50 \pm 0·22 \times 10^{-4}$
	0·0099 M		0·0576 M		$2·83 \pm 0·14 \times 10^{-4}$

1,2,3,4-Tetrachlorobenzene.

ArCl	0·0087 M	NaOMe	0·0288 M	k_2	$2·86 \pm 0·23 \times 10^{-3}$
	0·0092 M		0·0576 M		$2·65 \pm 0·36 \times 10^{-3}$

1,2,3,5-Tetrachlorobenzene.

ArCl	0·010 M	NaOMe	0·0173 M	k_2	$6·18 \pm 0·08 \times 10^{-3}$
	0·014 M		0·0173 M		$6·82 \pm 0·41 \times 10^{-3}$
	0·020 M		0·058 M		$6·89 \pm 0·49 \times 10^{-3}$

1,2,4,5-Tetrachloeobenzene.

ArCl	0·008 M	NaOMe	0·0288 M	k_2	$3·29 \pm 0·14 \times 10^{-3}$
	0·009 M		0·058 M		$2·47 \pm 0·10 \times 10^{-3}$
	0·0139 M		0·0173 M		$2·42 \pm 0·10 \times 10^{-3}$

Pentachlorobenzene.

ArCl	0·0092 M	NaOMe	0·0115 M	k_2	0·134 ± 0·010
	0·0077 M		0·0115 M		0·145 ± 0·011

Hexachlorobenzene.

ArCl	0·0025 M	NaOMe	0·0058 M	k_2	2·17 ± 0·81
	0·0067 M		0·0058 M		2·17 ± 0·24

Pentachloroanisole.

ArCl	0·0062 M	NaOMe	0·0115 M	k_2	$2{\cdot}60 \pm 0{\cdot}06 \times 10^{-2}$
	0·0083 M		0·0288 M		$2{\cdot}43 \pm 0{\cdot}09 \times 10^{-2}$

2,3,5,6-Tetrachloro-4-iodoanisole.

ArI	0·005 M	NaOMe	0·0576 M	k_2	$10{\cdot}16 \pm 1{\cdot}04 \times 10^{-6}$
	0·008 M		0·0115 M		$9{\cdot}52 \pm 0{\cdot}87 \times 10^{-6}$

o-(α,α,α-Trifluoromethyl)iodobenzene.

ArI	0·018 M	NaOMe	0·0288 M	k_2	$1{\cdot}48 \pm 0{\cdot}08 \times 10^{-4}$
	0·0109 M		0·0115 M		$1{\cdot}43 \pm 0{\cdot}06 \times 10^{-4}$
	0·020 M		0·0576 M		$1{\cdot}40 \pm 0{\cdot}07 \times 10^{-4}$

m-(α,α,α-Trifluoromethyl)iodobenzene.

ArI	0·011 M	NaOMe	0·115 M	k_2	$6{\cdot}22 \pm 0{\cdot}32 \times 10^{-6}$
	0·0178 M		0·115 M		$6{\cdot}12 \pm 0{\cdot}24 \times 10^{-6}$
	0·053 M		0·0576 M		$5{\cdot}77 \pm 0{\cdot}62 \times 10^{-6}$

p-(α,α,α-Trifluoromethyl)iodobenzene.

ArI	0·012 M	NaOMe	0·115 M	k_2	$5{\cdot}63 \pm 1{\cdot}3 \times 10^{-5}$
	0·010 M		0·0173 M		$2{\cdot}79 \pm 0{\cdot}34 \times 10^{-5}$
	0·0118 M		0·0288 M		$4{\cdot}03 \pm 0{\cdot}54 \times 10^{-5}$

2-(α,α,α-Trifluoromethyl)-4-bromoiodobenzene.

ArI	0·0064 M	NaOMe	0·0173 M	k_2	$5{\cdot}97 \pm 0{\cdot}62 \times 10^{-3}$
	0·0105 M		0·0576 M		$5{\cdot}45 \pm 0{\cdot}27 \times 10^{-3}$
	0·0057 M		0·00576 M		$5{\cdot}84 \pm 0{\cdot}39 \times 10^{-3}$

2-(α,α,α-Trifluoromethyl)-4-nitroiodobenzene.

ArI	0·0073 M	NaOMe	0·0115 M	k_2	3·24 ±0·16 x 10^{-2}
	0·009 M		0·0288 M		2·81 ± 0·12 x 10^{-2}

2,6-Dichloro-4-bromoiodobenzene.

ArI	0·008 M	NaOMe	0·0159 M	k_2	0·230 ± 0·060
	0·008 M		0·0079 M		0·215 ± 0·05

1,3-Dichloro-2,5-diiodobenzene.

ArI	0·0122 M	NaOMe	0·0159 M	k_2	0·151 ± 0·093
	0·0142 M		0·0148 M		0·224 ± 0·016

2,6-Dichloro-4-nitroiodobenzene.

ArI	0·0078 M	NaOMe	0·0074 M	k_2	ca. 0·21

Pentabromoiodobenzene.

ArI	0·0047 M	NaOMe	0·008 M	k_2	1·84 ± 0·32
	0·0036 M		0·008 M		1·95 ± 0·47

2,3,4-Trichloro-6-methyliodobenzene.

ArI	0·0078 M	NaOMe	0·0115 M	k_2	2·00 ± 0·34 x 10^{-2}
	0·0166 M		0·0173 M		1·75 ± 0·43 x 10^{-2}

2,6-Dimethyl-3,4,5-trichloroiodobenzene.

ArI	0·0063 M	NaOMe	0·0115 M	k_2	2·49 ± 0·49 x 10^{-4}
	0·0075 M		0·0029 M		1·04 ± 0·32 x 10^{-4}

Tetrachloro-m-xylene.

ArCl	0·006 M	NaOMe	0·0115 M	k_2	6·52 ± 0·48 x 10^{-5}
	0·0073 M		0·0288 M		6·18 ± 0·51 x 10^{-5}

2,4,5-Trichloroiodobenzene + Fluorene.

ArI	0·009 M	Fluorene	0·017 M	NaOMe	0·0115 M	k_2	6·20±0·32x10^{-2}
	0·0115 M		0·011 M		0·0115 M		6·76±0·59x10^{-2}

Detailed Kinetic analysis; 2,3,4,5 - tetrachloroiodobenzene

$[ArI] = 0{\cdot}00924$ M

$[NaOMe] = 0{\cdot}01152$ M

T = 323 K

Solvent; DMSO - methanol, 9:1, v/v.

$[AgNO_3] = 0{\cdot}05$ M

Volume of sample taken = 5·00 ml.

Time/mins.	VAg^+/ml.	ΔV/ml.	%	$10^3(a-x)$	$10^3(b-x)$	$10^2 \log \frac{b(a-x)}{a(b-x)}$	k_2
0	2·005	-	-	11·52	9·24	-	-
1·5	2·095	0·090	9·7	10·62	8·34	0·9178	0·103
2	2·295	0·200	21·6	9·52	7·24	2·3118	0·195
3	2·605	0·310	33·5	8·42	6·14	4·136	0·232
4	2·960	0·355	38·4	7·97	5·69	5·057	0·213
5	3·410	0·450	48·7	7·02	4·74	7·478	0·252
9	4·020	0·610	66	5·42	3·14	14·13	0·264
15	4·705	0·685	74	4·67	2·39	19·51	0·219
24	5·500	0·795	86	3·57	1·29	34·63	0·243

By Least squares analysis,

Mean $k_2 = 0{\cdot}246 \pm 0{\cdot}009$ l. $mol.^{-1}s.^{-1}$

Details of studies of the protiodeiodination mechanism.

Pentachloroidobenzene (0·010M) in solutions of sodium methoxide (0·01M) in methanol at 323K gave no iodide ion ($<10^{-4}$%) after three hours when either diethyl malonate (1% v/v) or dimedone (5,5-dimethylcyclohexa-1,3-dione; 1% w/v) had been added. A similar solution of pentachloroiodobenzene (0·01M) and sodium methoxide (0·01M) in methanol was split into three 25ml. portions which were treated respecitively with 1,3,5-trihydroxybenzene (1·0g.), 3,5-dimethylphenol (1·0g.), and 3,5-dimethylanisole (1·0g.). After 12 hours at 323K, each residue from the evaporation of the solvent residue under reduced pressure was subjected to mass spectrometry. In addition to the phenols or ether present, each spectrum showed the presence of pentachloroiodobenzene ($^{12}C_6{}^{35}Cl_5{}^{127}I$ requires m/e, 374) and the pentachlorophenyl radical but no pentachlorobenzene. Nor was iododimethylphenol (m/e, 248), its methyl ether (m/e, 262), or iodotrihydroxybenzene (m/e,252) detected.

The effect of additives upon the rate of protiodeiodination of pentachloroiodobenzene (0·005M) by sodium methoxide (0·005M) in DMSO - methanol (9:1, v/v; 323K) was measured by adding liquids (1% v/v) after about 2 minutes (ca.1 half life). The four points comprising the second section of the kinetic plot after nitrobenzene had been added were an exact continuation of the line defined before the addition (k_2,1·5±0·1 l.mol.$^{-1}$s.$^{-1}$) and gave the same rate constant (k_2, 1·5±0·2 l. mol.$^{-1}$s.$^{-1}$). When diethyl malonate was added, the four titres found after the addition (0·59,0·60,0·58,0·61 ml.) were the same so that taken immediately before the addition (0·57 ml.) although the kinetic plot gave the expected rate constant (k_2,1·4 l.mol.$^{-1}$s.$^{-1}$) until this event.

A similar study using 2,4,6-trichloroiodobenzene (0·01M) and sodium methoxide (0·01M) in DMSO-methanol (9:1,v/v;323K) showed no change of rate before (k_2,0·32±0·01 l.mol.$^{-1}$s.$^{-1}$) or after (k_2,0·31 l.mol.$^{-1}$s.$^{-1}$)

the addition of 1% nitrobenzene at about 30% completion, and the complete cessation of iodide ion production (V_{Ag}+/0·05$\underline{\underline{M}}$, 0·72ml. at time of mixing) by the addition of 1% diethyl malonate (V_{Ag}+,0·70,0·69,0·74ml.).

Kinetic studies of either aryl iodide in the presence of 1% dimedone gave no iodide ion over one hour.

The irradiation (150 watt tungsten filament lamp immediately above the Pyrex reaction vessel) of a reacting solution of o-chloroiodobenzene (0·21$\underline{\underline{M}}$) and sodium methoxide (0·28$\underline{\underline{M}}$) in DMSO-methanol (9:1,v/v;323K) for two hours, two days after the reaction had been initiated and when four points had defined the rate constant (k_2,6·6 x 10^{-7} l.mol.$^{-1}$s.$^{-1}$), caused no change in the kinetic plot studied over the next two days. (k_2,6±0·6 x 10^{-7} l.mol.$^{-1}$s.$^{-1}$).

Products of reactions with additives

Pentachloroiodobenzene or 2,4,6-trichloroiodobenzene (10 mmoles) in benzene (40ml.) was treated with a solution of sodium methoxide (0·4$\underline{\underline{M}}$,25ml.) in DMSO-methanol (9:1,v/v;323K). After five hours water was added. The benzene layer was separated, dried, and removed under reduced pressure. The residue showed (m.s.) the presence of the parent aryl iodide and of penta- or trichlorobenzene, but no peaks in the region m/e, 320 - 335 ($^{12}C_{12}{}^{1}H_5{}^{35}Cl_5$ requires m/e, 324) or the region m/e, 250 - 265 ($^{12}C_{12}{}^{1}H_7{}^{35}Cl_3$ requires m/e, 256), under conditions in which pentachlorobiphenyl gave the expected isotopic molecular ions.

The addition of fluorene (1·66g, 10mmoles) to a solution of sodium methoxide (10mmoles) in DMSO-methanol (9:1,v/v;50ml.) gave a red solution. A drop of this solution instantly decolourised on addition to water, giving a white precipitate, m.p., 103 - 108° (fluorene, m.p., 111 - 113°). The addition of pentachloroiodobenzene (10mmoles) or of 2,4,6-trichloroiodobenzene (10mmoles) intensified and deepened the red colour. After an hour at 50°, the DMSO-methanol solution was poured into water, and the light red precipitate was washed with dilute acid (2$\underline{\underline{M}}$) and with water. A small amount

showed (g.l.c.) the presence of penta- or of trichlorobenzene; this was confirmed, and the further presence of bifluorenylidene indicated, by mass spectrometry.

The organic product, dissolved in the minimum of chloroform, was applied to an alumina column (30cm. x 1 cm.) which was washed with light petroleum (b.p., 60 - 80°). Pentachlorobenzene (8·7 mmoles, m.p., 72 - 81°) or 1,3,5-trichlorobenzene (7·2mmoles, m.p., 50 - 60°) was eluted first. Pure samples (^{1}H n.m.r., m.p. and mixed m.p., g.l.c.) were obtained by further recrystallisation from ethanol.

Further elution of the column, using light petroleum containing increasing proportions of chloroform to hasten elution, gave 9,9'-bifluorenylidene (2·6mmoles in each case) as red needles, m.p.,196-8°, whose m.p. was not altered by the presence of authentic material (m.p., 198 - 200°) made by treating 9-bromofluorene (5g.) with an excess of sodium methoxide in DMSO-methanol.

5. REFERENCES.

1. H. Euler, Ann. 1902, 325, 292.
2. R.J. Gillespie, E.D. Hughes and C.K. Ingold, J.C.S., 1950, 2552.
3. R.J. Gillespie, J. Graham, E.D. Hughes, C.K. Ingold and E.R.A. Peeling, J.C.S., 1950, 2504.
4. O. Redlich and L.E. Nielsen, J.A.C.S., 1943, 65, 654.
5. J. Chédin, C. r. hebd. Séanc. Acad. Sci. Paris, 1935, 200, 1397.
6. C.K. Ingold, D.J. Millen and H.G. Pool, J.C.S., 1950, 2576.
7. J. Chédin and J.C. Pradier, C. r. hebd. Séanc. Acad. Sci. Paris, 1936, 203, 722.
8. E. Grison, K. Ericks and J.L. DeVries, Acta. Crystallogr., 1950, 3, 290.
9. R.A. Marcus and J.M. Fresco, J. Chem. Phys., 1957, 27, 564.
10. J. Chédin, Annls. Chim., 1937, 8, 243.
11. J. Chédin, Mém. Servicés Chim. Etat., 1944, 31, 113.
12. S. Fénéant and J. Chédin, Mém. Servicés Chim. Etat., 1955, 40, 292.
13. H. Martinsen, Z. Phys. Chem., 1905, 50, 385.
14. H. Martinsen, Z. Phys. Chem., 1907, 59, 605.
15. E.G. Cox, G.A. Jeffry and H.R. Truter, Nature, 1948, 162, 258.
16. C. Melander, Ark. Kemi., 1950, 2, 211.
17. R.T. Morrison and R.N. Boyd, 'Organic Chemistry', 3rd ed., Allyn and Bacon Inc., Boston.
18. W. Moffit, Proc. Roy. Soc. Ser. A, 1950, 202, 548.
19. J.D. Roberts and V.C. Chambers, J.A.C.S., 1951, 73, 5030.
20. G. Kortüm, W. Vogel and K. Andrussow, 'Dissociation constants of organic acids in aqueous solution', Butterworth, London.
21. Lange's 'Handbook of Chemistry', 12th ed., McGraw-Hill Inc.
22. R. Bolton, 'Organic Mechanisms', Penguin, 1972, p.29.
23. N. Bjerrum, Zeits. f. physik. Chemie, 1926, 106, 219.

24. J.G. Kirkwood and F.H. Westheimer, J. Chem. Phys., 1938, 6, 506, 513.

25. M. Brickman and J.H. Ridd, J.C.S., 1965, 6845.

26. S.R. Hartshorn and J.H. Ridd, J.C.S., 1968, 1063.

27. M. Brickman, J.H.P. Uttley and J.H. Ridd, J.C.S., 1965, 6851.

28. J.H. Ridd, 'Nitro Compounds - Proceedings of International Symposium, Warsaw, 1963', Pergamon Press, London.

29. T.A. Modro and J.H. Ridd, J.C.S., B, 1968, 528.

30. F.H. Westheimer and M.W. Shookhoff, J.A.C.S., 1939, 61, 555.

31. C.K. Ingold, A. Lapworth, E. Rothstein and D. Ward, J.C.S., 1931, 1959.

32. C.K. Ingold and M.S. Smith, J.C.S., 1938, 905.

33. M.L. Bird and C.K. Ingold, J.C.S., 1938, 918.

34. F.G. Bordwell and K. Rhode, J.A.C.S., 1948, 70, 1191.

35. C.K. Ingold and F.R. Shaw, J.C.S., 1949, 575.

36. C.K. Ingold, 'Structure and Mechanism in Organic Chemistry', Bell, London, p.246.

37. H.C. Brown and W.H. Bonner, J.A.C.S., 1954, 76, 605.

38. A.F. Holleman, Chem. Rev., 1925, 1, 187.

39. J.W. Baker and I.S. Wilson, J.C.S., 1927, 842.

40. J.W. Baker, K.E. Cooper and C.K. Ingold, J.C.S., 1928, 426.

41. J.W. Baker and W.G. Moffitt, J.C.S., 1931, 314.

42. L.P. Hammett, J.A.C.S., 1937, 59, 96.

43. L.P. Hammett, Trans. Farad. Soc., 1938, 34, 156.

44. M. Charton, J.A.C.S., 1969, 91, 615, 619, 624.

45. M. Charton. Can. J. Chem., 1960, 38, 2493.

46. H.C. Brown and Y. Okamoto, J.A.C.S., 1957, 79, 13.

47. H. Jaffé, Chem. Rev., 1953, 53, 191.

48. E. Grünwald and S. Winstein, J.A.C.S., 1948, 70, 846.

49. G. Wittig, Naturwiss., 1942, 30, 696.

50. F.W. Bergstrom, R.E. Wright, C. Chandler and W.A. Gilkey, J. Org. Chem., 1936, 1, 170.

51. J.D. Roberts, D.A. Semenow, H.E. Simmons and L.A. Carlsmith, J.A.C.S., 1956, 78, 601.

52a. J.D. Roberts, H.E. Simmons, L.A. Carlsmith and C.W. Vaugham, J.A.C.S., 1953, 75, 3290.

52b. E.F. Jenny and J.D. Roberts, Helv. Chim. Acta., 1955, 38, 1248.

53. R.A. Benkeser and W.E. Buting, J.A.C.S., 1952, 74, 3011.

54. P.L. Coe, R. Stephens and J.C, Tatlow, J.C.S., 1962, 3227.

55. G. Wittig and L. Pöhmer, Angew. Chem., 1955, 67, 348.

56. J.S. Bradshaw and W.E. Lambert, Unpublished work at the California Institute of Technology (through J.F. Bunnett and D.A.R. Happer, J. Org. Chem., 1966, 31, 2369).

57. R. Escales, Chem. Ber., 1835, 18, 893

58. A. Hälssig, J. Prackt. Chem., 1897, 56, 213.

59. J.F. Bunnett and D.A.R. Happer, J. Org. Chem., 1966, 31, 2369.

60. J.F. Bunnett and F.J. Kearley, J. Org. Chem., 1971, 36, 184.

61. J.A. Zoltewicz and J.F. Bunnett, J.A.C.S., 1965, 87, 2640.

62. G.E. Hall, R. Piccolini and J.D. Roberts, J.A.C.S., 1955, 77, 4540.

63. J.H. Wotiz and F. Huba, J. Org. Chem., 1959, 24, 595.

64. J.F. Bunnett and T.K. Brotherton, J.A.C.S., 1956, 78, 155.

65. A.F. Holleman, W.J. DeMooy and J. Ter Weel, Rec. Trav. Chim., 1915, 35, 1.

66. J.F. Bünnett, E.W. Garbisch and K.M. Pruitt, J.A.C.S., 1957, 79, 385.

67. J.F. Bunnett and R.E. Zahler, Chem. Rev., 1951, 49, 273.

68. J.F. Bunnett and R.J. Morath, J.A.C.S., 1955, 77, 5051.

69. B.A. Bolto, J. Miller and V.A. Williams, J.C.S., 1955, 2926.

70. G.P. Briner and J. Miller (and in part, M. Liveris, P.G. Lutz), J.C.S., 1954, 1265.

71. F. Del Cima, G. Biggi and F. Pietra, J.C.S. Perkin II, 1973, 55.

72. C.W.L. Bevan and G.C. Bye, J.C.S., 1954, 3091.

73. J. Miller, Austr. J. Chem., 1953, 9, 191.

74. J. Miller and J.M. Wrightson, Abstracts of papers presented at the 12th meeting of the American Chemical Society, New York, September 1947, p.16J, (through J.F. Bunnett and R.E. Zahler, Chem. Rev., 1951, 49, 273).

75. J. Miller and A.J. Parker, J.A.C.S., 1961, 83, 117.

76. H. Suhr, Chem. Ber., 1964, 97, 3277.

77. C.A. Kingsbury, J. Org. Chem., 1964, 29, 3262.

78. J. Murto and A.M. Hiito, Suomen Kemisthil, 1964, B37, 177.

79. J.H. Wotiz and F. Huba, J. Org. Chem., 1959, 24, 595

80a. J.F. Bunnett and C.E. Moyer, J.A.C.S., 1963, 85, 1891.

80b. J.F. Bunnett and C.E. Moyer, J.A.C.S., 1971, 93, 1183.

81. G. Wittig and R.W. Hoffman, Chem. Ber., 1962, 95, 2729.

82. G.B.R. DeGraaf, H.J. DenHertog and W.C. Melger, Tetr. Lett., 1965, 963.

83. D.J. McLennan and J.F. Bunnett, J.A.C.S., 1971, 93, 1198.

84. J.F. Bunnett and D.J. McLennan, J.A.C.S., 1968, 90, 2190.

85. C.W. Bird, Chem. Commun., 1969, 1486.

86. J.F. Bunnett and G. Scorrano, J.A.C.S., 1971, 93, 1190.

87. S. Gronowitz, Advanc. Heterocycl. Chem., 1963, 1, 75.

88. M.G. Reinecke and H.W. Adickes, J.A.C.S., 1968, 90, 511.

89. D.A. deBie and H.C. van der Plas, Tetr. Lett., 1968, 3905.

90. W.G. Kofron and C.R. Hauser, J.A.C.S., 1968, 90, 4126.

91. R.G. Jones and H. Gilman, Org. Reactions, 1951, 6, 339.

92. R. Alexander, E.C.F. Ko, A.J. Parker and T.J. Broxton, J.A.C.S., 1968, 90, 5049.

93. E. Hayon, T. Ibata, N.N. Lichtin and M. Simic, J.A.C.S., 1970, 92, 3898.

94. M.M. Mach and J.F. Bunnett, J.A.C.S., 1974, 96, 936.

95. C. Walling and A. Padiva, J. Org. Chem., 1962, 27, 2976.

96. J.F. Bunnett, Accounts Chem. Res., 1972, 5, 139.

97. D.A.R. Happer, Work carried out at the Brown University (U.S.A.) in 1964 (through J.F. Bunnett, D.A.R. Happer, M. Patsch, C. Pyun and H. Takayama, J.A.C.S., 1966, 88, 5250).

98. J.F. Bunnett and H. Takayama, J.A.C.S., 1968, 90, 5173.

99. J.F. Bunnett and C.C. Wamser, J.A.C.S., 1967, 89, 6712.

100. J.F. Bunnett and C.C. Wamser, J.A.C.S., 1966, 88, 5534.

101. M. Anbar and E.J. Hart, J.A.C.S., 1964, 86, 5633.

102. H.E. Bachofner, F.M. Beringer and L. Meites, J.A.C.S., 1958, 80, 4269, 4274.

103. F.M. Beringer and P.S. Forgione, Tetr., 1963, 19, 739.

104. C. Walling, 'Free Radicals in Solution', Wiley, New York, 1957.

105. J.K. Kim and J.F. Bunnett, J.A.C.S., 1970, 92, 7463.

106. M. Szwarc, Prog. Phys. Org. Chem., 1968, 6, 379.

107. D.E. Bartak, W.C. Danen and M.D. Hawley, J. Org. Chem., 1970, 35, 1205.

108. N. Kornblum, R.E. Michel and R.C. Kerber, J.A.C.S., 1966, 88, 5661.

109. R.A. Rossi and J.F. Bunnett, J. Org. Chem., 1973, 38, 1407.

110. R.A. Rossi and J.F. Bunnett, J. Org. Chem., 1973, 38, 3020.

111. J.F. Bunnett and B.F. Gloor, J. Org. Chem., 1974, 39, 382.

112. J.F. Bunnett and X. Creary, J. Org. Chem., 1974, 39, 3173.

113. J.F. Bunnett and X. Creary, J. Org. Chem., 1974, 39, 3611.

114. J.F. Bunnett and X. Creary, J. Org. Chem., 1974, 39, 3612.

115. J.F. Bunnett and R.P. Traber, J. Org. Chem., 1978, 43, 1867.

116. J.F. Bunnett and S.J. Shafer, J. Org. Chem., 1978, 43, 1877.

117. J.F. Bunnett and S.J. Shafer, J. Org. Chem., 1978, 43, 1873.

118. J.F. Bunnett, R.G. Scamehorn and R.P. Traber, J. Org. Chem., 1976, 41, 3677.

119. R.G. Scamehorn and J.F. Bunnett, J. Org. Chem., 1977, 42, 1449.

120. T. van der Linden, Rec. Trav. Chim., 1938, 57, 781.

121. C.E. Moyer, Diss. Abs., 1965, 25, 4412.

122. J.F. Bunnett and R.R. Victor, J.A.C.S., 1968, 90, 810.

123. G.A. Russell and S.A. Stevens, J. Org. Chem., 1966, 31, 248.

124. I. Collins and H. Suschitzky, J.C.S., 1969, 2337.

125a. R. Bolton and J.P.B. Sandall, J.C.S. Perkin II, 1976, 1545.

125b. R. Bolton and J.P.B. Sandall, J. Fluor. Chem., 1976, 7, 540.

126. R. Bolton and J.P.B. Sandall, J.C.S. Perkin II, 1977, 278.

127. E. Buncel and H. Wilson, Advanc. Phys. Org. Chem., 1977, 14, 192.

128. J.F. Norris and A.A. Ashdown, J.A.C.S., 1925, 47, 842.

129. A. Vogel, 'A Textbook of Practical Organic Chemistry', 4th ed., Longman, London, 1978.

130. A.F. Holleman, Rec. Trav. Chim., 1915, 34, 223.

131. C. Willergodt and M. Böllert, Chem. Ber., 1910, 43, 2642.

132. F. Ullman, Ann. 1904, 332.

133. W. Körner and A. Contardi, Atti. Accad. Lincei., 1913, (V) 22i, 823.

134. H.H. Hodgson and A.P. Mahadevar, J.C.S., 1947, 173.

135. C. Willergodt and K. Wilcke, Chem. Ber., 1910, 43, 2746.

136. A.C. Tas and R.H. de Vos, Environ. Sci. Technol., 1971, 5, 1216.

137. G.B. Deacon, J.M. Miller and B.S.F. Taylor, Austr. J. Chem., 1975, 28(7), 1499.

138. S.I. Pombik et. al., J. Organometal. Chem., 1977, 136(2), 185.

139. S.A. Brazier and H. McCombie, J.C.S., 1912, 101, 968.

140. H.A.J.Schoutissen, J.A.C.S., 1933, 55, 4531.

141. H.Goldschmidt and M Hönig, Chem. Ber., 1886, 19, 2440.

142. J.B. Cohen and H.D. Dakin, J.C.S., 1902, 81, 1333.

143. S.R. Birch, R.A. Dean, F.A. Fiddler and R.A. Lowry, J.A.C.S., 1949, 71, 1362.

144. R.L. Datta and F.V. Fernandes, J.A.C.S., 1916, 38, 1809.

145. R.C. Jones, J.A.C.S., 1947, 69, 2346.

146. G.C. Finger and M.L. Kanowski, Trans. Illinois State Acad. Sci., 1944, 66.

147. M.R. Petit and J.C. Tatlow, J.C.S., 1951, 3459.

148. E.T. McBee, O.R. Pierce, R.D. Lowry and E. Rapkin, J.A.C.S., 1951, 73, 3932.

149. R. Filler and H. Novar, J. Org. Chem., 1961, 26, 2707.

150. H.H. Hodgson and J. Walker, J.C.S., 1933, 1620.

151. F. Challenger and E. Rothstein, J.C.S., 1934, 1258.

152. A. Schaarschmidt, H. Balzerkierwicz and J. Gante, Ber., 1925, 58, 501.

153. A.L.J. Beckwith, J. Miller and G.D. Leahy, J.C.S., 1952, 3552.

154. N. Kornblum, A.E. Kelley and G.D. Cooper, J.A.C.S., 1952, 74, 3074.

155. G.F. Hennion and J.G. Anderson, J.A.C.S., 1946, 68, 424.

156. A.J. Parker, Quart. Rev., 1962, 16, 163.

157. J. March, 'Advanced Organic Chemistry', 2nd ed., McGraw-Hill, p.227.

158. C.Y. Meyers and M.L. Hsu, Abstracts, 170th meeting of the American Chemical Society, Chicago, August 1975 (through R.G. Scamehorn and J.F. Bunnett, J. Org. Chem., 1977, 42, 1449).

159. D.J. Cram, B. Rickborn and G.P. Knox, J.A.C.S., 1960, 82, 6412.

160. R.F. Bridger and G.A. Russell, J.A.C.S., 1963, 85, 3754.

161. R. Bolton and J.P.B. Sandall, Personal Communication.

162. W.J. Boyle and J.F. Bunnett, J.A.C.S., 1974, 96, 1418.

163. J.A. Zoltewicz and T.M. Oestreich, J.A.C.S., 1973, 95, 6863.

164. L.A. Pinck and G.E. Hilbert, J.A.C.S., 1946, 68, 377.

165. C.R. Hauser, W.R. Brasen, P.S. Skell, S.W. Kantor and A.E. Brodhag, J.A.C.S., 1956, 78, 1653.

166. F.G. Bordwell and W,T. Brannen, J.A.C.S., 1964, 86, 4645.

167. J. Miller, 'Aromatic Nucleophilic Substitution', Elsevier, Amsterdam, 1968.

168. W.K. McEwen, J.A.C.S., 1936, 58, 1124.

169. E.C. Steiner and J. Gilbert, J.A.C.S., 1963, 85, 3054.

170. J.H. Ridd, Advanc. Phys. Org. Chem., 1978, 16, 1.