Dediazoniation Reactions as Potential Routes to Fluoroaromatics.

Brian Sexton

Dediazoniation Reactions as Potential Routes to Fluoroaromatics.

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Statement

The work described in this thesis was carried out in the Chemistry Department of the University of Newcastle upon Tyne between October 1994 and September 1997. Except where otherwise acknowledged it is entirely the work of the author.

I would like to thank my supervisor Howard Maskill for his help and support during my time preparing this thesis. I would also like to thank him for allowing me to attend a Winter School on Organic Reaction Mechanisms in Italy and a European Symposium on Organic Reactivity in Spain. I would like to thank Dr. Dave Moody, my industrial supervisor at Zeneca for making my time at Grangemouth enjoyable and productive, and for his valuable contributions during my studies at Newcastle.

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Finally I would like to thank my parents for their support and encouragement over the years.

Abstract

The reactions of arenediazonium ions have been studied intensely by organic chemists. Besides the azo chemistry (of interest to the dye industry), dediazoniation reactions have also been investigated. In these processes, a carbon nitrogen bond cleaves to give an aryl cation and a nitrogen molecule. The aryl cation is a short lived species which is captured by a nucleophile or a solvent molecule (Figure 1).

$$Ar{-}N_2^+ \xrightarrow{-N_2} Ar^+ \xrightarrow{Nu} Ar{-}Nu$$

Figure 1

The objective of our investigation was to attempt to identify reaction conditions that would allow trapping of the aryl cation by fluoride. By using either fluoride donor solvents, fluoride or fluoride containing anions such as BF_4^- or PF_6^- as the solute in a very weakly nucleophilic solvent, we hoped to develop a viable industrial process for the production of fluoroaromatic compounds. At present, their method of production includes the use of liquid hydrogen fluoride which is an extremely poisonous and corrosive material. Our work mainly involved a kinetic study of the heterolytic dediazoniation of several substituted arenediazonium salts in a variety of possible fluoride donor solvents and an analytical study of the product distribution from reactions of arenediazonium salts with possible fluoride donor solvents and added fluoride ions. This study also looked at the photolytic decomposition of arenediazonium salts to see if this route was a viable industrial alternative to thermal dediazoniation.

The choice of solvent to facilitate heterolytic dediazoniation is important. It has been shown that the solvents in which the heterolytic dediazoniation mechanism is predominant have low nucleophilicities (but are highly ionising) whereas, in solvents of high nucleophilicity, homolysis of arenediazonium salts is favoured.

Hence trifluoroethanol, hexafluoroisopropanol, trifluoroacetic acid, ethanol and water were chosen as solvents in which to study the reaction. The use of trifluoromethoxybenzene and difluoromethyl 2,2,2-trifluoroethyl ether as co-solvents in trifluoroethanol were investigated as well as the use of inorganic fluorides in trifluoroethanol and water.

Finally, a short study of the reduction of *m*-nitrobenzenediazonium tetrafluoroborate in ethanol was undertaken to investigate the reduction mechanism.

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Chapter 1. Introduction.

1.1 General.

The reactions of arenediazonium ions are amongst the oldest to be studied intensively by organic chemists. They have their roots in the formation of the dye industry and their discovery is attributed to P. Griess.[1] On account of their reactivity, a large range of products are known, the most important of which technically are the azo dyes.

Azo compounds of the general formula ArN_2X are diverse, but a broad classification into two main groups is possible:

1) diazonium salts, $ArN_2^+X^-$,

2) azo compounds in which the atom or group X is covalently bound to the ArN_2 residue.

The high reactivity of arenediazonium ions is because nitrogen is an exceptionally good leaving group.[2] Arenediazonium salts are normally prepared from the reaction of an aniline derivative with nitrous acid in the presence of a dilute aqueous mineral acid. Unlike their aliphatic counterparts which decompose readily to molecular nitrogen and a carbocation, arenediazonium salts are relatively stable. Although their reactions are extensive, two main mechanisms predominate for the majority of reactions. The C-N bond can be cleaved either by a heterolytic or a homolytic mechanism.

1.2 Azo Dyes.

1.2.1 History of the dye industry.

W. H. Perkin was given the credit for producing the first synthetic organic dye in 1856.[3] He obtained Mauveine, a violet cationic dye by oxidation of a mixture of aniline bases. His discovery attracted the attention of other chemists which resulted in Griess discovering the azo compounds in 1859.[3] Several German industrialists realised the importance of these aniline dyes and founded companies to manufacture them. Although the names of these companies have been shortened today, their original historical names betray their origins in the aniline dye industry. The word Farbe is German for colour or dye and can be clearly seen in the names of these companies (*Farbenfabriken vorm. Friedrich*) Bayer, (*Farbwerke vorm. Meister Lucius und Brüning*) Hoechst and BASF (*Badische Anilin und Soda-Fabrik*). The dyestuff industry provided the platform for

these companies to launch into other markets (Bayer introduced aspirin in 1899 and BASF developed ammonia for fertilisers and explosives).

Arenediazonium salts undergo a coupling reaction with activated aromatic rings to yield azo compounds (Figure 1.1).

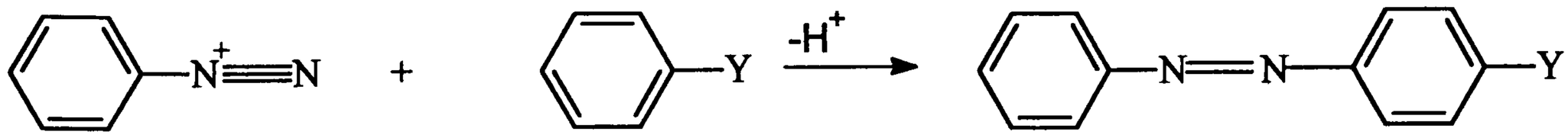


Figure 1.1

Diazonium coupling reactions are typical electrophilic aromatic substitution processes in which the positively charged diazonium ion is the electrophile that reacts with the electron rich ring of a phenol or arylamine. The reaction almost always occurs at the para position although ortho attack may take place if the para position is blocked (Figure 1.2).

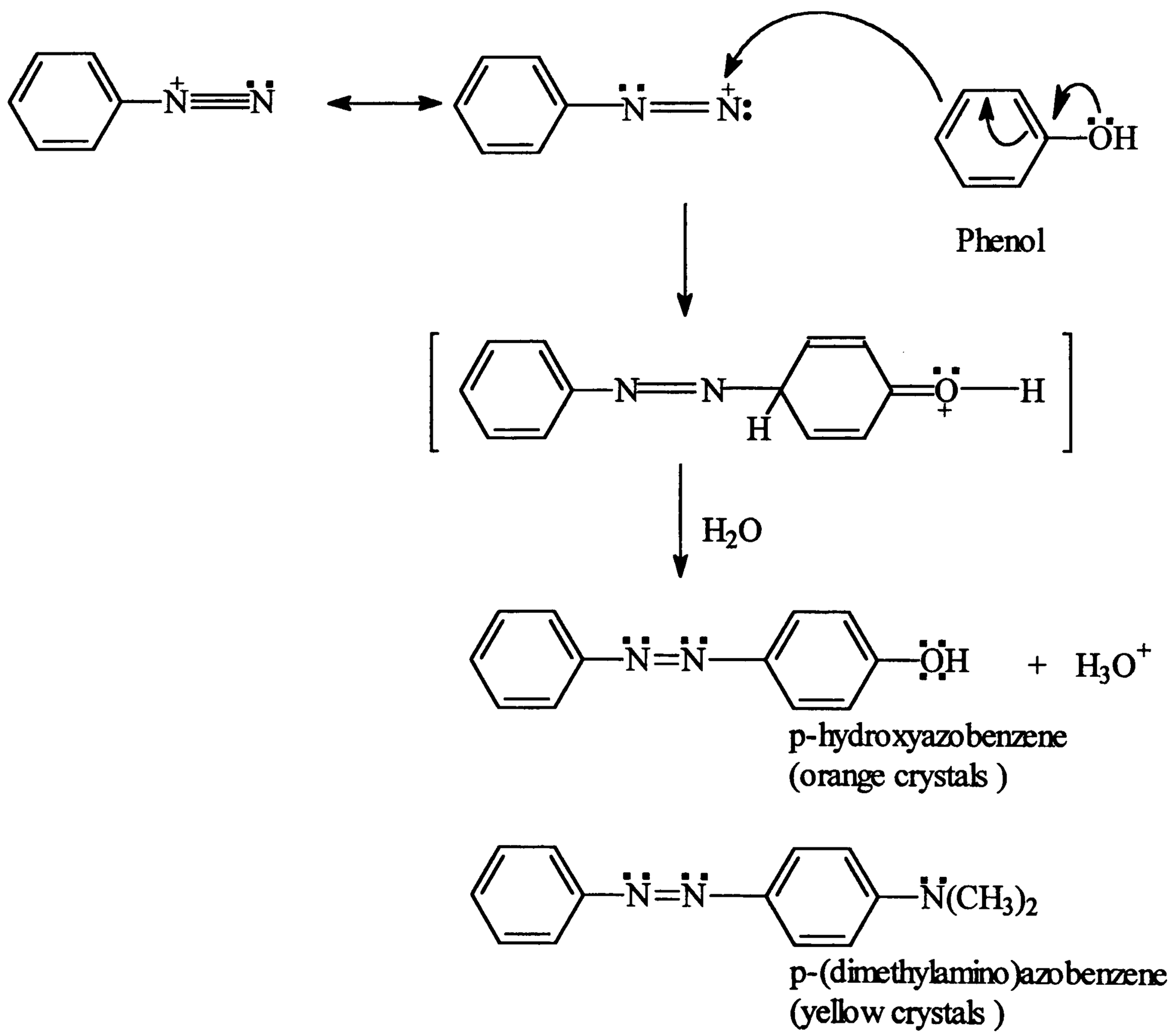
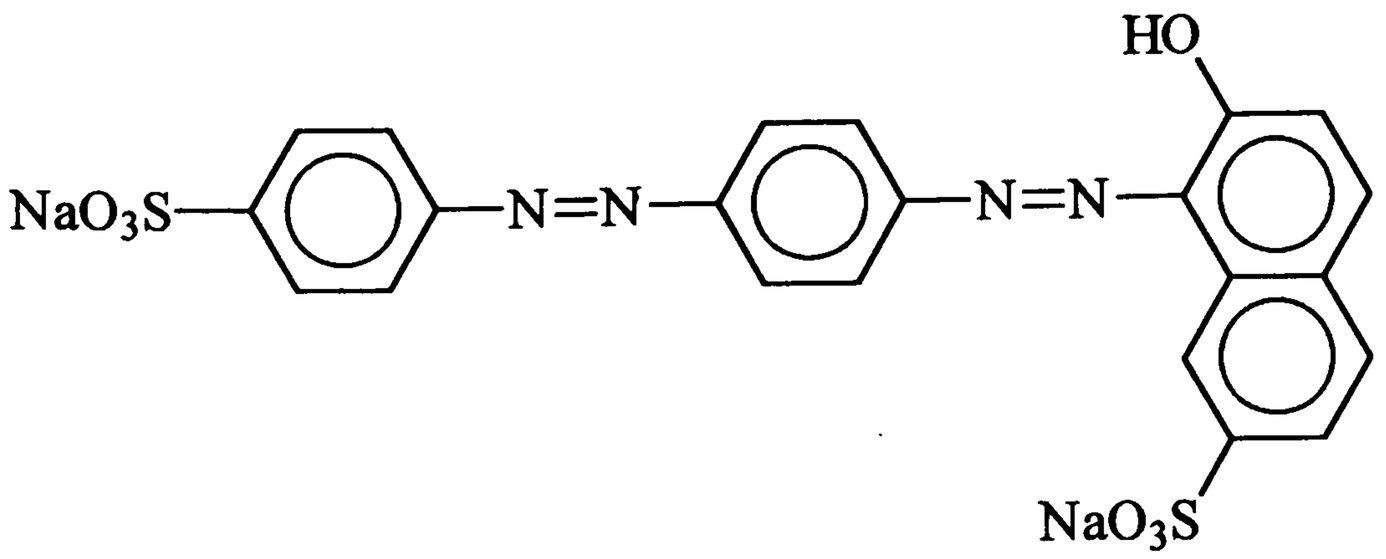
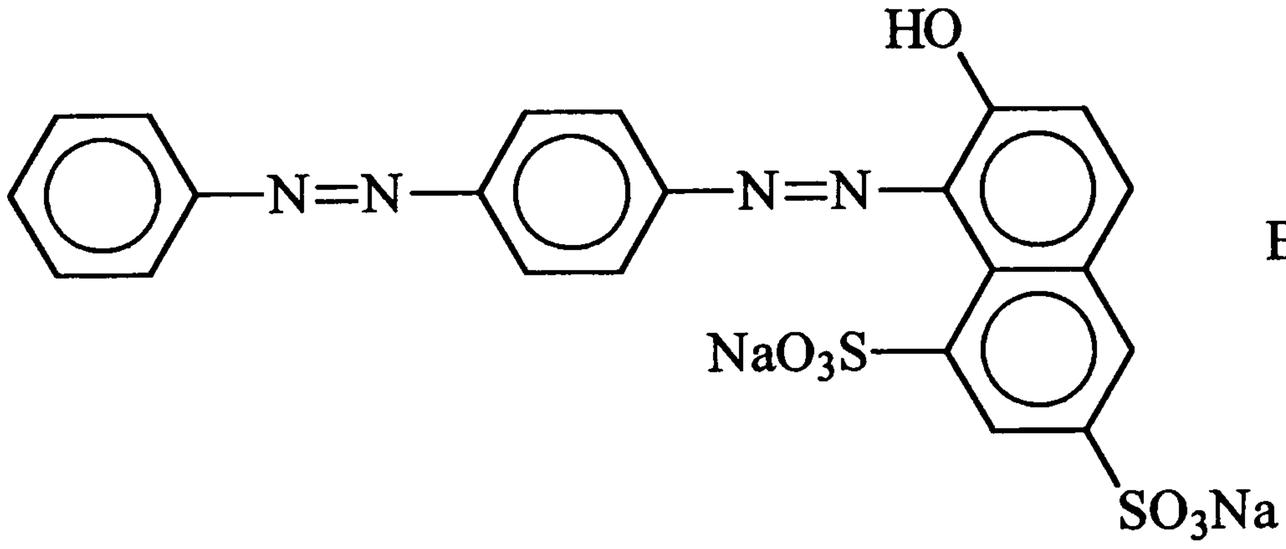


Figure 1.2

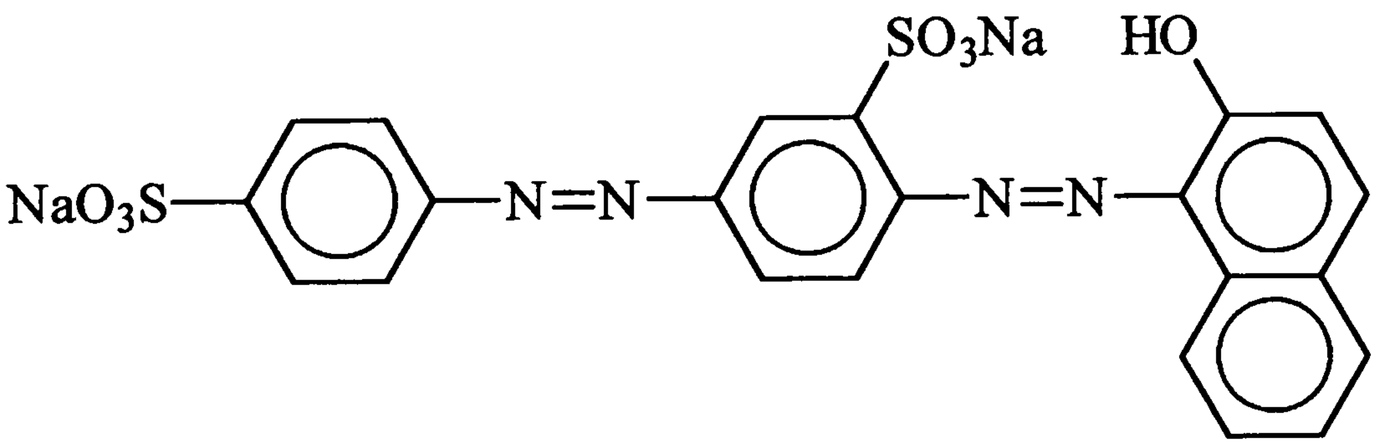
Colour, which is the most important property of dyestuffs, is due to the absorption of light, i.e radiant energy, to give the photo excited state of the molecule. Absorption of this energy raises certain electrons into higher energy orbitals. The difference in energy between the excited state and ground state (ΔE) is directly proportional to the frequency (ν) of the light absorbed. The electronically excited molecules lose the energy by collisions with other molecules, emission of radiation of longer wavelength, or photochemical reactions. Electrons in molecules fall into one of three classes: σ electrons, π electrons, and non-bonding electrons (called n electrons). Single bonds between atoms involve only σ electrons, multiple bonds involve π electrons, and molecules with atoms to the right of carbon in the periodic table (e.g. N, O, or halogen) have n electrons i.e. lone pairs. In general, the σ electrons are most firmly bound to the nuclei and hence require a great deal of energy to undergo transitions, while the π and n electrons require less energy. Saturated hydrocarbon molecules, which can only undergo high energy $\sigma \rightarrow \sigma^*$ transitions corresponding to UV radiant energy are not coloured. More pronounced colours are observed in unsaturated systems especially when two or more multiple bonds are conjugated in the molecule. In these cases, the $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions correspond to light absorption at longer wavelengths and higher intensities. With the amount of conjugation in azo dyes, these transitions correspond to the visible region of the spectrum. Azo dyes can be tailored to absorb light of a particular frequency by introducing various groups into the compound. The simplest azo dyes containing only benzene rings are yellow. By increasing the molecular weight or number of functional groups attached, the colour can be changed from yellow to red/brown. Introducing naphthalene rings produces azo dyes that are violet-blue or black in colour. Green azo dyes are formed when nitro groups are introduced into the azo compound. The introduction of a sulphonate group increases the solubility of the azo compound in water. The position of this group in the molecule can influence the colour of the dye as shown with the three isomeric compounds in Figure 1.3. The compounds shown give three distinct shades of red.



Crocein Scarlet



Brilliant Crocein



Biebrich Scarlet

Figure 1.3

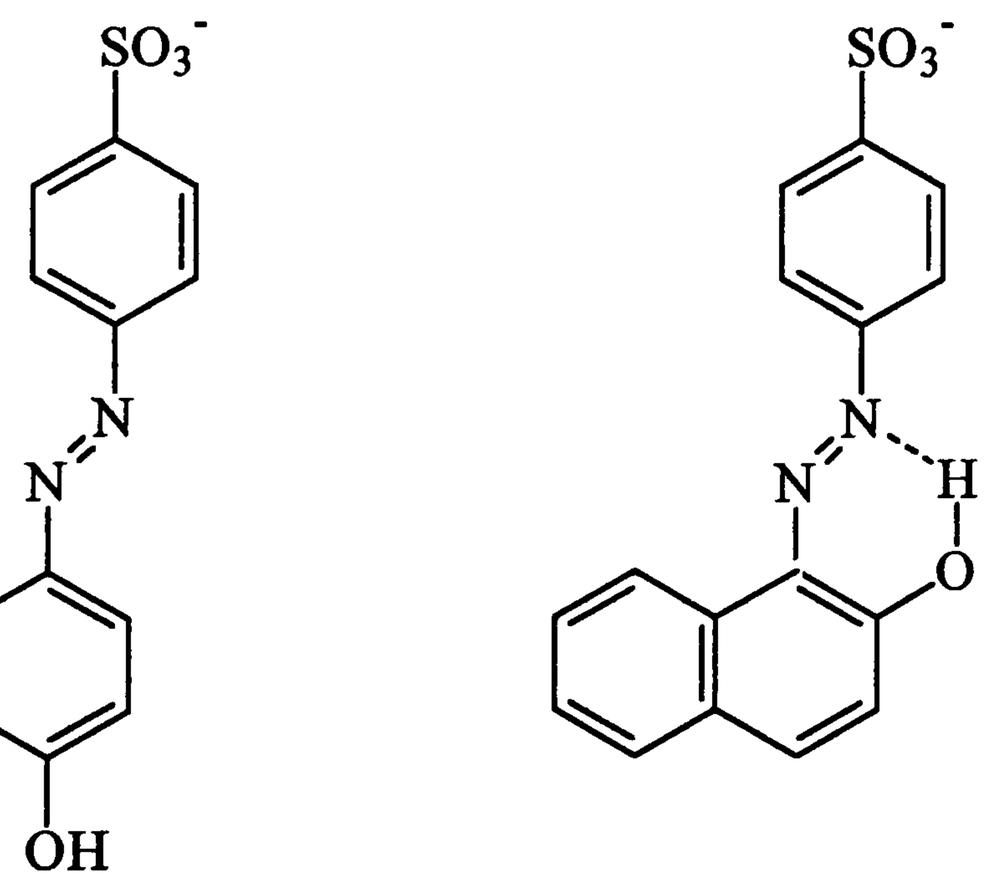
Azo dyes make up the largest group of industrial dyes, both in number and the amount produced, and can be divided into types.

1.2.2 Anionic monoazo dyes.

These dyes need the presence of one or more water solubilizing ionizable substituents which in nearly all cases are sulphonic acid groups. This is due to their complete dissociation in all activity ranges occurring in aqueous solutions. The main application of these dyes is for dying protein and synthetic polyamide fibres. The dye is applied to wool, silk and polyamides in weakly acidic conditions hence the term acid dye. The dye contains a residue which is capable of condensation with hydroxyl groups of cellulose (cotton) and with the amino groups of protein fibres of wool.

5-Pyrazolone derivatives are used as nucleophilic substrates in coupling to produce yellow dyes while naphthol and naphthylamine derivatives are used for orange to bluish violet dyes. It is important that the hydroxyl or amino groups are in the ortho position to

the azo bridge so a hydrogen bond can form between the hyroxyl or amino group and the azo nitrogen in the beta position. This displaces the pK of the acid-base equilibria of the hydroxyl or amino groups into pH regions outside the practical application of these dyes. This is important because dissociation of the hydroxyl group or protonation of the amino group leads to undesirable colour changes. An example of this is the isomeric dyes Naphthalene Orange I and Naphthalene Orange G (Figure 1.4). Orange G is little used now because of the tint changes in soda and washing tests. The pK_2 values show that Orange I is already present as a dibasic anion above pH 8.2 while Orange G releases its phenolic proton in a pH range not attainable in washing.



Naphthalene Orange I pK_2= 8.2 Naphthalene Orange G pK_2= 11.4

Figure 1.4

1.2.3 Disperse azo dyes.

These dyes are almost completely insoluble in water and are used for dying cellulose acetate fibres and synthetic fibres in aqueous suspensions. Most yellow, orange and red disperse dyes are azobenzene derivatives. In contrast to anionic monoazo dyes, benzene, not naphthalene, derivatives are the most important coupling components. For this reason the N-(2-hydroxyethyl)- and N-(2-methoxyethyl)anilines are significant because these compounds are not completely insoluble in water but possess the low water solubility necessary for the dying process. Nitrodiazobenzenes are used frequently as diazo components for disperse azo dyes (e.g. Celliton Scarlet B Figure 1.5). Caution

is needed when diazotizing di- and trinitro derivatives of aniline because of the danger of explosion at high temperatures.

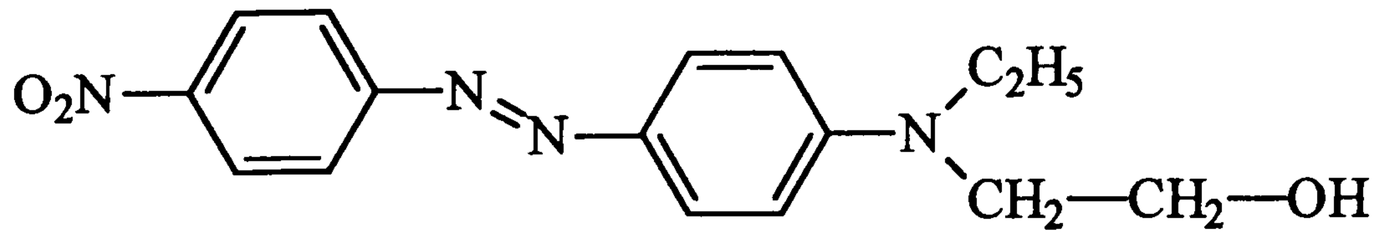


Figure 1.5 Celliton Scarlet B.

1.2.4 Complex forming monoazo dyes.

These dyes consist mainly of chromium and cobalt complexes and are used for dying protein and polyamide fibres. Complex forming dyes are predominantly trifunctional but can in some cases be bi, tetra and hexa functional. An example of a bifunctional complex forming dye containing salicyclic acid as the coupling component is Alizarine Yellow R (Figure 1.6). Two coordination sites (B) in the complex are available for bonding to groups in the fibre which posses lone pairs of electrons. These linkages are the cause of the increased wet fastness of these dyes.

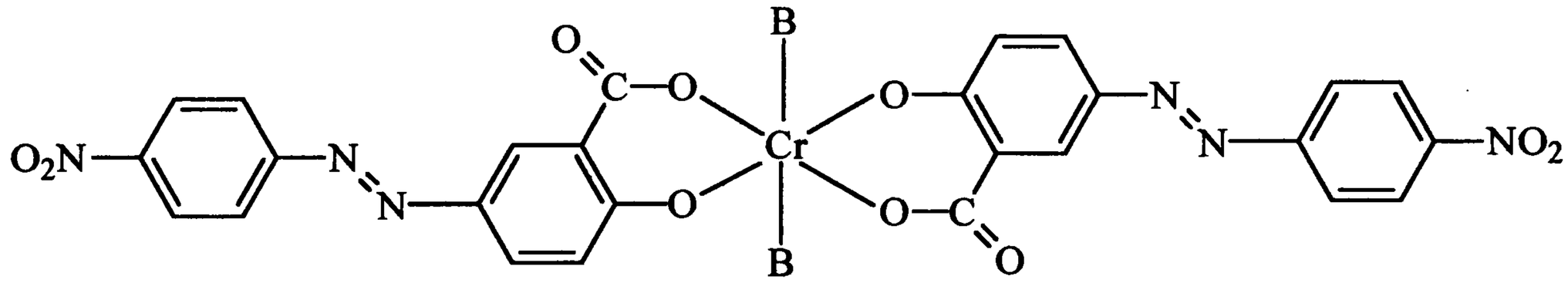


Figure 1.6. Alizarine Yellow R.

1.3 Diazonium Salt Preparation (Diazotisation).

1.3.1 Diazotisation of anilines.

This is carried out by addition of sodium nitrite to an aqueous solution or suspension of the amine in the presence of acid (Figure 1.7).[4]

$$ArNH_2 + 2HX + NaNO_2 \rightarrow ArN_2X + 2H_2O + NaX$$

$$X = Cl, Br, NO_3, HSO_4, BF_4 \text{ etc}$$

Figure 1.7

The free amine $ArNH_2$ is in equilibrium with the corresponding $ArNH_3^+$ ammonium ion. Several techniques are in use depending on basicity and solubility of arylamine. For the preparation of solid arenediazonium chloride or sulphate, the reaction is conducted in the

absence of water as far as possible, so the source of nitrous acid is one of its organic esters (amyl nitrite) and a solution of hydrogen chloride gas in alcohol. The addition of ether causes the diazonium salt to precipitate out.

1.3.2 Diazotisation in concentrated mineral acids.

With amines of very low basicity, use of aqueous media is not possible as the amines are incompletely protonated and the amine itself is insoluble. These amines are soluble in anhydrous acids so concentrated sulphuric acid is used.[5] It is possible to dissolve sodium nitrite in 90 - 96% sulphuric acid without evolution of nitrous fumes at 0 - 10°C.

1.3.3 Mechanism of diazotisation.[6]

The rate of diazotisation of aniline in aqueous perchloric acid varies between pH 3 to 9M acid (Figure 1.8). At low acidities pH (H_0) 1-3 (region A), the rate of diazotisation decreases with acidity but at pH 1 the rate passes through a minimum and then increases rapidly to reach a maximum in 7M perchloric acid (region B). At higher acidities the rate of diazotisation falls off very rapidly, eventually becoming negligible (region C). Diazotisation is a multistage reaction.

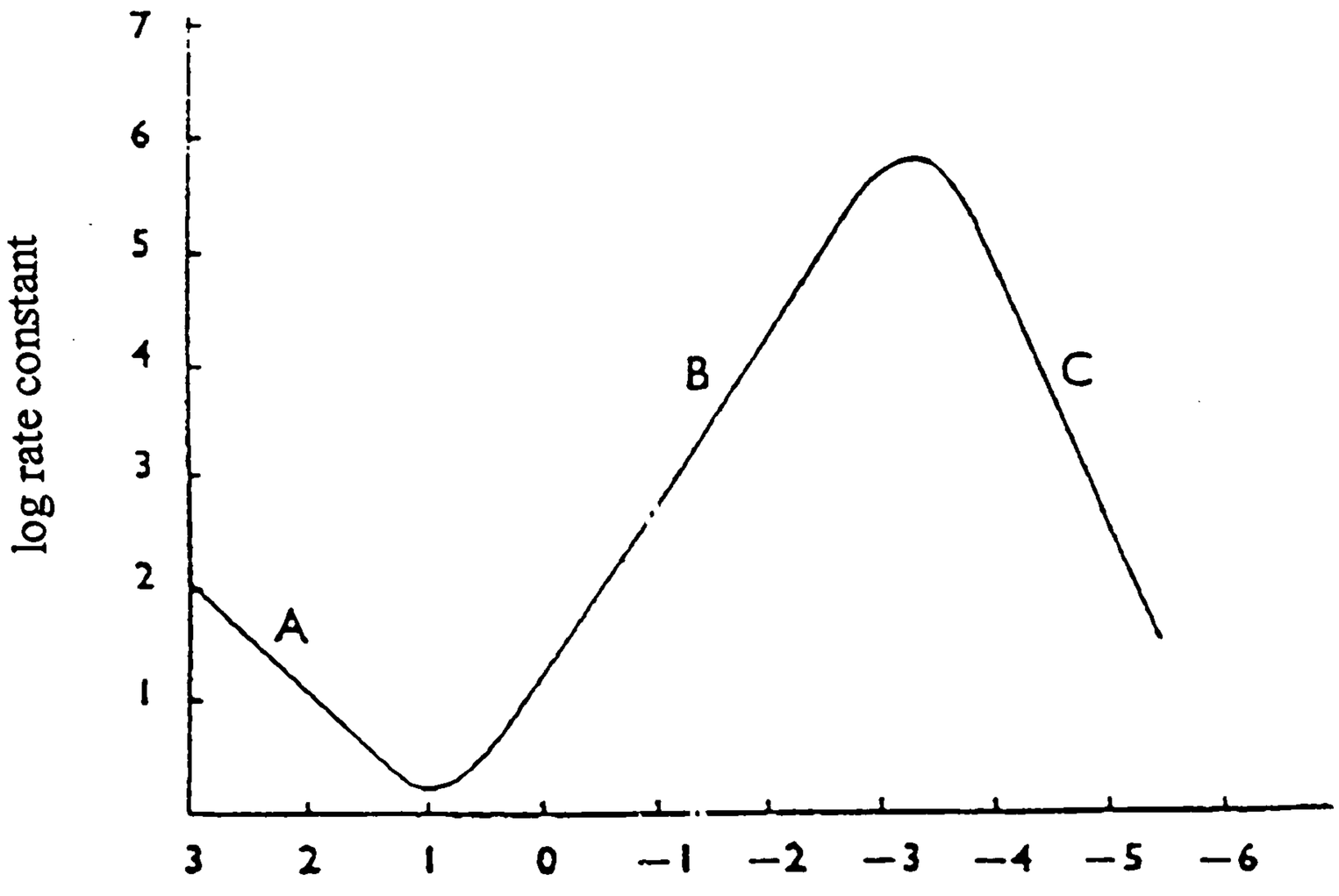


Figure 1.8 Variation in rate constant of diazotisation of aniline with H_0 acidity function.

For diazotisation at intermediate and high acidities, the reaction stages are more complex than illustrated. However, the view that diazotisation proceeds through slow formation of the primary nitrosamine is correct. The reason diazotisation rates vary with acidity is complex, the dependency partly arises from equilibria that involve the reactants.
Amines are Bronsted bases (eq. 1) so for amines such as aniline (pKa of anilinium = 4.6) protonation is virtually complete under normal reaction conditions of diazotisation.

$$ArNH_2 + H^+ \rightleftharpoons ArNH_3^+ \qquad (1)$$

The equilibria involving nitrous acid also include formation of nitrous anhydride and nitrosonium.

$$2HNO_2 \rightleftharpoons N_2O_3 + H_2O \qquad (2)$$

$$HNO_2 + H^+ \rightleftharpoons NO^+ + H_2O \qquad (3)$$

At low acidities the main component of nitrous acid is molecular HNO_2 but the concentration of nitrosonium ions increases rapidly with acidity, and this is the main nitrous species present in 8 M perchloric acid.

Low acidity regions (region A Figure 1.8).

Rate of diazotisation = k_{obs} [amine]$_T$[nitrous acid]^2

$$[amine]_T = [ArNH_2] + [ArNH_3^+]$$

The rate constant varies inversely with concentration of H^+ ions. This is as a consequence of reaction through the free amine and dependency of the reaction rate on the square of the nitrous acid concentration as a result of nitrosation by nitrous anhydride.

$$ArNH_3^+ \overset{\text{fast}}{\rightleftharpoons} ArNH_2 + H^+$$

$$2HNO_2 \overset{\text{fast}}{\rightleftharpoons} N_2O_3 + H_2O$$

$$N_2O_3 + ArNH_2 \xrightarrow{\text{slow}} ArNH_2^+NO + NO_2^-$$

$$ArNH_2^+NO \xrightarrow{\text{fast}} ArN_2^+ + H_2O$$

Electron withdrawing substituents increase the rate of diazotisation as they increase the concentration of free amine in the solution. The effects of a weak electron withdrawing substituent (Cl) and an electron donating substituent (OMe) can be seen in table 1.1, region A.

Table 1.1. Effect of substituents on Rate of diazotisation relative to H = 1.

X	region A	region B	region C
p-OMe	0.35	9.4	-
p-Me	-	7.3	ca 1
p-Cl	1.68	0.24	ca 1
H	1	1	1

Intermediate acidity region (region B Figure 1.8).

With increasing acidity, the rate constant of diazotisation of aniline increases rapidly. At the same time the kinetic form changes so that at a given acidity, the reaction obeys

$$\text{rate} = k_{obs}\,[\text{amine}]_T[\text{nitrous acid}].$$

The change in kinetic order with respect to nitrous acid indicates nitrous anhydride is no longer the nitrosating agent, but it is some species such as the nitrosonium ion whose equilibrium concentration increases rapidly with acidity. Between 0.5M and 3 M perchloric acid the rate constant increases more than a hundred fold. Ridd observed that the reaction had unusual features, notably in the pattern of substituent effects.[6] For *p*-substituents the reverse of that in region A occurs (Table 1.1). From these and other considerations, Ridd deduced that the nitrosating agent attacks the protonated amine and is loosely associated with the aromatic ring in the transition state. The main features of the kinetics under these conditions can be understood in terms of the reactions shown in Figure 1.9.

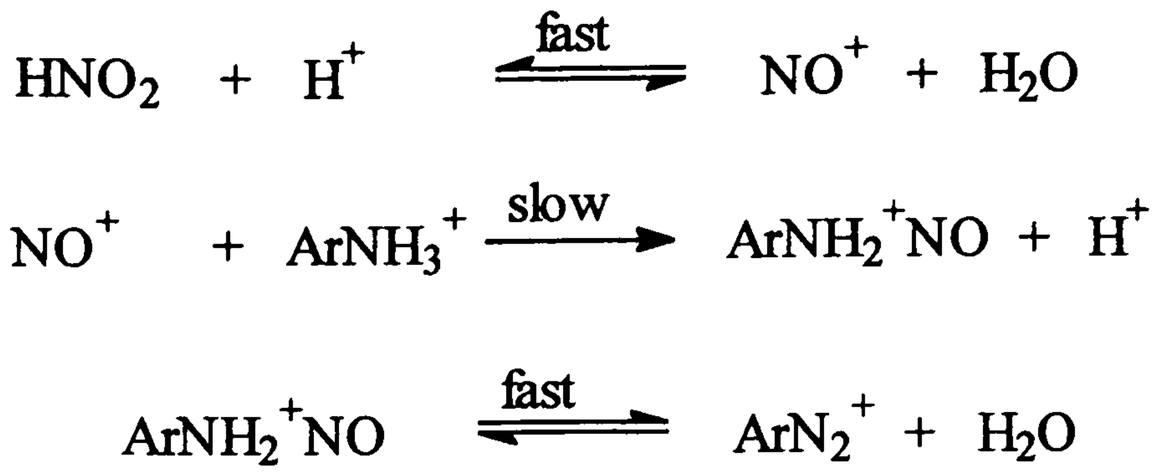


Figure 1.9

The dominance of reaction through the protonated amine in region B occurs not because protonation is necessary before the amine will undergo diazotisation but because the concentration of the free amine is then so small that its rapid reaction with nitrosating agents contributes little to the overall rate of diazotisation.

High Acidity Region (region C Figure 1.8).

The rate constant for diazotisation of aniline reaches a maximum but then in region C, decreases rapidly with increasing acidity. The maximum depends on the nature of the substituents attached to the aniline, i.e. is pKa dependent. The order with respect to the amine and nitrous acid remains unchanged (second order overall). The reason for this change from strong acid catalysis in region B to strong acid inhibition in region C is that there is a change in the rate determining step. The rate determining step now involves the loss of a proton to the medium and requires the participation of a Bronsted base which becomes more difficult as the acidity is increased.

1.4 Diazonium Ion Structure.

The elucidation of the structure of arenediazonium ions has concerned chemists for over a hundred years. Intense discussion has centered on the relative contributions of canonical structures 1, 2 and 3 (Figure 1.10).

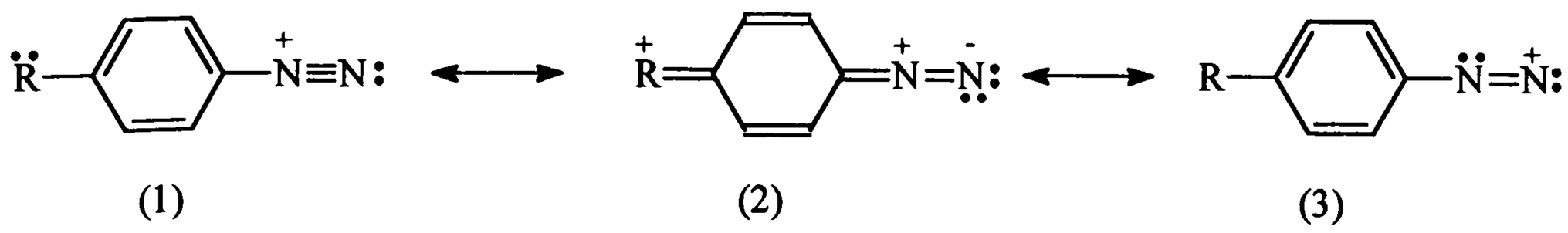


Figure 1.10

It has been with the advent of techniques such as ^{15}N and ^{13}C NMR spectroscopy, X-ray crystallography and infra-red spectroscopy that this problem has been studied. The ^{13}C

and ^{15}N NMR shifts of 4-substituted benzenediazonium salts were studied by Roberts and co-workers.[11] They found that the chemical shifts for N(2) of the arenediazonium ions studied were more sensitive to substituent changes than the N(1). This indicated to the authors that substantial positive charge existed on the terminal nitrogen which they believed to be proof for a quinoid canonical. However evidence against a quinoid type structure was published by Elofson and Gadallah.[12] They studied the ^{13}C and ^{15}N chemical shifts of 4-substituted benzenediazonium salts in sulfolane solutions and compared the chemical shifts of C(1) to the polarographic half-wave potentials of the same benzenediazonium salts. In agreement with previous studies, they observed highfield shifts of C(1) carbons and lowfield shifts of diazo nitrogens. The authors reported a good linear correlation between polarographic half-wave potential (direct measure of electrophilicity) and ^{13}C shifts of C (1).

In contrast to the ^{13}C chemical shifts, those of ^{15}N shift downfield as the substituents become more electron donating. The ^{15}N resonance moves generally to highfield as the half-wave potential, $E_{1/2}$ increases. The authors explained this by using the following resonance structures (Figure 1.11).

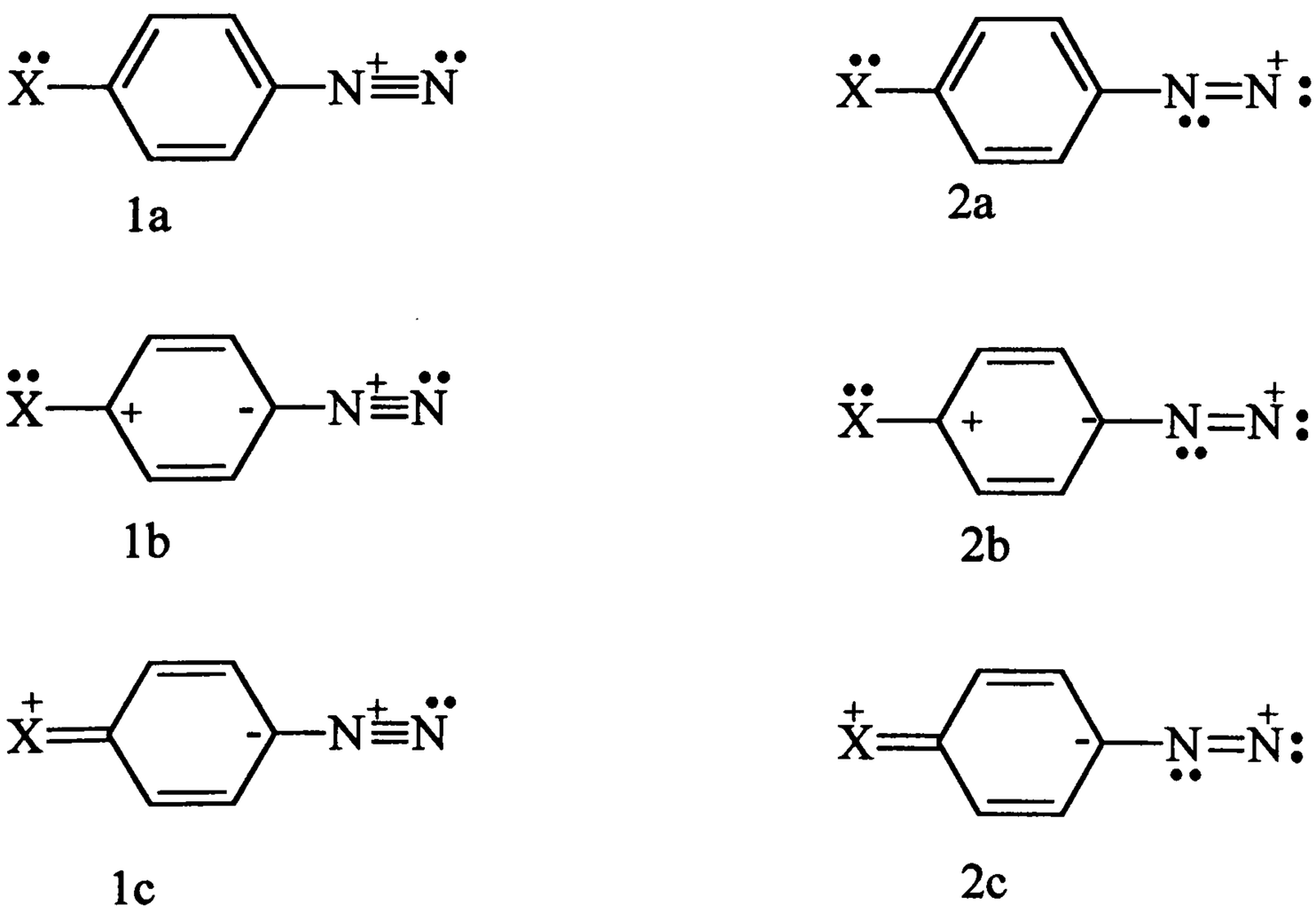


Figure 1.11

These resonance structures are also compatible with the slight lengthening observed for the N-N bond. The ^{15}N chemical shift of N(1) moves downfield by gaining a lone pair, and N(2) by gaining a positive charge (1a ↔2a, 2b or 2c).

Further evidence against the quinoid structure was provided by Axenrod, Watnick and Huang.[13] They analysed the ^{13}C-^{15}N coupling constants and ^{13}C chemical shifts for substituted benzenediazonium salts. They observed that only one-bond coupling is sensitive to the ring substituent with values of $^{1}J(^{13}C$-$^{15}N)$ ranging from 10.0 Hz in 3,5-dimethylbenzenediazonium ion to 19.8 Hz in the 2,4,6-tribromobenzenediazonium ion, and that the magnitude is enhanced by both electron withdrawing and releasing substituents. Evidence against a change in the C(1)-N(1) bond order was highlighted when the authors observed the effect of sterically inhibiting the resonance interaction of the nitro group. With 3,5-dimethyl-4-nitrobenzenediazonium ion (Figure 1.12) C(1) experiences reduced deshielding, but the magnitude of ^{1}J (^{13}C-^{15}N) is unaffected indicating no change in the C(1)-N bond order.

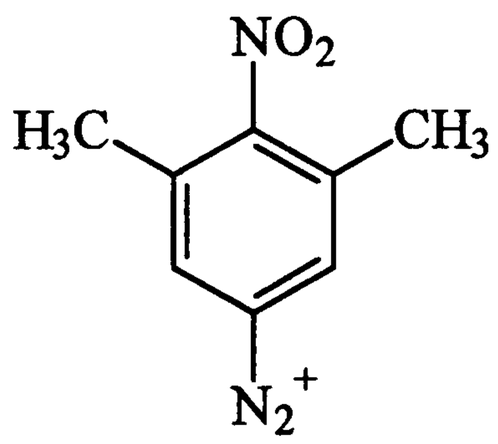


Figure 1.12

Olah demonstrated the ambident nature of benzenediazonium ions by analysing the changes in the charge distribution of the aromatic carbons as different substituents were put into the ring. He studied the ^{13}C NMR for a series of benzenediazonium tetrafluoroborates and hexafluorophosphates in sulphur dioxide solutions at -30°C.[10] He observed a marked upfield shift of the C(1) carbon bearing the $-N_2^+$ substituent. This effect was further enhanced when a para substituent Y on the ring is electron releasing. The carbon bearing the substituent is shifted downfield indicating these carbons are electron deficient compared to benzene. The largest downfield shifts occurred for carbons that could accommodate positive charge. Olah proposed the following canonical structures determined on the basis of ^{13}C chemical shifts (Figure 1.13), provide a significant resonance contribution to benzenediazonium salts.

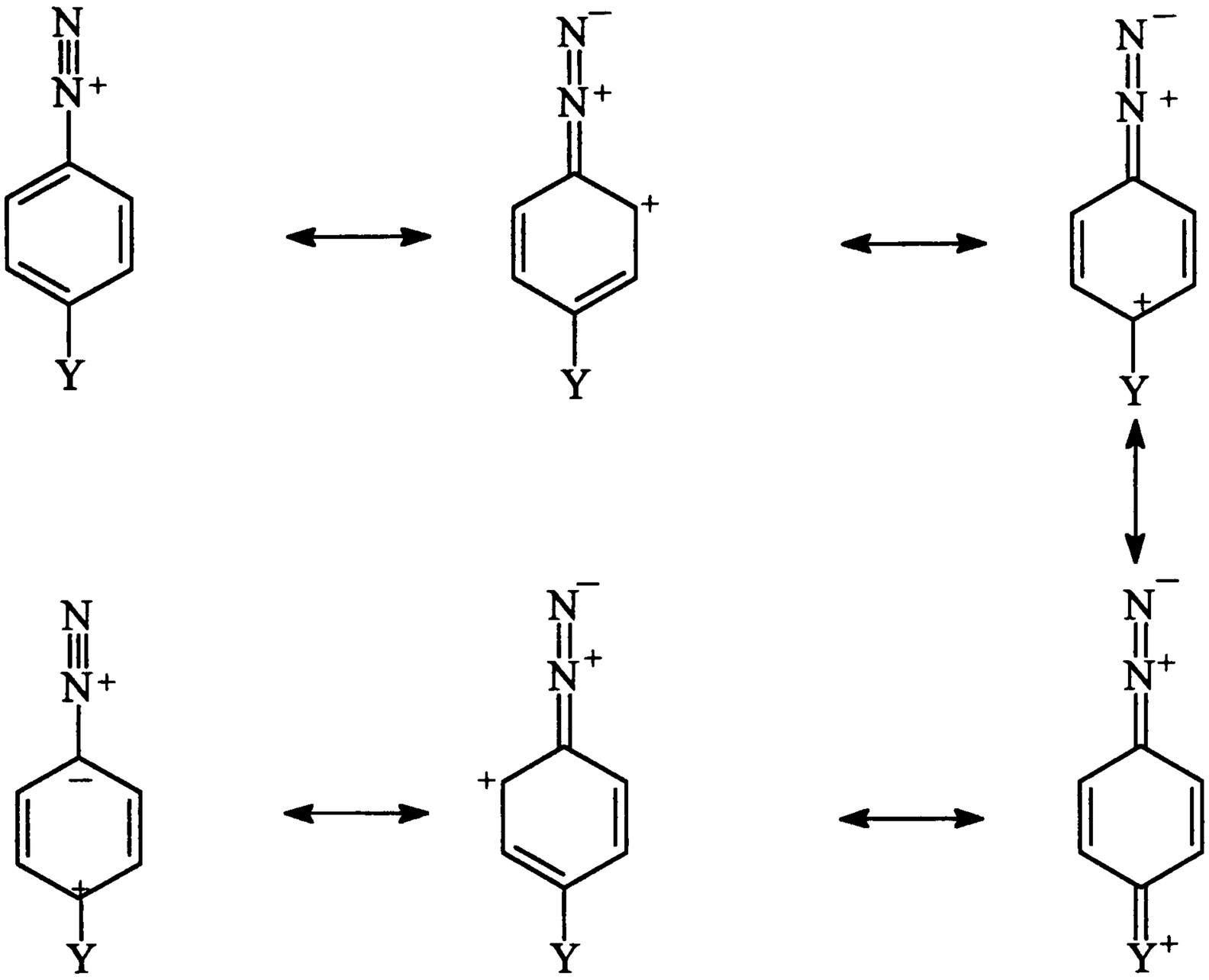


Figure 1.13

Various X-ray crystallography studies supported the case against structure (2) Figure 1.10. The dominance of structure (1) Figure 1.10 for the ground state of benzenediazonium chloride was established by Romming in 1963.[7] His X-ray investigations showed that the C(1)-N(1) bond length corresponds to that of a C-N single bond and N(1)-N(2) to a triple bond. Similar results were obtained for a number of substituted diazonium salts with complex anions. In *p*-benzenebisdiazonium tetrachlorozincate (p-$N_2C_6H_4N_2$)($ZnCl_4$)$_2$, Romming found, in addition to N triple and C-N single bonds, an appreciable deviation from hexagonal symmetry of the benzene ring showing the antiquinoid geometry.[8] From this he concluded that there was no evidence for the contribution of (2).

Cygler, Przybylska and Elofson obtained the crystal structure for benzenediazonium tetrafluoroborate.[9] They found the bond lengths and angles agreed well with those of Romming for benzenediazonium chloride (Table 1.2). The C-N and N≡N triple bond lengths are 1.415 and 1.083 Å respectively. The bonds of the benzene ring do not show any difference as they vary from 1.371 to 1.383 Å. The ion is seen to have an approximate plane of symmetry passing through the N(2), N(1), C(1) and (C4) atoms.

Table 1.2 Bond lengths and angles in benzenediazonium tetrafluoroborate and in benzenediazonium chloride (esd's in parentheses).

Bond	Length (Å)	
	$C_6H_5N_2BF_4$	$C_6H_5N_2Cl$
N (1)-N(2)	1.083(3)	1.097(6)
N(1)-C(1)	1.415(3)	1.385(9)
C(1)-C(2)	1.377(4)	1.374(8)
C(2)-C(3)	1.382(4)	1.383(10)
C(3)-C(4)	1.376(5)	1.376(8)
C(1)-C(4)	2.682(4)	2.689(8)

Bond Angle (Å)	Compounds	
	$C_6H_5N_2BF_4$	$C_6H_5N_2Cl$
C(1)-C(2)-C(3)	115.9(3)	117.6(7)
C(2)-C(3)-C(4)	120.5(3)	119.8(7)
C(3)-C(4)-C(5)	121.3(3)	121.192)
C(6)-C(1)-C(2)	126.0(2)	126.1(2)

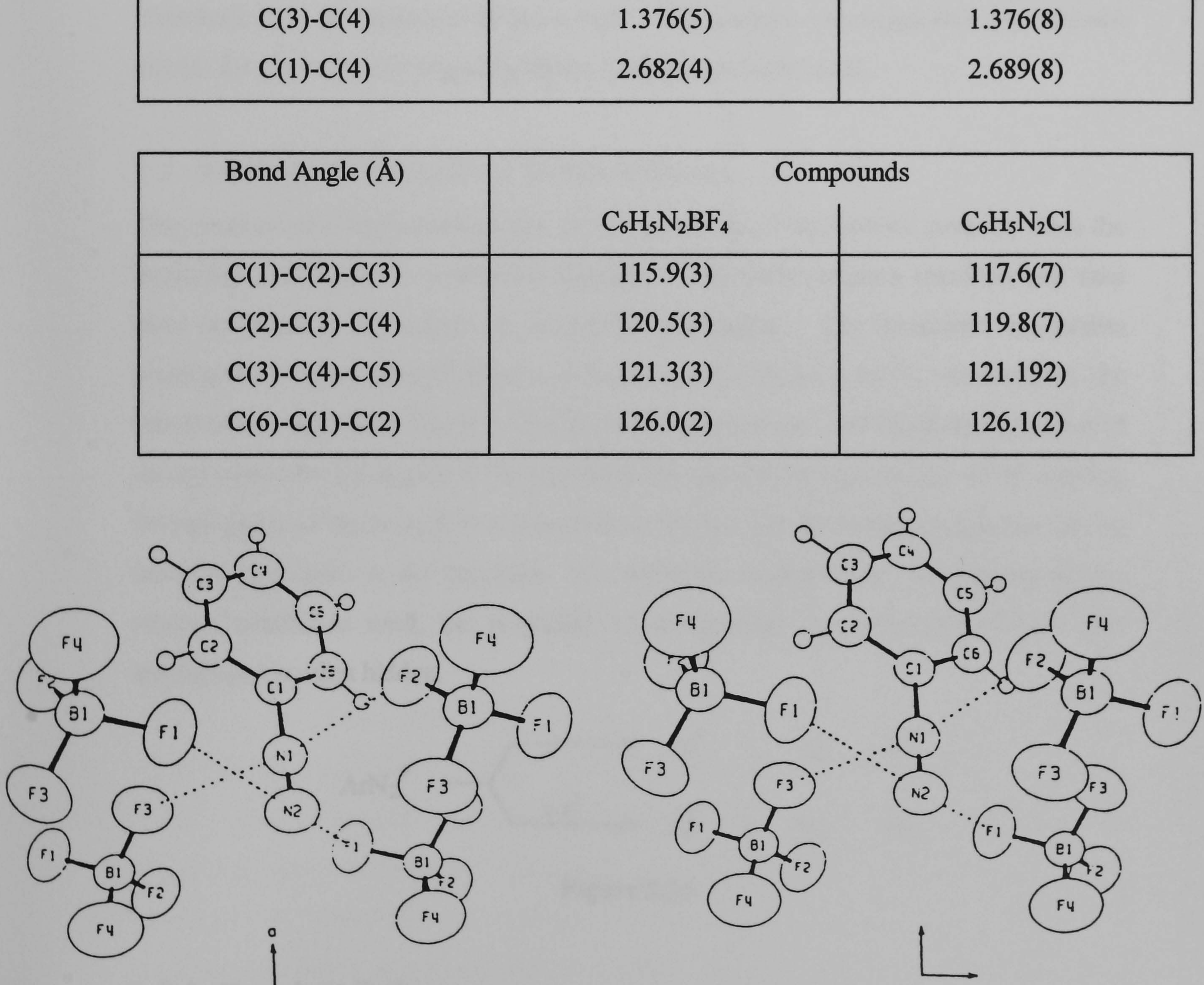


Figure 1.14 A stereoscopic view of benzenediazonium cation with surrounding BF_4^- groups. The closest N to F contacts are shown by broken lines.

The C(1)-C(4) distance is observed to be shorter than in benzene. The packing of BF_4^- ions surrounding the benzenediazonium cation is shown in Figure 1.14. Each nitrogen atom makes 4 short contacts <3.1Å with F of each of the four anions. However 3 contacts N(1)-F(2), N(1)-F(3) and N(2)-F(1) are slightly shorter than the sum of the van der Waals radii (2.85Å). The close proximity of F to N(1) suggests that electron density of the N(1)-N(2) triple bond may be displaced towards the N(1) atom resulting in sharing of the positive charge between the two nitrogen atoms. This would suggest that in addition to the main resonance form (1) Figure 1.10, the form (3) Figure 1.10 makes a contribution to the structure of the cation. The authors concluded that no evidence existed for the resonance form (2) Figure 1.10 (quinoid structure).

1.5 Mechanistic Details of Dediazoniation.

The reactions of arenediazonium ions ArN_2^+ have aroused mechanistic curiosity since the beginning of their use in preparative chemistry. The dediazoniation reactions may take place by either a heterolytic or homolytic mechanism. The homolytic mechanism requires an electron transfer from a reducing agent (Figure 1.16 b). In contrast, the heterolytic counterpart (Figure 1.16 a) is an S_N1 mechanism. Although the formation of an aryl cation would appear to be less likely, in view of the high energy of the species, the energetics of the homolytic and heterolytic are not too dissimilar because the driving force in both cases is the formation of a molecule of dinitrogen. Depending on the reaction conditions used, the possibility of competition or coexistence of the two mechanisms is often hidden.

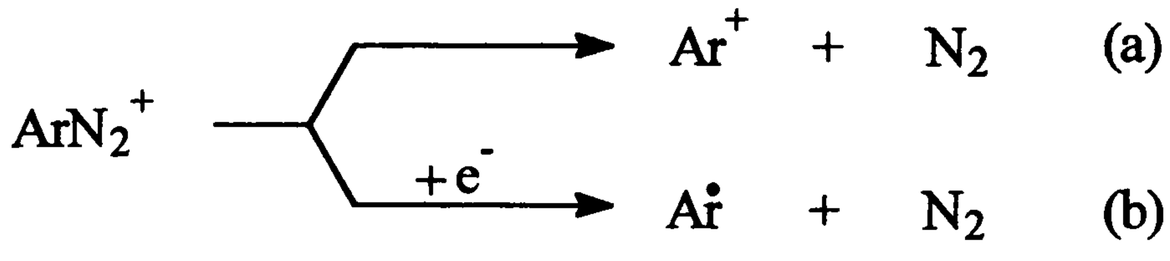


Figure 1.16

1.5.1 Homolytic Pathway.

The homolytic mechanism has a wider diversity of pathways than the heterolytic. This is due to the numerous reducing agents that have been used to generate the intermediate $Ar^{\bullet}$.

1.5.1.1 History.

In 1864 Griess noticed the ready replacement of the diazonium group by iodide to give ArI.[14] However, he found replacement of N_2 by Br^- or Cl^- to be more difficult as it required stronger reaction conditions which mainly led to phenol in water.[14] In 1884 Sandmeyer found that the use of copper (I) chloride or bromide allowed chloro or bromo dediazoniations to proceed more easily.[14] A couple of years later, Gattermann discovered copper powder could be utilised in the formation of chlorobenzene from benzenediazonium chloride.[14] The main breakthrough in this field occurred when Balz and Schiemann discovered the thermal decomposition of arenediazonium tetrafluoroborate in the absence of solvent afforded a good yield of aryl fluoride.[15]

In addition to the halodediazoniations, other dediazoniation reactions appeared in the meantime. Notably, Sandmeyer observed the preparation of cyanoarenes by the use of cuprous cyanide and an aromatic nitration taking place under cuprous catalysis.[14] At about the same time Pschorr developed an intramolecular arylation without copper catalysis while Mai described the reduction of arenediazonium salt to ArH by means of hypophosphorous acid as opposed to Griess's older method of employing ethanol.[14]

In 1924 Gomberg and Bachmann decomposed arenediazonium ions in a heterogeneous arene/alkali mixture through an intermediate aryl diazotate resulting in an intermolecular arylation to give unsymmetrical biaryls (Figure 1.17).[14]

$$ArN_2^+ + 2OH^- \xrightarrow{-H_2O} ArN{=}NO^- \xrightarrow{Ar'H} ArAr' + OH^- + N_2$$

Figure 1.17

The formation of aryl radicals in the dediazoniation reactions was proposed for the first time by Grieve and Hey in 1934.[16] The true mechanistic breakthrough was made by Waters. On the basis of concepts already advanced in a review with Hey, he explained that Sandmeyer's cuprous salt functioned as a reducing agent to give an aryl radical (Figure 1.18). The aryl radical was suggested to react subsequently with a halide ion to give the aryl halide or with another aryl radical to give a biaryl. In the presence of a suitable hydrogen atom donor, the aryl radical could also be reduced to the arene.[17]

$$ArN_2^+ + Cu^I \longrightarrow Ar^\bullet + N_2 + Cu^{II}$$

Figure 1.18

On the grounds of electrochemical evidence, Waters linked the uniqueness of the cuprous salt to its correct potential for bringing about the reductive step. Weaker reductants such as Cd(II), Mn(II), Ni(II), Co(II), and Zn(II) were simply not able to give the electron transfer step. Waters also suggested that a single electron transfer mechanism could operate with iodide ions as well. In contrast, the other halide ions are poorer reductants and therefore unable to transfer an electron. These halide ions require the assistance of an accompanying cuprous cation in order to react. Waters also suggested that besides the iodide ion, other nucleophiles such as nitrite, thiolate, xanthate, and sulfur dioxide, having a redox potential close to that of Cu(I) could replace the diazo group in the absence of a cuprous cation by giving the direct transfer of an electron to ArN_2^+.

1.5.1.2 How the homolytic dediazoniation takes place.

This section examines the conditions under which the homolytic step (Figure 1.16 b) can be made to occur.

1) Reduction at the electrode.

The most straightforward way of promoting step b in Figure 1.16 is at the surface of an electrode. When a diazonium salt acquires an electron, it forms a diazenyl radical which in turn gives up dinitrogen to form an aryl radical (Figure. 1.19). Electrochemical studies show that diazonium salts are reducible species (Table 1.3). The polarographic half wave reduction potential ($E_{1/2}$) of benzenediazonium tetrafluoroborate in sulfolane is +0.295V (vs SCE) according to Elofson and Gadallah.[18] The $E_{1/2}$ increases to 0.45V with a *p*-nitro substituent and decreases to +0.14V with a *p*-methoxy group. A linear relationship with a slope of 0.22 has been found by these authors, between the $E_{1/2}$ values and the σ^+ substituent constants. The correlation obtained indicates that electron-withdrawing substituents increase the ease of reduction of the substrate while electron releasing substituents stabilise the starting diazonium salt decreasing its tendency to acquire an electron.

Table 1.3 Half-wave reduction potentials of arenediazonium ions in tetramethylene sulfone (sulfolane).

substituent	$E_{½}$ (vs SCE), V	substituent	$E_{½}$ (vs SCE), V
p-NO_2	+ 0.450	*p*-SO_3^-	+ 0.297
p-CN	+ 0.433	H	+ 0.295
p-Cl	+ 0.350	*p*-CH_3	+ 0.250
p-Br	+ 0.383	*p*-OCH_3	+ 0.140

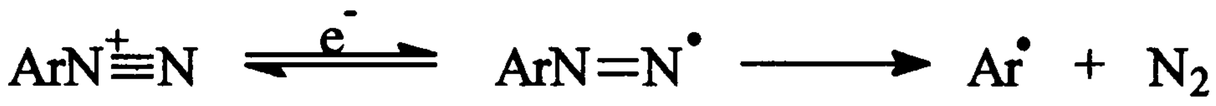


Figure 1.19

2) Radiolytic Reactions.

Another way of supplying an electron to a diazonium salt is by a radiolytic technique (Figure 1.21). Solvated electrons produced in water solution by γ-radiation from a ^{60}Co source have been used by Packer et al. to induce a free radical chain reaction between arenediazonium ions and a variety of reducing agents (RH_2).[19]

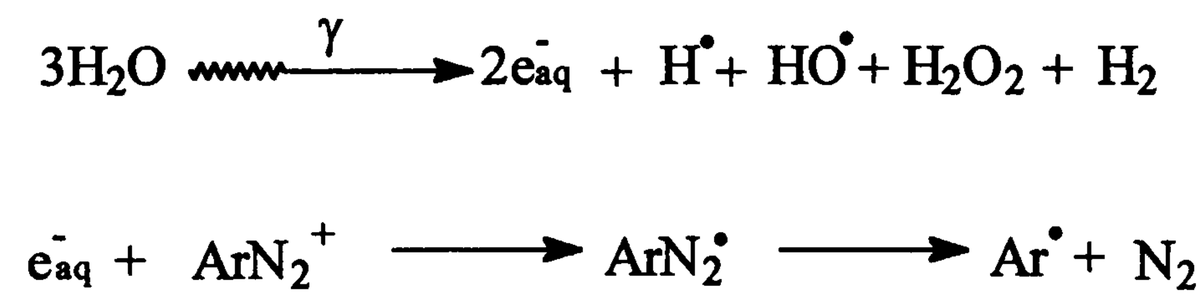


Figure 1.21

The aryl radicals produced by a solvated electron in the primary radiolytic step abstracts hydrogen from the reducing agent (RH_2 which can be either ethanol or propan-2-ol), forming a new radical ($^{\bullet}RH$) which then reduces the diazonium ion in a chain-propagation process (Figure 1.22).

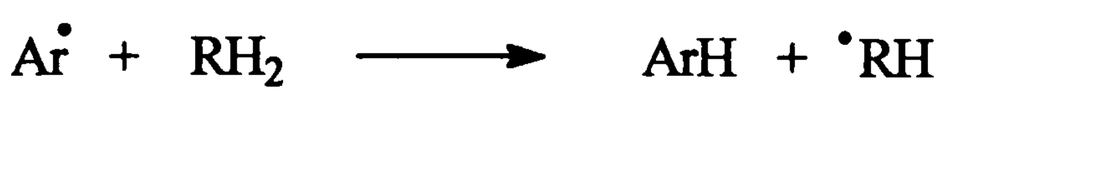


Figure 1.22

The overall reaction is a hydrodediazoniation (Figure 1.23).

$$ArN_2^+ + RH_2 \longrightarrow ArH + N_2 + R + H^+$$

Figure 1.23

These authors used alcohols, aldehydes, or formate ion as reducing agents.[19] They indicate that the reaction between $^{\bullet}RH$ and ArN_2^+ is a true electron transfer and does not involve prior addition of the radical to the diazonium nitrogen with subsequent dissociation. They were also able to measure quantitatively the rate of electron transfer between the •RH derived from benzyl alcohol and para-substituted diazonium salts. Correlating these results with σ^+ constants gave a good linear relationship with a ρ value of 0.55. These results uphold a reductive process via electron transfer and are consistent with Elofson and Gadallah's polarographic reduction of diazonium salts.[18]

3) Photoinduced Electron Transfer

A third method of formation of $Ar^{\bullet}$ from diazonium salts is by photochemical decomposition. Work by Ando and co-workers indicates that the primary process is a homolytic scission of the C-N bond of the diazonium salt, and electron transfer from the counterion.[20] This follows from the excitation of a charge transfer (CT) complex between the electron donor (X^-) and the arenediazonium ion leading to an electron transfer.

$$ArN_2Cl \xrightarrow{h\nu} [\, Ar^{\bullet} + N_2 + Cl^{\bullet}] \xrightarrow{-N_2} ArCl$$

$$ArN_2BF_4 \xrightarrow{h\nu} ArF + N_2 + BF_3$$

Figure 1.24

In an alcoholic solution, homolysis is followed by hydrogen abstraction resulting in an overall hydrodediazonation. In addition, Ando reports light induced photolytic dediazoniation occurs in the solid state when X^- is Cl^- or BF_4^-, leading to aryl halides (Figure 1.24).

4) Reduction by Metal Cations.

The most familiar method of dediazoniation is the one induced by metal cations. Good yields of ArX (X = Cl, Br, CN) are obtained if cuprous salts are used as reducing agents as they have the correct redox potential (0.16V) for release of an electron to the arenediazonium ion. Other cations such as Sn(II), Cr(II), Ti(III), V(II) and Fe(II) possess the correct potential for reduction of the arenediazonium ion.[17] The reducing ability of the donors reflects their redox potential. The better the reductant, the more efficient the X-dediazoniation process. A threshold value appears beyond which the electron transfer (E.T.) no longer occurs efficiently.

In the presence of CuX the electron transfer from univalent copper to the diazonium ion is very easy and gives the $ArN_2^{\bullet}$ radical; which rapidly decomposes to $Ar^{\bullet}$ and N_2. The aryl radical then combines with $X^{\bullet}$ from the salt of divalent copper ($Cu^{II}X_2$). ArX is formed and CuX is regenerated, hence the process is catalytic (Figure 1.25).

$$ArN_2^+ + CuCl_2^- \longrightarrow Ar^{\bullet} + N_2 + CuCl_2 \longrightarrow ArCl + N_2 + CuCl$$

Figure 1.25

5) Anion induced dediazoniation.

The anion induced dediazoniation is related to the cation induced one, as it is based on the redox potential of the electron donor species.

$$ArN_2^+ + Y^- \longrightarrow ArN_2^{\bullet} + Y^{\bullet}$$

Figure 1.26

A nucleophile present as the counterion of the diazonium ion (Figure 1.26), or purposely added in solution may give an outer-sphere E.T. to ArN_2^+, or form a covalent adduct with the cationic functionality due to the favourable electrostatic interaction.[21] The choice depends on the oxidation potential of the nucleophile and on the solvent features. The nucleophile can also be the solvent.

An iodide ion can behave as a nucleophile as it has the correct redox potential (E^o = 1.3 V). The first step involves a direct release of an electron to the arenediazonium ion (Figure 1.27).[22,23] The diazenyl radical then fragments to give Ar•.

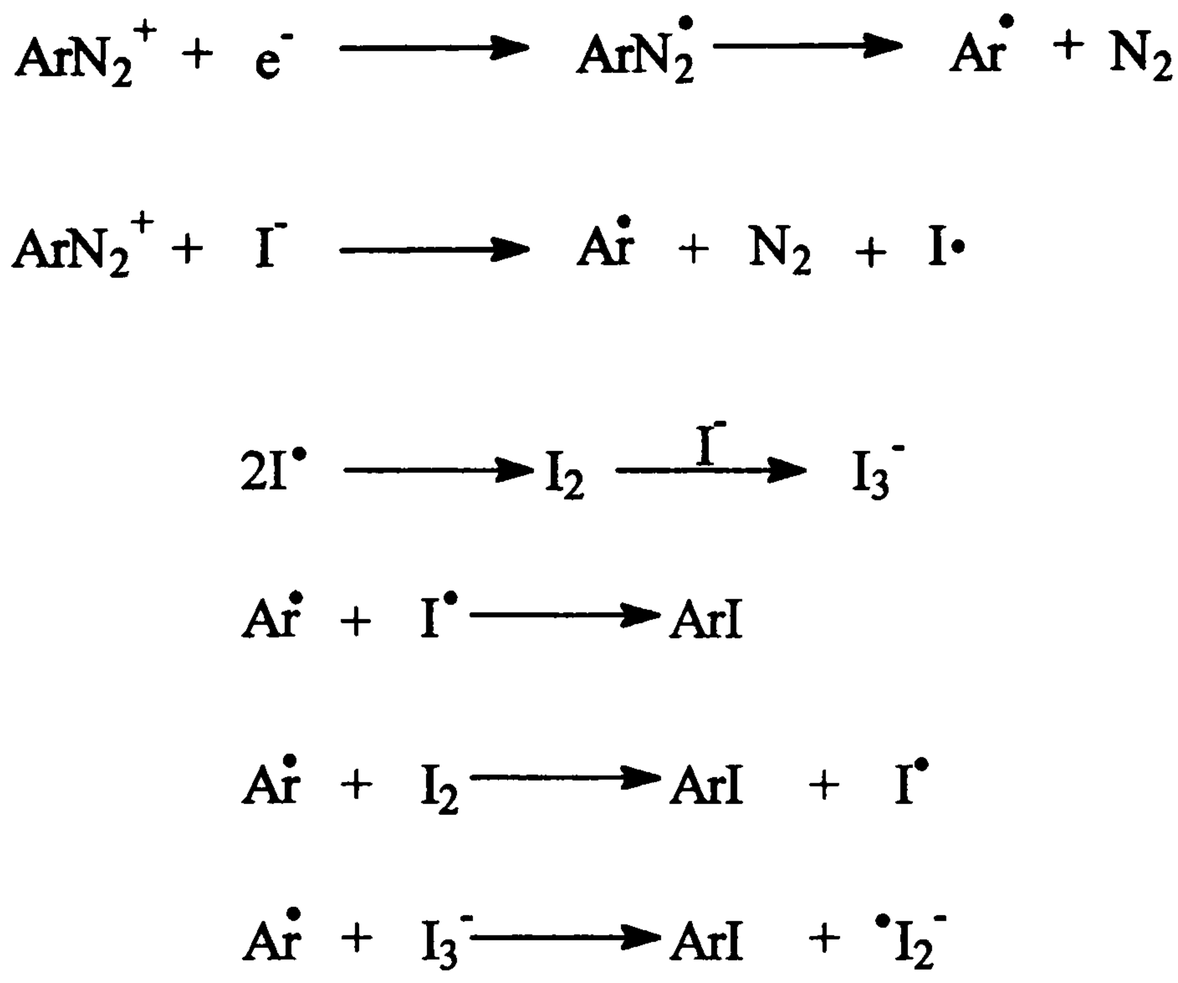


Figure 1.27

This radical may then couple with I•, iodine or I_3^- to produce aryl iodide.[24] In view of the high efficiency of the reaction of Ar• with iodine ($k = 1 \times 10^{10}$ M^{-1} s^{-1}) it would appear that this is the species that is responsible for the formation of ArI. Chloride (E° = 2.6 V) and fluoride (E° = 3.6 V) have redox potentials much higher than that of iodide, therefore they are not capable of a direct E.T. to ArN_2^+ but must rely on a cuprous cation purposely added to fulfill that task.[25]

6) Solvent-Induced dediazoniation.

Finally in this section, the thermal homolytic dediazoniation induced by the solvent is mentioned. Szele and Zollinger have shown that the thermal homolytic dediazoniation is favoured by increasing the nucleophilicity of the solvent or by increasing the electrophilicity of the β nitrogen atom of the diazonium ion by placing suitable substituents on the aromatic ring.[26,27] The net result is the solvent can act as an electron donor to the nitrogen atom. The higher the electron donor capacity of the solvent or the electrophilicity of ArN_2^+ the more the reaction follows the homolytic decomposition pathway (Figure 1.28).

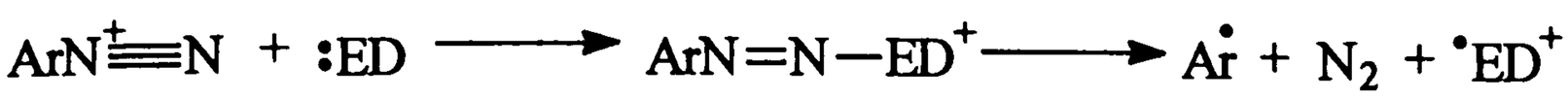


Figure 1.28

1.5.2 Heterolytic dediazoniation.

The heterolytic dediazoniation of arenediazonium salts is a reaction which has been studied intensely by various authors over many years. Most of the work has been concerned with the elucidation of the mechanism. As early as 1940 Hammett postulated and Crossley verified experimentally a slow unimolecular heterolytic dissociation of arenediazonium ions into aryl cations and N_2.[28,29] The highly reactive cations formed in both cases were assumed to react very rapidly with nucleophiles (including solvent) in subsequent steps (Figure 1.29).

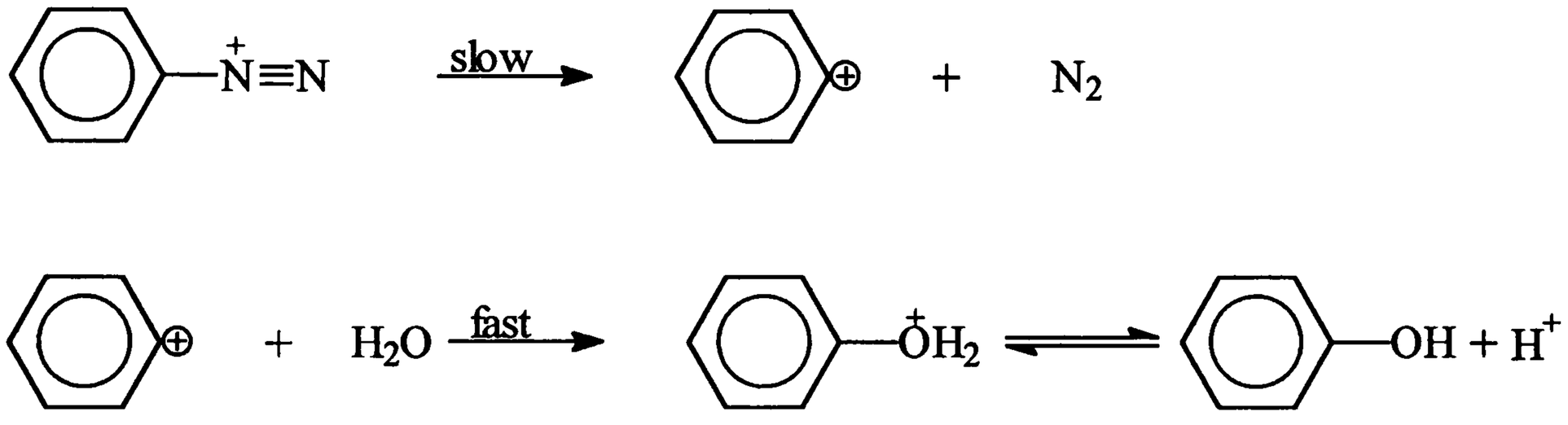


Figure 1.29

Lewis and Hinds found in 1952 that some of these dediazoniations were not only first order with respect to diazonium ions but also to nucleophiles.[30] Lewis postulated a bimolecular process involving as a first step attack of the nucleophile on the diazonium ion.[31] However this mechanism was not supported by later evidence such as substituent effects and kinetic isotope effects.[32-34]

Subsequent work by several groups showed that the rate of decomposition of benzenediazonium ion in water is first order in benzenediazonium tetrafluoroborate and shows little dependence on the concentration of added nucleophile.[35-38] In 1964 it was shown for the first time that a rearrangement reaction accompanies the heterolytic dediazoniation (Figure 1.30).[39]

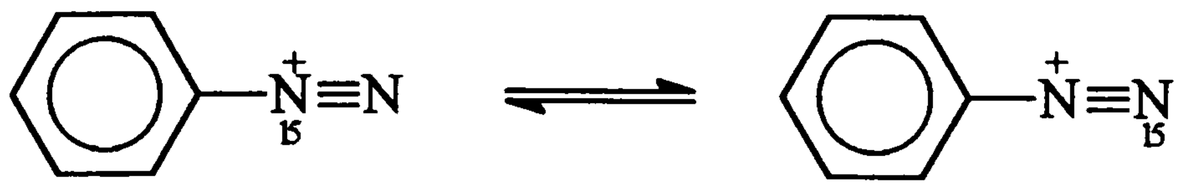


Figure 1.30

Zollinger found that the Nα-Nβ rearrangement takes place to a significant extent when TFE was used as a solvent.[40] The rate ratio of rearrangement to solvolysis (k_r/k_s) is 0.072 at 30°C and 0.079 at 50°C. This contrasts with the value obtained in water at

35°C of 0.016 which is in agreement with Lewis's value of 0.014 and Swain's value of 0.016.[41,42]

These results suggested to the authors that a phenyl cation intermediate exists, that can undergo a reversible reaction with the nitrogen molecule present.

DeTar showed that the rates of the thermal decomposition in aqueous solution of benzenediazonium, 2,3,4-trimethylbenzenediazonium, 3-bromobenzenediazonium and the 3-chlorobenzenediazonium ions had no dependency on the anions present.[35] The consistency of the rate constants in solutions as diverse as H_2SO_4, CH_3CO_2H and CH_2Cl_2 provided further evidence for a rate-determining step (R.D.S.) that involved the formation of a phenyl cation. In 1975 Swain and coworkers published a series of papers studying reactions of arenediazonium salts in a variety of solvents.[43] To the authors, there appeared to be 8 possibilities for the R.D.S. (Figure 1.31) where the nucleophile Y may be H_2O, Br^-, Cl^-, or F^-. The first possibility shown is the one-step bimolecular displacement which was adopted in 1969 as the preferred mechanism for the reaction of arenediazonium ions with H_2O, SCN^-, Br^- or Cl^- in aqueous solutions. The main evidence that excludes all mechanisms except 3 is that, changing from 80 to 105 % H_2SO_4, the rate constant for hydrolysis changes less than 2%. Since the activity of water changes more than 1000 times throughout this solvent range, and given the fact that HSO_4^- is a much poorer nucleophile than water, the solvent molecules can not be involved in the R.D.S. This means the extent of covalent bond formation between carbon and the nucleophile (water molecules or HSO_4^-) at the transition state (T.S.) is extremely small or zero. This is confirmed by the large positive entropy of activation and by the absence of a solvent isotope effect.

The authors also measured the rate of solvolysis of benzenediazonium tetrafluoroborate in three solvents of very different polarities CH_2Cl_2, CH_3CO_2H and H_2SO_4. They found the rate constants for these reactions to be similar. This indicated to the authors that the R.D.S does not change and the solvents only solvate the intermediate very weakly. Mechanisms involving benzyne as an intermediate were excluded as no isomerized products were obtained in aqueous solution. By a process of elimination, the only mechanism that was found to accommodate all the data seen involved a phenyl cation intermediate (3).

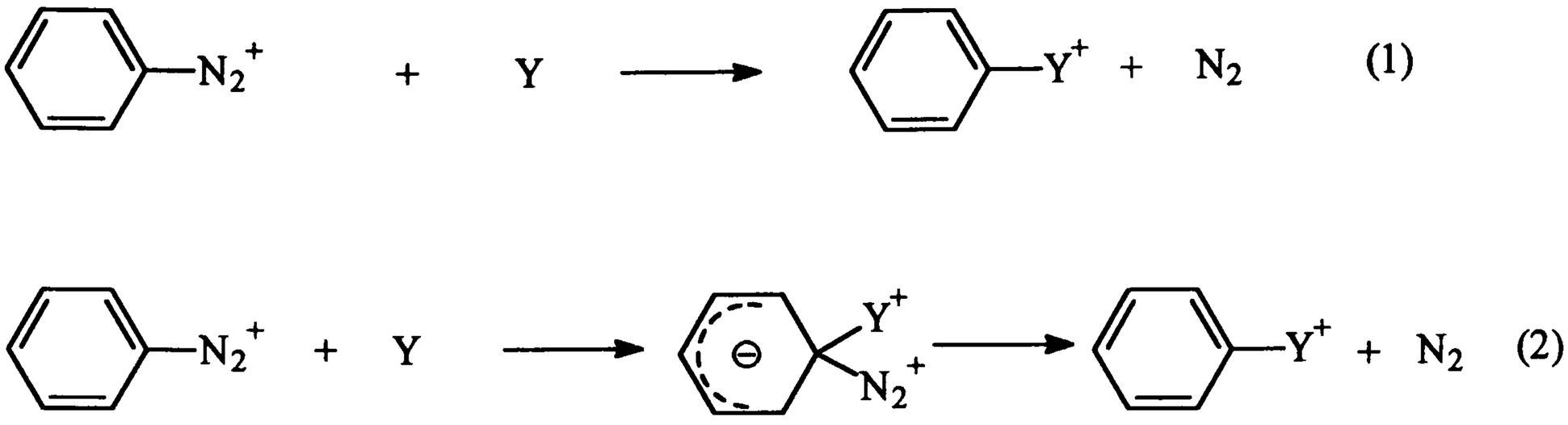


Figure 1.31

1.5.2.1 Exclusion of an aryne mechanism.

Although Zollinger and Swain independently proposed the aryl cation intermediate, Cadogan et al. showed under certain conditions with suitably substituted arene-diazonium salts a dediazonation mechanism involving an aryne intermediate occurs (Figure 1.32).[44]

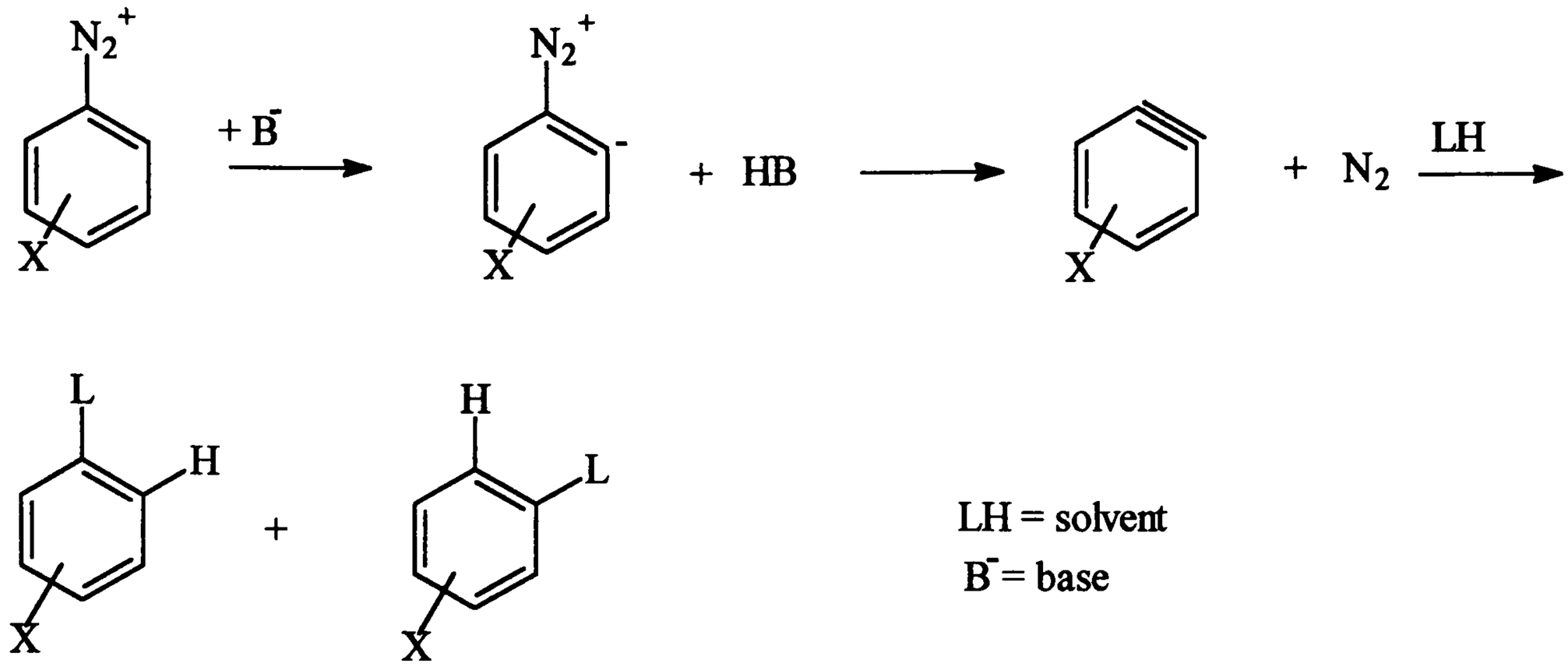


Figure 1.32

Zollinger checked for this possibility in the TFE system, aware that such a mechanism might explain the N_α-N_β rearrangement of the two nitrogen atoms of an arenediazonium ion.[45] In TFE he found that the isotopic scrambling occurred to a much higher degree than in aqueous solution (1-2%). If this mechanism were occurring, isomeric solvolysis products would be expected. Zollinger investigated the dediazoniation products of 4-chlorobenzenediazonium tetrafluoroborate in TFE. GLC analysis of the products showed no meta derivatives to be present. Therefore the authors concluded the reaction does not occur via this mechanism.

1.5.2.2 Kinetic Isotope Effect evidence for an aryl cation.

Work by Swain and co-workers on the hydrogen and nitrogen kinetic isotope effects for the heterolytic dediazoniation provided further information on the aryl cation intermediate.[33] They reported an α-nitrogen kinetic isotope effect k_{14}/k_{15} of 1.0384 for the solvolysis of benzenediazonium ion in aqueous 1% H_2SO_4 at 25°C. From this value they calculated the β-nitrogen kinetic isotope effect to be 1.0106, which gave them an overall nitrogen isotope effect of 1.0245 for normal benzenediazonium tetrafluoroborate. This value was found to be in agreement with previous studies of nitrogen isotope effects by Lewis and Insole who reported a k_{14}/k_{15} value of 1.019 for 4-toluenediazonium tetrafluoroborates.[41] Brown and Drury obtained a value of 1.022 which they showed to be insensitive to substituents (H, 2-CH_3, 3-CH_3, 4-CH_3) and temperature 7-68°C.[46] Swain concluded that the very large α-nitrogen isotope effect (1.0380) indicated that the

C-N bond has a greatly reduced vibrational frequency at the transition state which corresponds to almost complete formation of phenyl cation. The smaller value for the β-nitrogen isotope effect suggested that the N_2 leaving group cannot be considered as a rigid unit of 28 or 29 amu. This suggested that the transition state has an almost completely broken C-N bond which is consistent with a phenyl cation. If as earlier suggested a spirodiazirine intermediate was involved, a much smaller α-nitrogen K.I.E would be observed since the C-N bond would be much stronger in the transition state. Swain and co-workers produced further evidence that the mechanism of the reaction of benzenediazonium ion in solution in the absence of strong bases, reducing agents or light is slow decomposition to form the singlet cation.[33] He argued that delocalisation of the positive charge of the phenyl cation into the ring is not possible since the vacant orbital lies in the plane of the ring. The only means of stabilisation available is hyperconjugation with the ortho hydrogens and to lesser extents with the meta and para hydrogens. Swain stated that since hyperconjugation should strongly stabilise a localised carbonium ion, large secondary deuterium isotope effects would be expected if the ortho hydrogens were replaced with deuterium. The values he obtained experimentally for the secondary isotope effects agreed with the theory. He obtained an isotope effect of 1.22 for each ortho position, 1.08 for each meta and 1.02 for each para position. These results provided proof that stabilisation by hyperconjugation with the ortho hydrogens can occur (Figure 1.33).

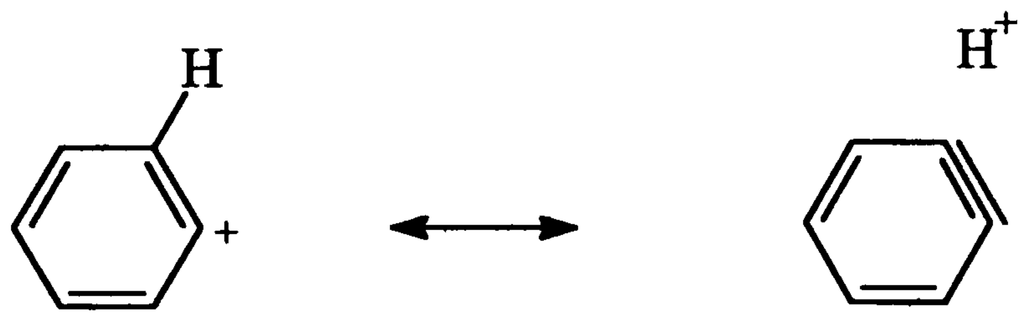


Figure 1.33

Further work by Swain showed that the hyperconjugation stabilisation of the positive charge in the phenyl cation results in decreased stretching and bending of the ortho C-H force constants.[33] The authors showed that, by introducing methyl groups, the isotope effect is decreased as electron donation from the methyl groups lessened the need for, and therefore the magnitude of, hyperconjugation. This can be seen with 3,5-dimethylbenzenediazonium 2,4,6-d_3 (1.48) compared to benzenediazonium 2,4,6-d_3 (1.52) tetrafluoroborates. The authors performed molecular orbital calculations using

the INDO method and showed the ground state of the phenyl cation to be a singlet, linear at C1 with the positive charge partially distributed throughout the molecule especially at the ortho hydrogens (Figure 1.34).

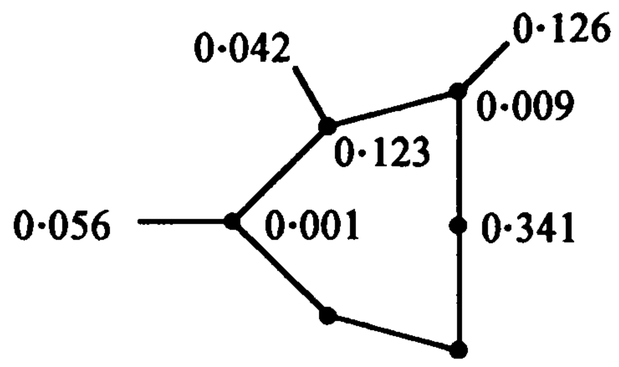


Figure 1.34 Charges on various atoms of singlet phenyl cation as calculated by the INDO molecular orbital method.

Zollinger studied the secondary deuterium isotope effects for the dediazoniation of 2,4,6-$^{2}H_3$ benzenediazonium tetrafluoroborate in TFE and HFIP and obtained the values 1.46 and 1.51 respectively, which were similar to results obtained by Swain.[47] He calculated the secondary deuterium isotope effect in the rearrangement in TFE to be 1.42. The fact that the isotope effect in the rearrangement is, within experimental error, the same as that during dediazoniation excludes the formation of a benzenespirodiazirine cation. If a benzenespirodiazirine existed, hyperconjugation would have no effect so the secondary deuterium isotope effect would be negligible. As this is not the case it must be assumed that rearrangement proceeds via a phenyl cation / N_2 molecular pair.

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1.5.2.3 The elucidation of the mechanism.

In a series of papers between 1976 and 1981 Zollinger and co-workers presented evidence supporting 2 steady state intermediates which led them to propose the now accepted mechanism for the heterolytic dediazoniation of arenediazonium ions in solution. They showed that rearrangement of the two nitrogen atoms of the diazonium group is greater by a factor of 3 to 4 in TFE, TFA and H_3PO_4 compared to water. This is explained by the fact that TFE is generally a poor solvating species for cations. In water the diazonium ion is well solvated and the reaction is slow. Once the process of splitting the C-N bond begins the aryl cation benefits much more from solvation than does the molecule ion pair; isotopic rearrangement is therefore low. In TFE the diazonium salt is poorly solvated and this reacts faster. The phenyl cation is not

appreciably stabilised and so the molecule-ion pair has a relatively longer lifetime allowing more rearrangement.

In 1974 Zollinger presented evidence for the first example of a reaction of nitrogen molecules with an organic reagent in solution.[40] The previous mechanism did not explain why the ratio k_r/k_s remained unaffected when the external N_2 pressure was increased to 1000 atm. Zollinger did not believe the phenyl cation to be the only steady state intermediate present. He investigated the possibility of external exchange of nitrogen molecules with benzenediazonium tetrafluoroborate in TFE and found that 2.46% of external nitrogen at 300 atm is incorporated into the diazonium salt. This value rose to 4.49% at 1000 atm. Another experiment which provided conclusive proof for the mechanism he later proposed was that under a pressure of 320 atm of carbon monoxide a solution of benzenediazonium tetrafluoroborate in TFE yielded 5.3% 2,2,2 trifluoroethyl benzoate in addition to the normal products (fluorobenzene and 2,2,2 trifluoroethyl ether). Zollinger proposed the following energy diagram for the reaction (Figure 1.35)

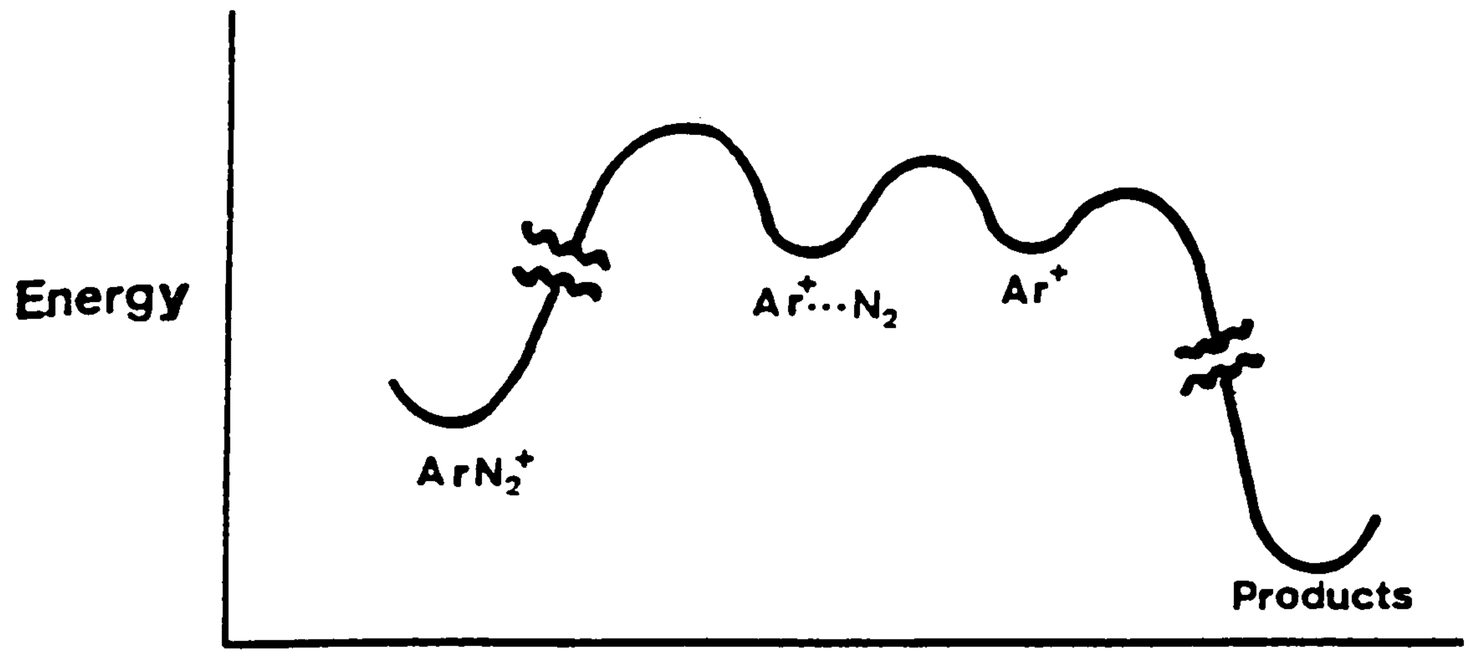


Figure 1.35

and the following mechanism (Figure 1.36).

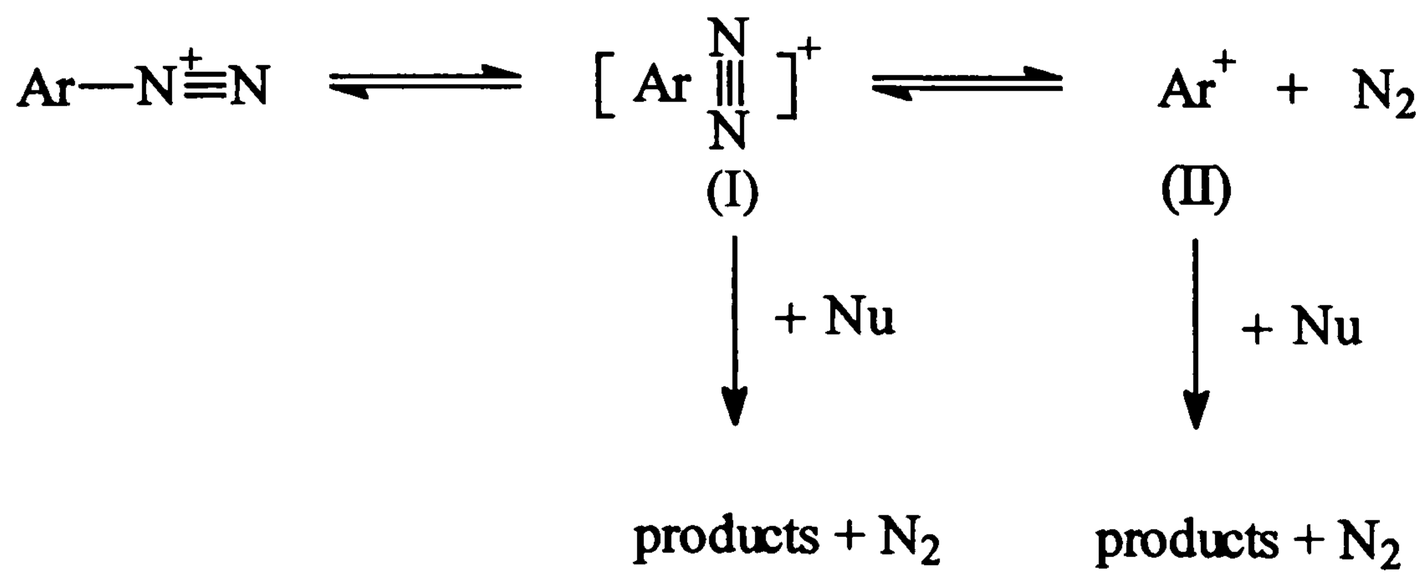


Figure 1.36

Two intermediates are proposed; the tight ion-molecule pair (I) and the free aryl cation (II). Previous work in the presence of high pressures of CO and using H_2O as the solvent led to no incorporation of the CO molecule, the reason for this according to Zollinger is H_2O is a solvent of high nucleophilicity so it reacts with the first intermediate to produce phenol thereby suppressing the formation of the free aryl cation.

The study of the solvolysis reaction of benzenediazonium tetrafluoroborate in TFE under high pressures of external nitrogen resulted in important observations (Figure 1.37). More rearrangement product (III) than exchange product (IV) was observed despite there being at least equal if not more external nitrogen in the solvation shell around the phenyl cation. Also observed is an increase in the amount of exchange product as the pressure of nitrogen is increased whereas no change is seen in the amount of rearranged product. The authors concluded that rearrangement occurs through the first intermediate and exchange through the second.

III

IV

Figure 1.37

1.5.3 Dediazoniation in the presence of alcohol.

Specific citations (e.g. Advanced Orgainc Chemistry), cites that the best and most effective method of reducing arenediazonium salts to their corresponding hydrocarbons is by the use of ethanol or hypophosphorous acid.[49] This report fails to mention that reduction by ethanol is substituent dependent. Griess reported in 1864 that benzenediazonium salts are reduced upon boiling with ethanol.[50] This report became accepted as a general method of obtaining arenes in spite of later evidence to the contrary. It soon became apparent that the decomposition of benzenediazonium salts with ethanol yields phenyl ethyl ether with only a small amount of benzene.

Remsen and Orndorff showed in 1887 that Griess had been in error in the case of benzenediazonium sulphate and nitrate.[50] They showed that these react to give phenyl ethyl ether contaminated with a little benzene. Hantzsch and Jochem confirmed their findings in 1901 when they made a careful study of the action of ethanol on benzenediazonium chloride and sulphate.[50] Despite the numerous demonstrations of the unreliability of ethanol as a reducing agent its use persisted. In 1909 Cain reported on the reaction of 2,3,5,6-tetramethyl-4-nitrobenzenediazonium ion with ethanol to give the 2,3,5,6-tetramethylnitrobenzene.[50] It was not until 1952 that it was recognised that the product was actually an aryl ether derivative.

Later work by various people in this field showed that electron donating substituents favoured the formation of aryl ethers whilst electron withdrawing groups such as nitro favoured the formation of benzenes.[116] Although it is widely accepted that substituents govern whether a heterolytic or homolytic mechanism occurs, the literature still tends to refer to this reaction incorrectly by ignoring substituent effects and generalising the reaction.

1.5.4 Factors affecting homolytic or heterolytic mechanisms.

A significant observation of DeTar and Kosuge was that product selection between ArH and ArOR was strongly dependent on the atmosphere above the reaction mixture for 4-bromo- and 4-methoxy- benzenediazonium salts.[51] They found that the reaction under O_2 gave mainly aryl ethers while the reaction under N_2 gave bromobenzene or anisole. The reasoning for suppression of the protodediazoniation reaction under O_2 , is O_2 is a prominent scavenger of radicals hence the reaction will proceed via the heterolytic route. Product studies by Broxton and Paik supported the observations of DeTar and Kosage that aryl ethers are formed by an ionic mechanism and hydrodediazoniation products by a radical mechanism.[52] Zollinger and co-workers also demonstrated that minor changes in reaction conditions, absence or presence of molecular oxygen or a change in the substituent, alter the nature of the products significantly indicating a change in mechanism. They reasoned that the heterolytic dissociation of an arenediazonium ion occurs easily as the leaving group forms a very stable product, N_2. In contrast, the homolytic cleavage of the C-N α bond of a diazonium ion would yield no primary product of reasonable stability as the formation of a dinitrogen radical cation ($N_2^{\cdot+}$) is not

an energetically favourable process. However, as products are formed via aryl radical intermediates, a mechanism must exist in which these radicals are formed by processes other than the monomolecular homolytic cleavage of the C-N bond.

The mechanism of the reaction of ArN_2^+ with the methoxide ion has been elucidated by Bunnett and co-workers.[53] A very fast formation of a covalent intermediate (arylazo ether) takes place in alkaline methanol (Figure 1.38).

Figure 1.38

This is followed by a one or two step homolytic decomposition (Figure 1.39), the cis arylazo ether being faster to fragment than the trans isomer.[54]

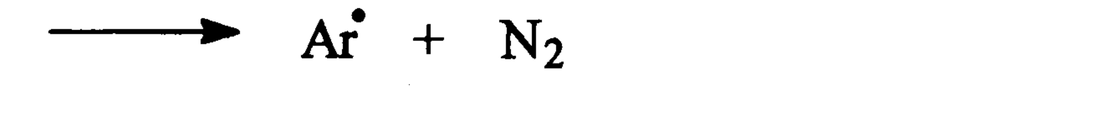


Figure 1.39

For the chain propagation steps, Bunnett's data support the following mechanism (Figure 1.40).

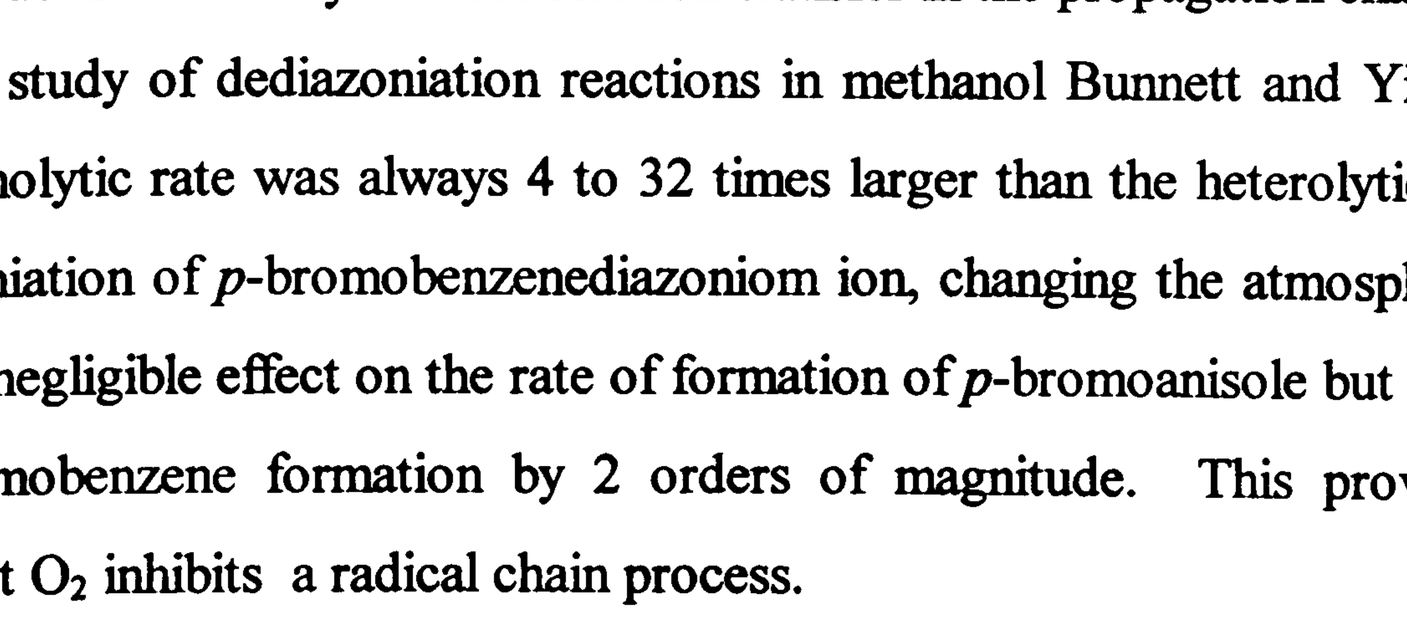


Figure 1.40

The overall hydro-dediazoniation comprises a preliminary homolytic decomposition of a covalent adduct followed by a direct electron transfer in the propagation chain.

In a careful study of dediazoniation reactions in methanol Bunnett and Yijima showed that the homolytic rate was always 4 to 32 times larger than the heterolytic rate.[55] For the dediazoniation of *p*-bromobenzenediazoniom ion, changing the atmosphere from O_2 to N_2 had a negligible effect on the rate of formation of *p*-bromoanisole but increased the rate of bromobenzene formation by 2 orders of magnitude. This provided further evidence that O_2 inhibits a radical chain process.

Zollinger showed that the addition of pyridine to TFE in the dediazoniation of benzenediazonium tetrafluoroborate increased the overall rate and yields of the products of homolytic decomposition.[56] He showed that the kinetics change from first order with respect to the diazonium salt in TFE to a non integral order between 0 and 1 in the TFE pyridine mixture. The magnitude of the order depends on the pyridine concentration. Using UV, NMR and CIDNP (chemically induced dynamic nuclear polarisation), Zollinger provided evidence of a covalent diazo intermediate which can undergo homolytic fragmentation to form an aryl radical, a nitrogen molecule and a gegenradical-cation (Figure 1.41).

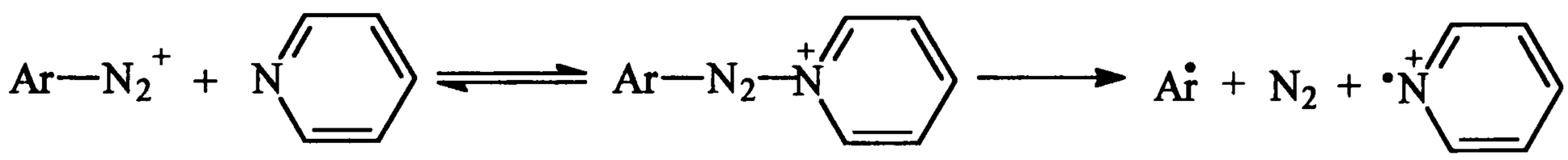


Figure 1.41

Zollinger further demonstrated that nitrite ions and diphenylhydroxylamine are good catalysts for the homolytic reaction as they both form stable radicals namely the $NO_2^{\cdot}$ molecule and diphenylnitroxide.[56] The following mechanism (Figure 1.42) explains why diphenylhydroxylamine can be used to catalyse the formation of biphenyl derivatives from arenediazonium salts.

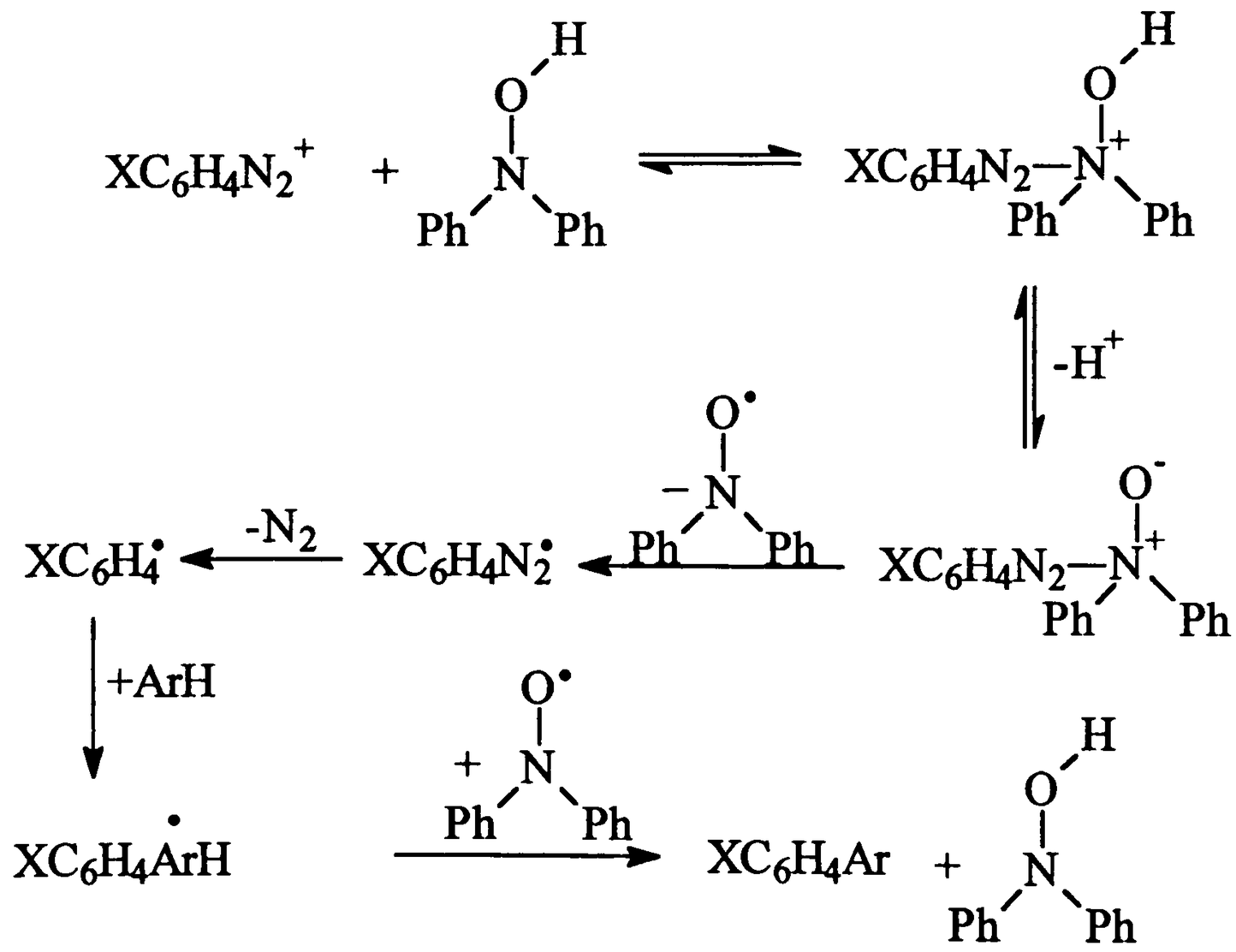


Figure 1.42

Zollinger concluded that not only the additives to solutions of diazonium salts catalyse the homolytic dediazoniation but also the solvent molecules if they are sufficiently nucleophilic. This is demonstrated in Table 1.4 which lists some solvents in which the products of dediazoniation were investigated. The last two columns contain parameters which give information on the nucleophilic character of the solvent (Koppel & Paju's B values and Schleyer's N_{BS} values).[57,58] It can clearly be seen that increasing the nucleophilicity of the solvent favours the formation of products of homolytic intermediates.

Table 1.4. Main products of substituted benzenediazonium salts in solvents of different nucleophilicities.

Solvent	Products				Solvent Parameters	
	p-NO_2	*p*-Cl	H	*p*-OCH_3	B	N_{BS}
HFIP	___	___	C	___	___	-3.93
TFE	C	C	C	C	___	-2.78
CH_3COOH	C	C	C	C	131	-2.05
H_2O (pH < 1)	C	C	C	C	156	-0.26
CH_3OH / O_2/ 0.1 M TsOH	C/R	C	C	C	218	+0.01
CH_3OH / N_2/ 0.1 M TsOH	R	C	C	C	218	+0.01
DMSO	R	___	C	___	362	___
HMPT	___	___	R	___	471	___
Pyridine	R	R	R	R	472	___

C= heterolytic (cationic products)

R = homolytic (radical products)

1.6 Substituent Effects.

The Hammett equation has been one of the most widely used means for the study and interpretation of organic reactions and their mechanisms (Figure 1.43).

$$\log \frac{k_X}{k_H} = \rho\sigma_X$$

k_X = the rate constant for the meta or para X-substituted benzene derivative and

k_H = the rate constant for the unsubstituted benzene derivative in its corresponding reaction.

Figure 1.43

The Hammett equation includes two parameters. One is a substituent parameter σ_X which is a measure of the effect of X upon the acidity of benzoic acid. The other is the reaction parameter ρ, which is a measure of the relative sensitivity of the reaction series under consideration to the introduction of substituents.

Hammett plot of para substituent effects on rate of dediazoniation of substituted benzenediazonium chlorides in 0.1M HCl at 25°C

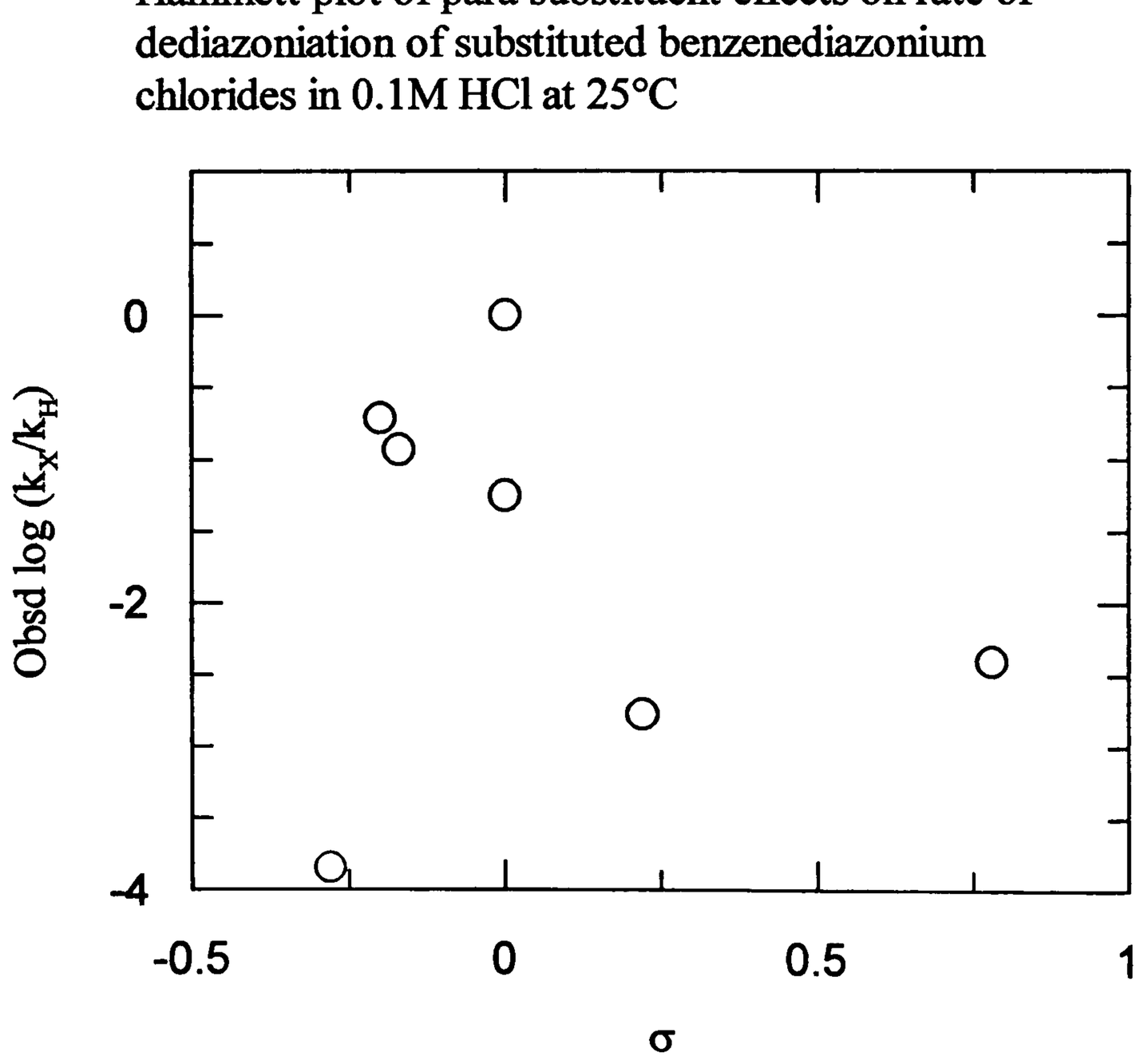


Figure 1.44

The effect of meta and para substituents on the rate of dediazoniation is considerable. All para substituents, including electron withdrawing nitro and electron donating alkyl,

decrease the rate of nitrogen loss. In the meta position the strongly withdrawing NO_2, Br, Cl groups decrease the rate but m-MeO and alkyl substituents increase the rate of reaction. Any attempt to correlate the data using a simple Hammett equation gives a scatter (Figure 1.44). The reason for this is the starting arenediazonium ion and the aryl cation can be resonance stabilised by electron donation to different degrees. However, Swain and Lupton obtained an excellent correlation using field and resonance parameters (Figures 1.45 and 1.46).[59]

$$\log\frac{k_X}{k_H} = f_m F + r_m \Re + i_m = (-2.74)F + (-3.18)\,\Re + (0.27)$$

$$\log\frac{k_X}{k_H} = f_p F + r_p \Re + i_p = (-2.60)F + (5.08)\,\Re + (-0.25).$$

Figure 1.45

Dual substituent constant plot of para substituent effects on rate of dediazoniation of substituted benzenediazonium chlorides in 0.1 M HCl at 25°C

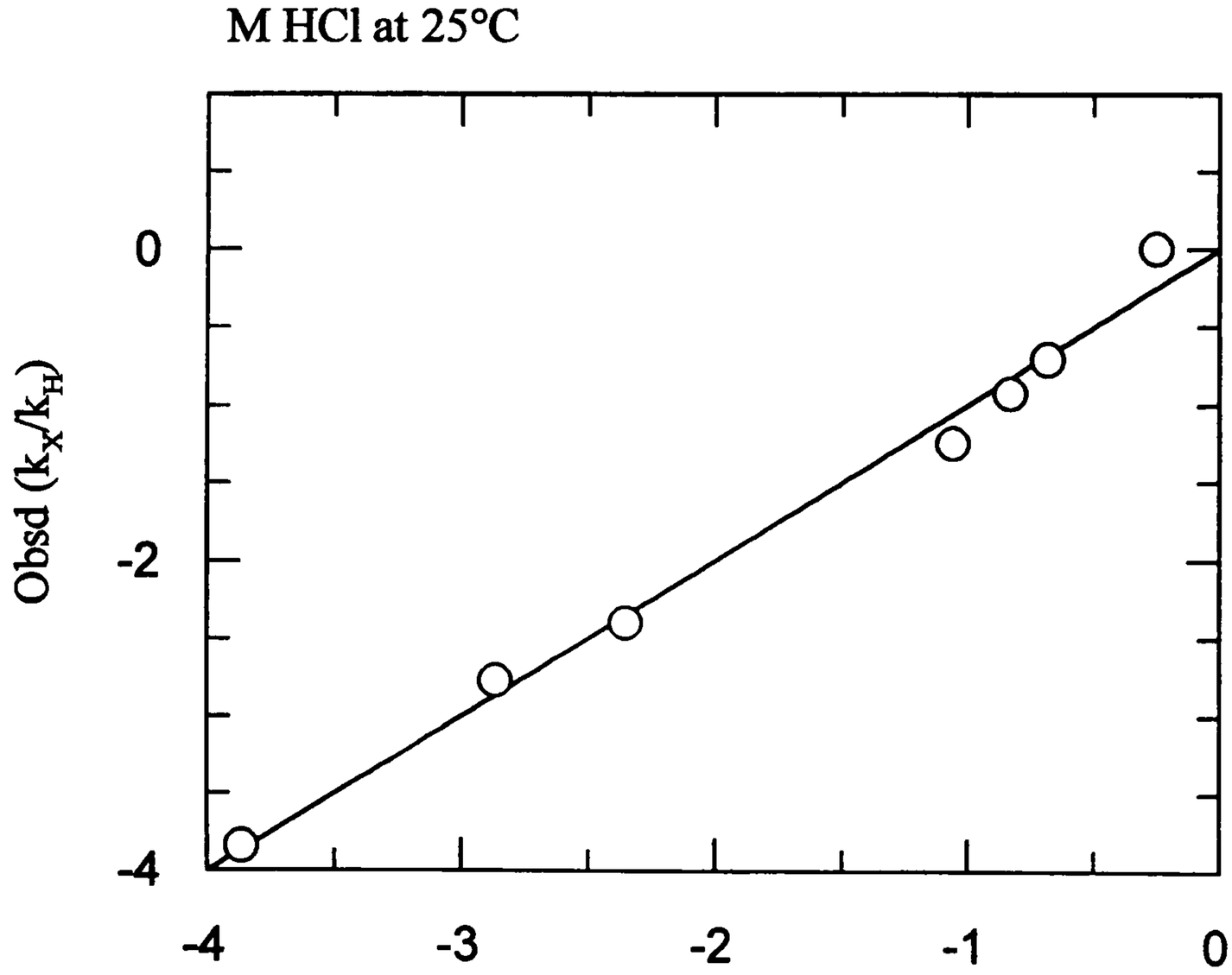


Figure 1.46

The f_m and f_p reaction constants represent the sensitivities of these reactions to the field constants F of meta and para substituents (representing all influences except those transmitted by resonance or π bonds). They are comparable (-2.74 and -2.60) and of the

expected sign and magnitude because electron supplying (negative F) substituents should facilitate departure of N_2 by stabilising the transition state much more strongly than the reactant.

The r_m and r_p reaction constants represent the sensitivities of these reactions to the resonance constants $\mathcal{R}$ of meta and para substituents. For meta substituents with electron supplying substituents, stabilization of the transition state leading to the phenyl cation occurs. This is due to the ortho carbons being supplied with electrons. As meta substituents are poor at stabilising the reactant, an increase in the C-N double bond character does not occur. This means that the sign of the sensitivity to resonance r_m due to meta substituents (-3.18) is the same as that of f_m and f_p.

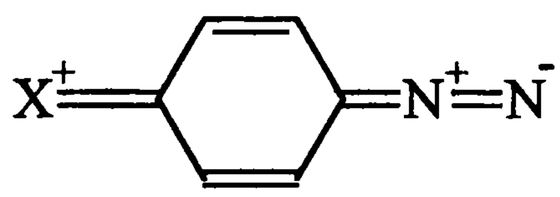


Figure 1.47

For para substituents, resonance with electron supplying substituents does increase the double bond character of the C-N bond in the initial reactant diazonium cation (Figure 1.47). This effect which stabilises the reactant and hinders cleavage of this bond considerably outweighs the kind of transition state resonance stabilisation exhibited by meta substituents and so causes r_p to be positive for para substituents (+5.08). Doubts existed about the accuracy of the field and resonance substituent constants used by Swain. Modifications were suggested by Taft, Charton and Swain himself.[60-62] Although these modifications give reaction constants with smaller standard deviations and better correlation coefficients, Swain's original parameters can still be used adequately in heterolytic dediazoniation reactions.

1.7 The Structure of the Aryl Cation.

The structure of the aryl cation intermediate formed in the decomposition of arenediazonium salts has been the subject of much discussion in the literature. Evidence supporting a singlet type cation has been put forward while at the same time suggestions that it might be a triplet have been voiced.

The questions concerning structure were first addressed by Taft who observed substantial enhancements in the rate due to electron donating substituents in the *meta* position of benzenediazonium salts.[63] He suggested this effect implied a high degree of radical-cation character in the transition state of the dediazoniation reaction, which could be attained by a π electron of the benzene ring being transferred into the vacant σ (sp^2) orbital of the cation. The net result being a triplet. This electronic rearrangement was believed to give a more stable structure due to resonance interaction of the π electrons (Figure 1.48).

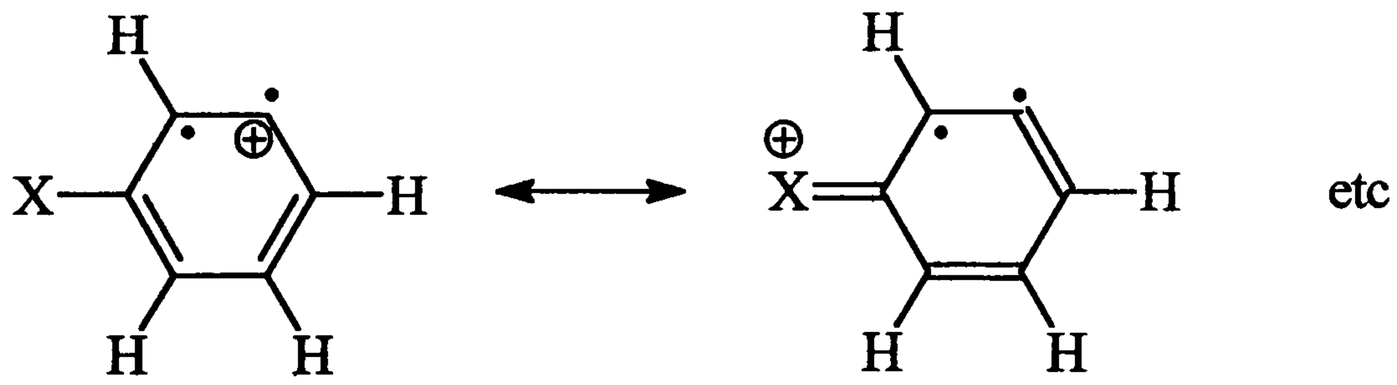


Figure 1.48

An investigation of the electronic state of the aryl cation was published by Evleth and Horowitz in 1971.[64] They performed INDO calculations on phenyl and 4-aminophenyl cations. For the phenyl cation, they found the lowest singlet and triplet states have σ structures (Figure 1.49).

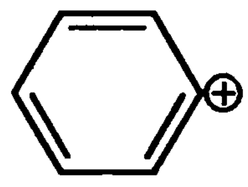


Figure 1.49

The lowest triplet state of phenyl cation is 3.5 eV above the ground singlet state. The INDO calculations were found to be contrary to Taft's suggestions as the calculations indicated both the σ and π triplets have energies higher than the filled shell singlet state. Similar calculations carried out on the 4-aminophenyl cation revealed a profound substituent effect. In this case, the calculations predicted a near degeneracy of the π

cation triplet state and the σ filled shell cation singlet, with the triplet state being slightly more stable. The triplet in this case exhibited a σ,π configuration (Figure 1.50).

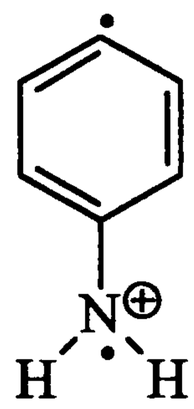
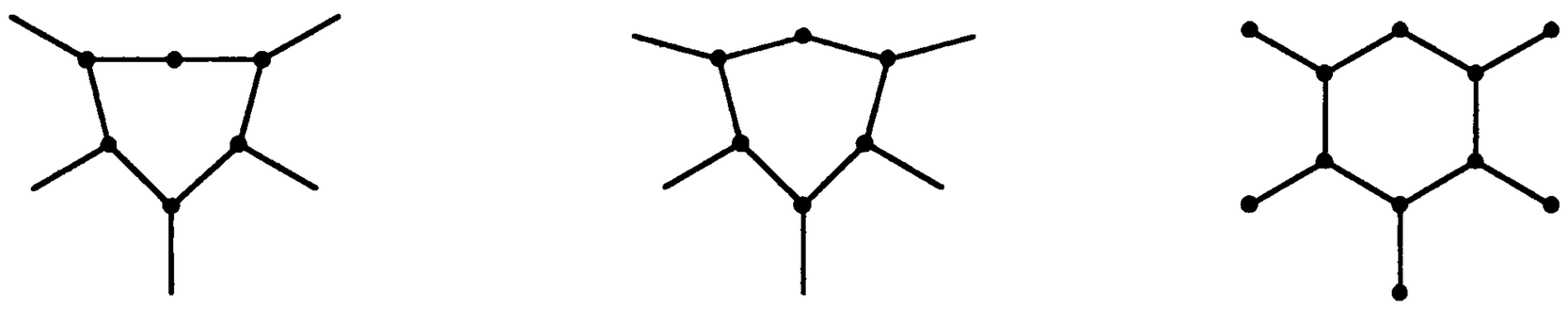


Figure 1.50

This work established that the aryl cation structure is very sensitive to the effect of electron donating substituents. The energy gap of 3.5 eV between the filled shell singlet and the lowest triplet in phenyl cation can be removed on substitution with an amino group.

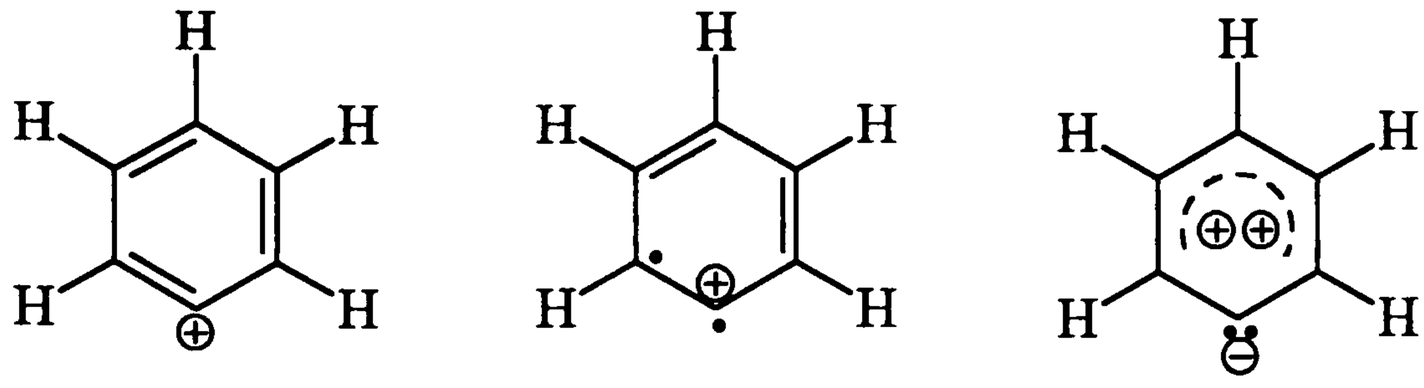
In 1975 Swain and coworkers reported INDO calculations with geometry optimisation (Figure 1.51).[33] They found C1, C2 and C6 are collinear in the ground state of the phenyl cation (I). This results in energy stabilisation of 4.05 eV compared to the symmetrical benzene geometry (III). They also showed that the linear triplet is 146 kcal mol^{-1} less stable than the linear INDO singlet.



I II III

Figure 1.51

Jaffé and coworkers in 1975 used CNDO/S calculations on 12 electronic states of phenyl cation in the symmetrical benzene geometry (III).[65] They found the ground singlet state to be more stable than the lowest σ,π triplet state by 0.87 eV and more stable than the lowest closed shell excited singlet state by 1.56 eV (Figure 1.52).



ground singlet triplet closed shell excited singlet

Figure 1.52

The extension of these calculations to two other geometrical configurations (I & II) revealed that the various electronic states of the phenyl cation can be divided into 3 geometrical categories. It was found that electronic states with a vacant C1 σ orbital prefer a highly distorted geometry in which C1, C2 and C6 are collinear (I) while those states with 2 electrons in the C1 σ orbital prefer the symmetrical benzene geometry (III). Electronic states with one electron in the C1 σ orbital either prefer an intermediate geometry (II) or show little discrimination between an intermediate geometry and that in which C1, C2 and C6 are collinear. It appears that conformational preferences of the various electronic states of the cation are related to the state of hybridisation of C1. When the C1 σ orbital is vacant it acquires 100 % p character (sp hybridisation of carbon), but when the C1 σ orbital contains two electrons, it tends towards maximum s character (sp^2 hybridisation of carbon). A single electron in the C1 σ orbital distorts the symmetric benzene geometry but not necessarily all the way to conformation I.

In 1975 Dill and coworkers reported *ab initio* molecular orbital calculations for the phenyl cation in singlet and triplet states.[66] They found that the singlet cation is highly distorted with a CC^+C angle of 145°. The reason for this they postulated was the singlet cation undergoes such a distortion in order to maximise charge delocalization into the p (C^+) orbital from the σ framework of the ring. The triplet geometries were found to be close to that of benzene.

A year later, Dill and coworkers studied the effect of a series of substituted phenyl cations by STO-3G calculations.[67] They found the singlet configuration is best stabilised by aryl cations substituted by σ donors (i.e. Li, HBe, H_2B and H_3C) in the order *ortho* > *meta* > *para* whereas the triplet configuration is best stabilised by π- donors (i.e. NH_2, OH and F) in the order *para* ~ *ortho* > *meta*. The extent of stabilisation is such that

triplet ground states are predicted for aryl cations having NH_2 and OH substituents. The reason for the π donor effect, is the variation in π charge (Figure 1.53);

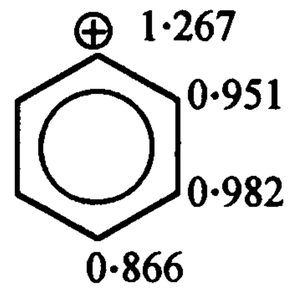


Figure 1.53

π electrons are polarised towards C1 where there is an excess of 0.267 relative to the π charge in benzene. These π electrons cannot be donated directly into the in-plane vacant orbital at C1 but positive charge can be delocalised by polarisation of the π electrons toward C1. Substituents that can increase electron density in the π system are favoured. Stabilisation also results from σ interactions (Figure 1.54). Contrasting the charges on hydrogen compared to hydrogens on benzene, high positive charges are observed on *ortho* H's as a result of hyperconjugation. Hence, introducing substituents at the *ortho* position increases stabilisation further.

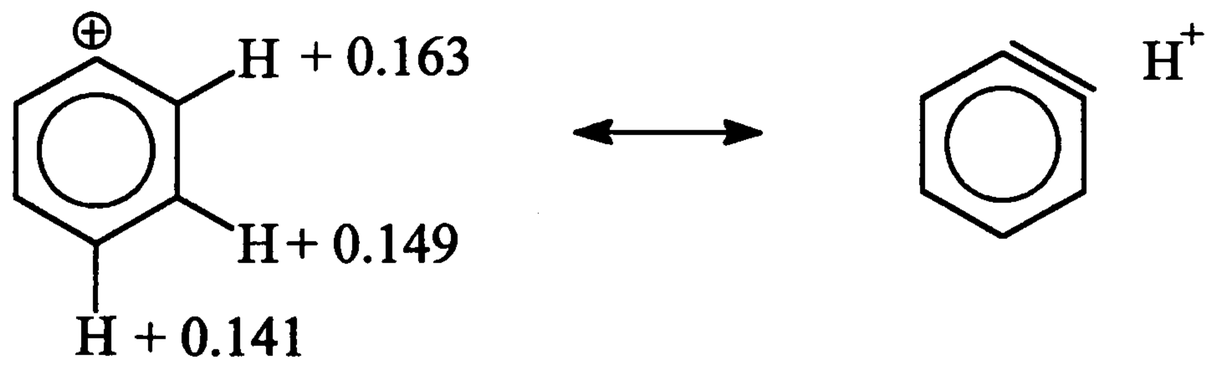


Figure 1.54

In conclusion to theoretical calculations on the aryl cation structure, the literature indicates the singlet structure is generally favoured as the ground state. However, the triplet state may be favoured if a suitable substituent is present that can stabilise this state.

1.8 Occurrence of Arenediazonium Ions in Nature.

The edible mushroom Agarious Bisporus contains several arylhydrazines and arenediazonium ions that are genotoxins.[68] The arenediazonium ions present are 4-(hydroxymethyl)benzenediazonium and 4-methylbenzenediazonium. The mechanism whereby arylhydrazines and arenediazonium ions are genotoxic is unknown but it is proposed that aryl radicals may cause DNA damage.

1.9 Fluoroaromatics.

1.9.1 Preparation of fluoroaromatics.

Of the 10 million compounds registered in the American Chemical Societies Chemical Abstracts, 6.2 % (620000) contain compounds possessing a C-F bond.[69] The interest in such compounds has increased significantly in the last 30 years. The number of organo fluorine research papers has increased more than 5 fold in this time. The increase in interest of industrial and academic scientists reflects the ability of fluorine to alter the physical and chemical properties of organic compounds. The three main reasons fluorine changes the properties of organic compounds are as follows.

1) The van der Waals radius of fluorine (ca 1.35Å) is very similar to that of hydrogen (ca 1.10 Å) and the C-F bond length (1.26 - 1.41 Å) is not much greater than the C-H bond length. (1.08 - 1.11 Å). This means the substitution of fluorine for hydrogen in a molecule will not dramatically alter the shape or steric bulk of the molecule.

2) The electronegativity of fluorine (4.0) greatly exceeds that of hydrogen (2.1) so a large electronic effect on reactions at neighbouring carbon centres may be anticipated. It may also function as a hydrogen bond acceptor, and replacement of hydroxyl by fluorine often has interesting results. Although it is a rather poor leaving group (from carbon), it may be displaced by nucleophiles at or near to the active sites of enzymes, with resultant covalent attachment of an organic moiety to the enzyme.

3) Carbon-fluorine bonds increase the lipophilicity of molecules. This obviously increases the fat-solubility of organofluorine compounds which is of considerable importance in drug design.

The first report on the application of selective fluorination to modify biological activity was by Fried in the preparation of 9-α-fluorohydrocortisone acetate.[70] This publication marked the beginning of a new era when medicinal chemists and biochemists routinely introduced fluorine as a substituent to modify reactivity. Since then, the uses of organofluorine compounds have become numerous especially in drug design. Systematic substitution of fluorine can help establish the effect of hydroxylation on the activity of a molecule (due to similar electronegativity of fluorine to oxygen). One case studied is the synthesis of fluorinated vitamin D_3 analogues. Once fluorine is introduced, the high carbon fluorine bond strength (452 kJ mol^{-1}) renders the fluorine substituent resistant to many metabolic transformations. Another use of fluorine is as a leaving group in

addition elimination processes. Its superior leaving group ability relative to hydrogen has been utilised in the development of mechanism based enzyme inhibitors. A major benefit of fluorine in drug design is that it has a non-naturally-occurring short lived isotope, fluorine-18 (^{18}F) which decays by positron emission. Positron emission tomography (PET) is a useful technique for the survey of living tissue. It complements traditional methods such as X-ray studies by allowing real time analysis of metabolic processes.[71] Introduction of isotopically labelled substituents is essential. While isotopes such as ^{11}C, ^{13}N and ^{15}O have half lives of 20, 10 and 2 minutes, ^{18}F has a half life of 110 minutes which is sufficient for synthesis and for administration of the radio labelled materials.[72] One application of ^{18}F PET is in the brain imagery of Parkinson's disease patients. By using ^{18}F labelled Fluorodopa (Figure 1.55), new insights into the chemistry and metabolism of the brain have been revealed.

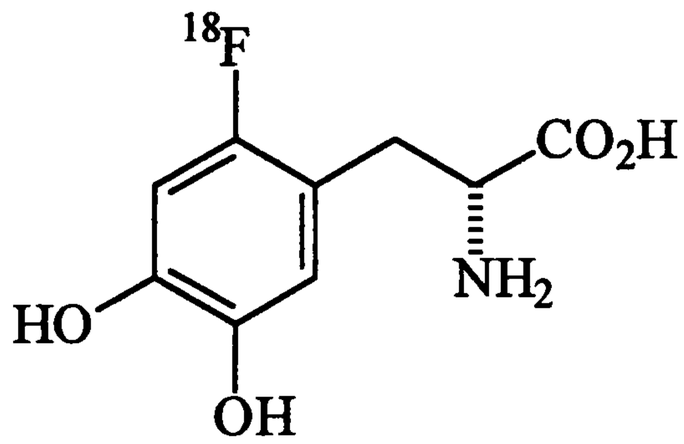


Figure 1.55. 6α-[^{18}F]-Fluoro-L-dopa.

The interest in fluoroaromatics to the chemical industry is as intermediates (building blocks) in the manufacture of pharmaceutical and agrochemical products.

Two products that the 1,3-difluorobenzene intermediate is used in are Diflubenzuron (DFB) a benzoylphenylurea derivative (Figure 1.56), and Diflunisal (Figure 1.57).[73,74]

DFB is a member of a group of insecticides first discovered in 1972. These pesticides are insect stomach poisons which interfere with the formation and deposition of cuticle chitin during larval moulting. DFB is effective against pests associated with fruit, cotton and soya beans as well as mosquito larvae.

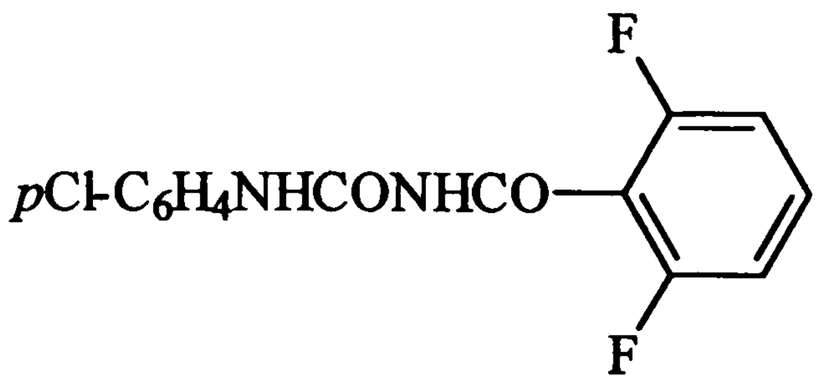


Figure 1.56. DFB

Diflunisal is a difluorophenyl derivative of salicylic acid. Chemically, Difunisal differs from aspirin (acetyl salicyclic acid) in two respects. The first is the presence of a difluorophenyl substituent at carbon 5. The second difference is the removal of the O-acetyl group from the carbon 2 position. Diflunisal is not metabolised to salicylic acid and the fluorine atoms are not displaced from the difluorophenyl ring structure.

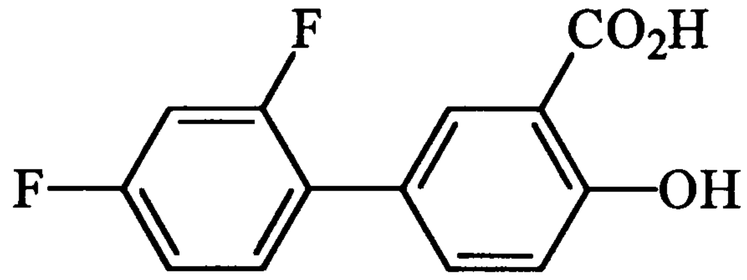


Figure 1.57. Diflunisal.

Before Diflunisal, the analgesia provided by aspirin could not be surpassed by usual doses of any other single entity oral agent. The only way analgesic efficiency was increased was by combining aspirin with a narcotic such as codeine. The discovery of Diflunisal was the culmination of a long search by the Merck Sharp and Dohme Research laboratories to produce a drug that was 5 to 10 times more potent than aspirin. The key to its success is the presence of the two fluorine atoms which increases the lipophilicity and the aqueous solubility. The precise mechanism of the analgesic and anti-inflammatory actions of Diflunisal are not known except that it is a prostaglandin synthetase inhibitor. In animals, prostaglandins sensitize nerves inducing pain. The mode of action is believed to involve a decrease of prostaglandin in peripheral tissues.

Diflunisal is marketed by Merk Sharp and Dohme as an anti-inflammatory agent for the treatment of osteoarthritis and as a post operative analgesic after orthopaedic and dental surgery.

1.9.2 The Balz-Schiemann Reaction.

While great progress in the methodology of fluorination of aromatic compounds has occurred, the classical Balz-Schiemann reaction remains a favoured means for introducing fluorine (Figure 1.58).[102]

$$ArN_2BF_4^+ \xrightarrow{heat} ArF + N_2 + BF_3$$

Figure 1.58

At present the main industrial method relies on using a diazonium ion intermediate in situ (Figure 1.59).[75]

ICI

$$PhNH_2 + NaNO_2 + HF \text{ (excess)} \rightarrow PhF + NaF + 2H_2O + N_2$$

(via $NaNO_2 + HF \rightarrow NaF + HNO_2 \rightarrow NOF + H_2O$)

Dupont

$$2PhNH_2 + N_2O_3 + HF \text{ (excess)} \rightarrow 2PhF + 3H_2O + N_2$$

(via $N_2O_3 + 2HF \rightarrow 2NOF + H_2O$)

Figure 1.59

The important fact to notice in both the ICI and Dupont procedures is that water is produced. This provides an unwanted complication as it leads to the formation of phenol which undergoes coupling with unreacted diazonium ions present to give diazo products. Lowering the amount of water produced provides a more efficient reaction (contrast the Dupont method, 1.5 moles water per diazonium ion with the ICI method which produces 2 moles of water per diazonium ion).

1.9.3 Alternatives to the Balz-Schiemann Reaction.

Incorporation of fluorine into organic molecules by nucleophilic substitution remains a difficult area. The small size of F^- (radius is 1.36Å) and its low polarizability encourages F^- to behave as a base rather than a nucleophile. In the following section alternative methods will be reported.

1.9.3.1 Halogen Exchange (HALEX).

An alternative method to the Balz-Schiemann process for aromatic fluorination is by halogen exchange between aromatic halides and potassium fluoride. The reaction normally takes place at an elevated temperature in a pressure reactor. The source of fluorine is normally potassium fluoride. Difficulties arise in the choice of solvent. Potassium fluoride is insoluble in most organic solvents so the choice is limited to only a few such as DMF and DMSO. However, high temperatures are required for the KF to

react with the aromatic halide, so these solvents are not suitable. An appropriate solvent for this reaction is tetramethylenesulfone (sulfolane, b.p. 285°C).

Problems with this reaction can occur due to its exothermic nature. Six people were injured in an explosion at the Shell fluoroaromatic plant at Stanlow, Cheshire in March 1990.[76] Fluoroanilines are prepared by a two-step batch process. The first step is halogen exchange in which 2,4-dichloronitrobenzene is converted to 2,4-difluoronitrobenzene (Figure 1.60).

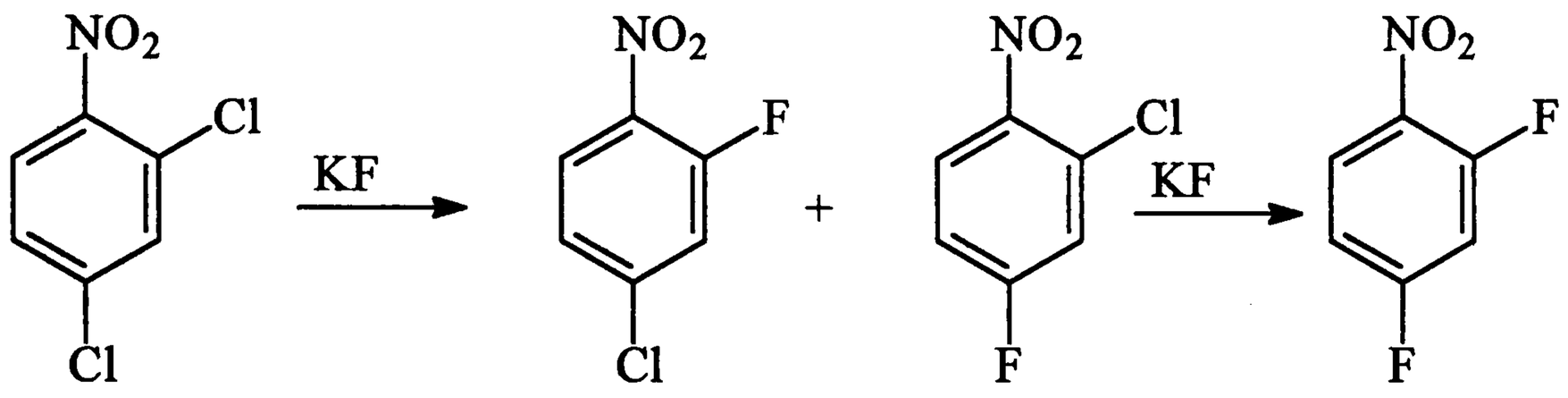


Figure 1.60

The second step involves the hydrogenation of the nitro aromatic compound to an aniline derivative. Although the reaction is exothermic the temperature of the process normally settles out at 170°C. On 20 March 1990, near the end of a campaign to manufacture 2,4-difluoronitrobenzene (2,4-DFNB), the Halex reactor was charged with 2,4-dichloronitrobenzene, potassium fluoride, N,N-dimethylacetamide (DMAC) as solvent, and tetramethylammonium chloride (TMAC) as catalyst. After heating from ambient temperature to 165°C in the normal time of 3 hours, the plant alarm went off when the reactor temperature continued to rise above 170°C. Even though the heating system was turned to cooling, the temperature and pressure continued to rise until an explosion occurred which destroyed the reactor and part of the plant. A subsequent investigation revealed DMAC had become contaminated with acetic acid. A few days before the explosion, the products of the Halex reaction were separated by distillation to give DMAC, (which is recycled) and 2,4-DFNB. Under the conditions of the azotropic distillation DMAC is partly hydrolysed to dimethylamine and acetic acid (Figure 1.61).

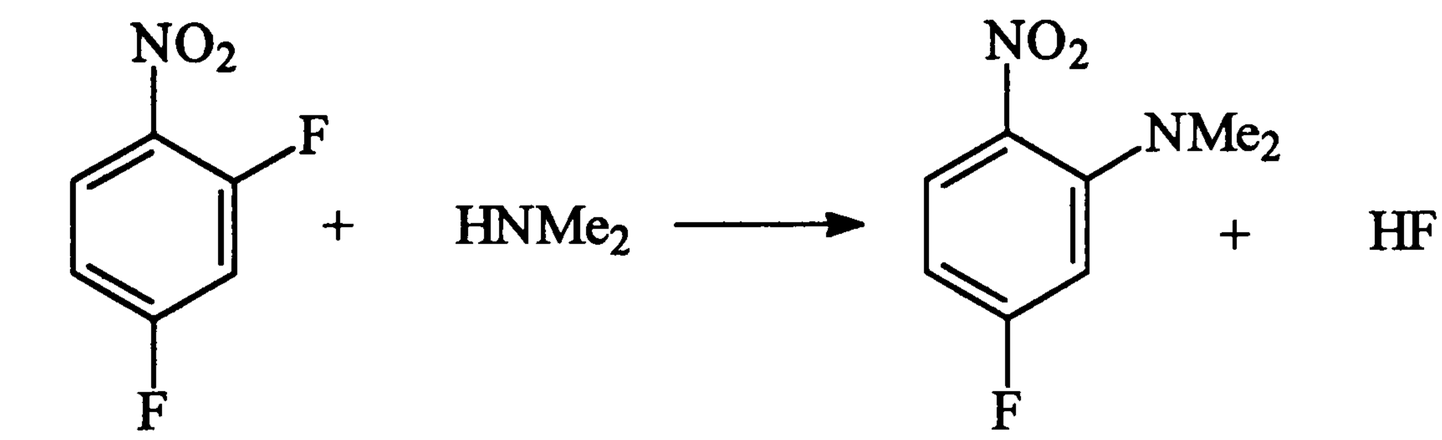


Figure 1.61

2,4-DFNB reacts with dimethylamine to give 2-dimethylamino-4-fluoronitrobenzene thereby shifting the equilibrium so acetic acid builds up in amounts equimolar with the water consumed. No separation between DMAC and acetic acid is achieved when the mixture is distilled after the hydrolysis because DMAC and acetic acid give an azeotrope close to the boiling point of DMAC. Unfortunately, the analytical methods used at Stanlow did not detect the presence of acetic acid in DMAC so this recycled DMAC was used in the Halex batch. The subsequent reaction that occurred was shown to produce poly(nitrophenyl) ethers, nitrohalophenols and tars. The gases produced consisted of ketene, hydrogen fluoride and carbon dioxide. An unexpected exotherm raised the temperature above 250°C, causing the nitro compounds to explode.

1.9.3.2 Alkali Metal Fluorides.

These fluorinating agents are used mainly in Halex reactions to substitute fluorine for other halogens. The main driving force is the formation of the thermodynamically favourable C-F bond. The presence of a high boiling solvent and anhydrous conditions are favoured to aid the solubility of the ionic fluoride and to encourages the formation of unsolvated fluoride anions ("naked fluoride"). The use of crown ethers has also been investigated.[77] Their main benefit is to solvate inorganic fluorides in non polar solvents by complexation.

Research in the area of alkali metal fluorides has been concerned with improving KF reagents. It has been found that the reactivity of KF can be improved by dispersion on suitable supports thereby increasing the reagent's surface area. An example is the use of KF on alumina.[78] Other support materials used are silica and zeolities. An alternative support system, which cuts down the intermolecular hydrogen bonding of F^- to the

support allowing an increase in the reactivity of F^-, is KF supported on CaF_2.[79] Another innovation in this area is polymer-supported KF.[80] The dispersion of KF on a cross-linked polystyrene support increases the yields of fluorination compared to KF/CaF_2 and KF alone.

1.9.3.3 Silver fluoride.

Silver fluoride was first used by Moissen in 1897 for fluorination of organic compounds.[117] It is a popular choice as a fluorinating reagent because of its high selectivity and its low basicity compared to KF. This minimises elimination over substitution resulting in cleaner reactions. Its main use is in selective halogen exchange reactions, e.g. RI→RF. Its disadvantages as a fluorinating agent are its high cost and that 2 moles of reagent are required per mole of substrate (Figure 1.62).

$$RX + 2AgF \longrightarrow RF + AgF.AgX$$

Figure 1.62

1.9.3.4 Use of pyridinium poly(hydrogen fluoride) for fluorination reactions.

Anhydrous hydrogen fluoride is an inexpensive fluorinating agent that is widely used, however its reactions are difficult due to its low boiling point (19.6°C) and corrosive nature. This problem has largely been overcome by using anhydrous hydrogen fluoride (AHF) in suitable donor solvents. Initially, THF was chosen as a solvent but more success came with the use of triethylamine and pyridine from which pyridinium poly(hydrogen fluoride) was made. Pyridinium poly(hydrogen fluoride) (PPHF) commonly known as Olah's reagent is a commercially available stable liquid.[81] In contrast to other pyridinium halides, pyridinum fluoride is difficult to prepare. Pyridinium fluoride was obtained by the reaction of pyridine with formyl fluoride through the decarbonylation of the intermediate N-formylpyridinium fluoride. The solution contains about 9 equivalents of HF to 1 equivalent of pyridine (70% w/w HF, 30% w/w pyridine) and is stable up to 55°C. It has mainly been used to fluorinate secondary and tertiary alcohols, alkenes, alkynes and in Halex reactions. Reacting pyridine with anhydrous hydrogen fluoride gives only bi- and poly(hydrogen fluorides).

Olah has shown that the poly(hydrogen fluoride) is in equilibrium with a small amount of free HF. ^{19}F NMR indicates the presence of a poly(hydrogen fluoride) species in which each fluorine atom is surrounded by four hydrogen atoms (Figure 1.63).

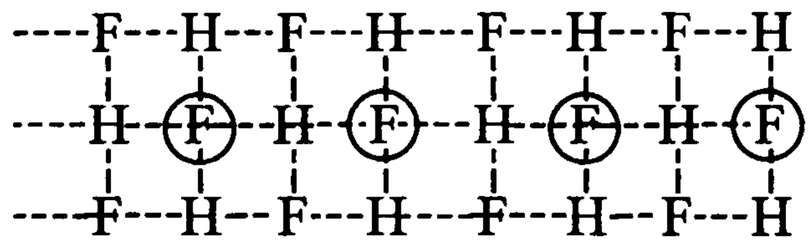


Figure 1.63

Olah showed that the reaction of α-amino acids in pyridinium poly(hydrogen fluoride) solution with excess sodium nitrite led via in situ diazotization followed by nucleophilic dediazoniation to the formation of 2-fluorocarboxylic acids in good to moderate yields. In general, pyridinium poly(hydrogen fluoride) is a convenient medium for the preparation of fluoroarenes. Yoneda and co-workers have shown that the diazotisation and dediazoniation reactions of a modified Balz-Schiemann reaction proceed smoothly at room or slightly higher temperatures to give the fluoroarenes in good yields in the presence of a poly(hydrogen fluoride) species.[82]

1.9.3.5 Zinc difluoride

Zinc difluoride is a highly toxic, colourless solid made by the action of fluorine on zinc, zinc oxide, zinc bromide and zinc sulfide.[83] Although this reagent is rarely used it has shown some promise in the fluorination of aromatic compounds (Figure 1.64).[84]

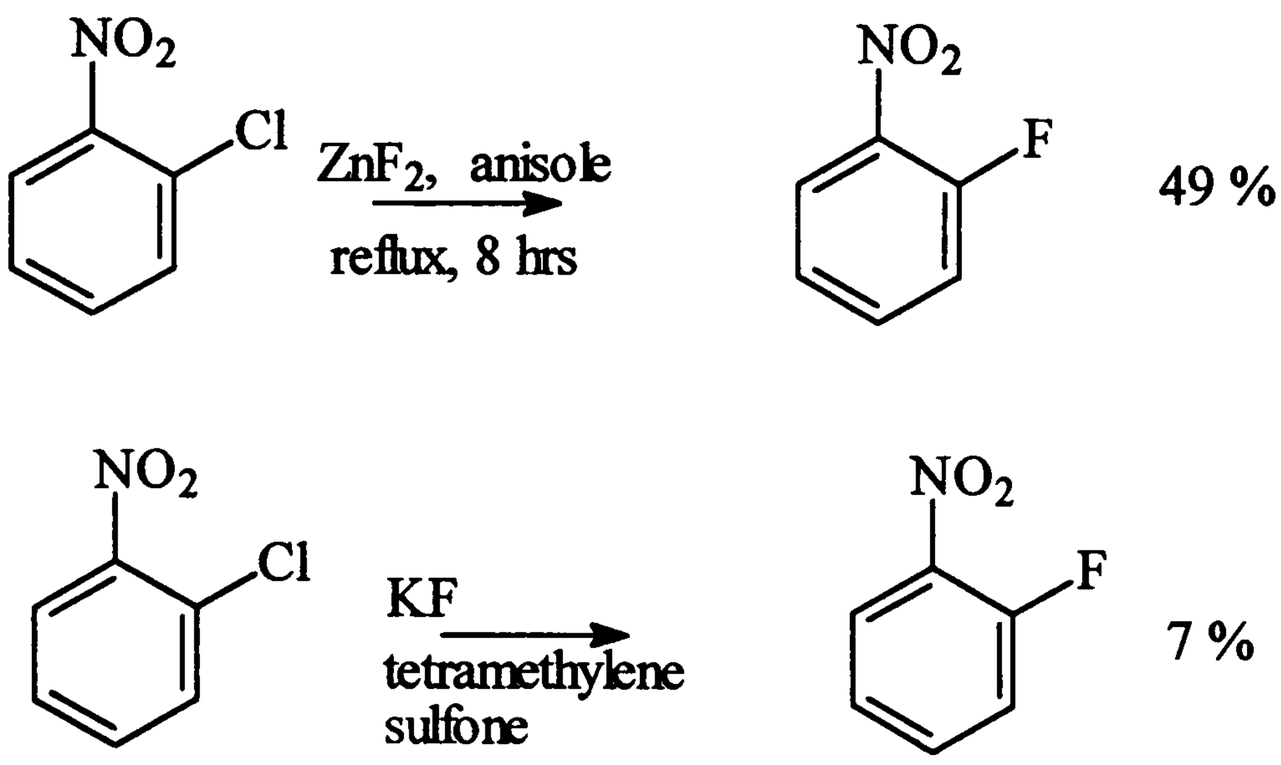


Figure 1.64

1.9.3.6 Modifications to the Balz-Schiemann method.

Milner reported the use of nitrosonium tetrafluoroborate with arylamines in dichloromethane to give corresponding fluoroarenes in good yield.[85] The reaction proceeds without isolation or drying of the diazonium tetrafluoroborate and is reported to be useful for arylamines bearing carboxyl and hydroxyl subtituents. These arylamines normally give poor yields of fluoroaromatics under Balz-Schiemann conditions but good yields are obtained using nitrosonium tetrafluoroborate (Figure 1.65).

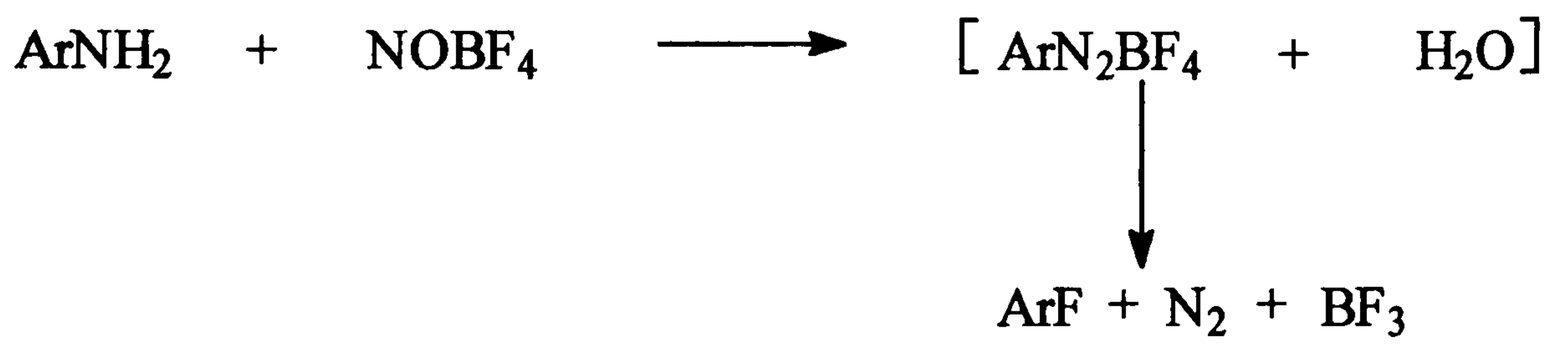


Figure 1.65

Shinhama and co-workers reported the conversion of a number of arenediazonium tetrafluoroborates to the corresponding fluoroaromatics in a boron trifluoride diethyl ether complex.[86] The boron trifluoride adduct was found to be a good solvent in view of its thermal and photochemical stability (b.p. 126°C).

Investigations into using different counteranion fluoride sources have been carried out by numerous workers. Two studies have concentrated on using hexafluoroantimonates and hexafluorophosphates. Sellers and Suschitzky reported that the thermolysis of arenediazonium hexafluoroantimonates gave better yields of the corresponding aromatic fluorides than the decomposition of arenediazonium tetrafluorbororates (Figure 1.66).[87] The differences were significantly highlighted when fluoroaromatics containing electron withdrawing substituents were prepared.

Figure 1.66

Rutherford and co-workers prepared arenediazonium hexafluorphosphates and decomposed them to give fluoroaromatics in better yields than the Balz-Schiemann method (Figure 1.67).[88]

Figure 1.67

The use of potassium hydrogen fluoride and silicon tetrafluoroborate was found to work as an efficient fluorinating agent by Tamura and co-workers (Figure 1.68).[89] They demonstrated that deaminative fluorination of aniline derivatives proceeds with KHF_2 and SiF_4 to give the corresponding aromatic fluoride in good yields. An advantage of this method is that KHF_2 is less corrosive than HF so handling is easier.

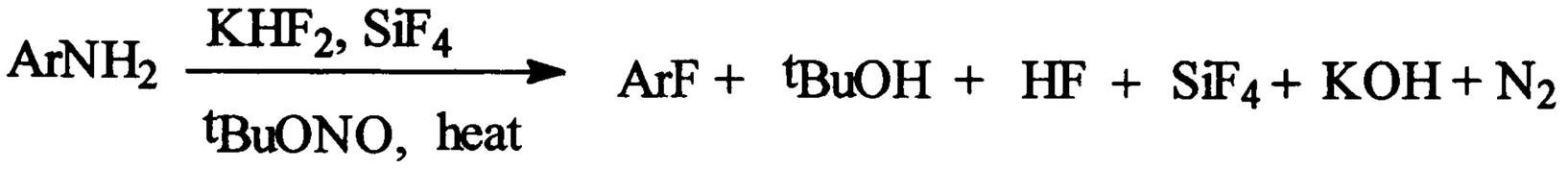


Figure 1.68

Sasaki and co-workers discovered that the addition of $SnCl_2$ or SnF_2 as low redox potential reductants at the fluorodediazoniation step afforded the corresponding fluoroaromatic in a good yield.[90] The yields of the fluoroaromatics were further increased by the addition of tetrabutylammonium dihydrogen trifluoride which acted as a nucleophilic source of fluoride.

Chapter 2. Methods and Results.

2.1 Preparations.

The arenediazonium salts used in the kinetic and product analysis were prepared using Starkey's general method.[4] This involved dissolving the amine in tetrafluoroboric acid and reacting it with an aqueous solution of sodium nitrite to give the arenediazonium tetrafluoroborate. The yields of the arenediazonium salts prepared were generally good. All of the compounds prepared were purified by recrystallisation prior to their use. Generally, the arenediazonium salts were white powders, the main exception to this was *m*-nitrobenzenediazonium tetrafluoroborate which was a light brown powder. As only small quantities were required for individual kinetic and product studies (less than 100 mg), the arenediazonium salts were only prepared in small quantities (generally between 3-6 g). Since arenediazonium salts are photolytically reactive and decompose at room temperature, they were stored in the dark at -5°C. Fresh arenediazonium salts were prepared when required.

The aryl ethers for the product analysis studies were prepared by reacting the arenediazonium salt with the solvent (i.e. trifluoroethanol, ethanol). The aryl ether was separated and purified from the product mixture by preparative GLC. Generally, only a small quantity of the aryl ether (less than 100 mg) was used in the product analysis so no yields were obtained for these preparations.

All materials obtained commercially were analysed by GLC for impurities. Generally, no further purification was required.

2.2 Kinetics.

The kinetic data were collected with a Cecil 5000 series spectrophotometer (5502 model) and fitted to a single exponential equation in the manner shown below (Figure 2.1). The manual plotting of data for one compound using the logarithmic integrated first-order rate law is shown below Figure 2.1. In nearly all cases, enough data points were taken to cover at least 3 half lives (only exception, *m*-CN compound in HFIP) whilst in some cases enough data points were possible for at least 4 half lives. With the exception of the reactions in HFIP, all reactions were carried out twice. Most of the

data from the reactions of the decomposition of arenediazonium compounds in solvolytic media fit first order kinetics. The only substrates that appear to be non first-order are those that are extremely unreactive. All of the data obtained for each individual diazonium salt in a particular solvent covered a minimum temperature range of at least 25°C. For some diazonium salts, their lack of reactivity meant the kinetics had to be followed at quite high temperatures, i.e TFE 70°C, water 80°C, whilst reactive arenediazonium salts could be followed down to room temperature.

The kinetic data for benzene-, 3-methylbenzene-, and 3-methoxybenzene-diazonium salts in water, trifluoroethanol, hexafluoroisopropanol, ethanol and trifluoroacetic acid are included in Tables 2.1-2.16. Tables 2.17-2.24 show the kinetic data for 3-trifluoromethylbenzene- and 3-cyanobenzene-diazonium tetrafluoroborates in the same solvents with the exception of trifluoroacetic acid. The rate constants for the dediazoniation reaction of 3-nitrobenzene- and 4-methylbenzene-diazonium tetrafluoroborates in water and trifluoroethanol are shown in Tables 2.25-2.28. Table 2.29.1-2.29.4 illustrate the kinetic data for 4-methylbenzenediazonium tetrafluoroborate in a mixed solvent system of trifluoroethanol and trifluoromethoxybenzene.

The rate constants listed in Tables 2.1-2.29 are average values of two experimental rate results. The full experimental results are given in appendix A (chapter 6). The reliability of the data could be assessed by viewing the standard deviation. This was determined by the software program and is a measure of the fitting of the data for an individual reaction to the calculated exponential curve. For all first order rate constants (k), the standard deviation was always less than 5 % and in the majority of cases less than 1%.

Once the rate constants at various temperatures for a given compound in a particular solvent were obtained, an Eyring plot could be constructed to determine the activation parameters for that reaction (e.g., Figure 2.2). Tables 2.30-2.34 include the activation parameters for the solvolysis of various substituted arenediazonium tetrafluoroborates in water, trifluoroethanol, hexafluoroisopropanol, ethanol and trifluoroacetic acid. The rate constants at 25°C are extrapolated values from the corresponding Eyring plots.

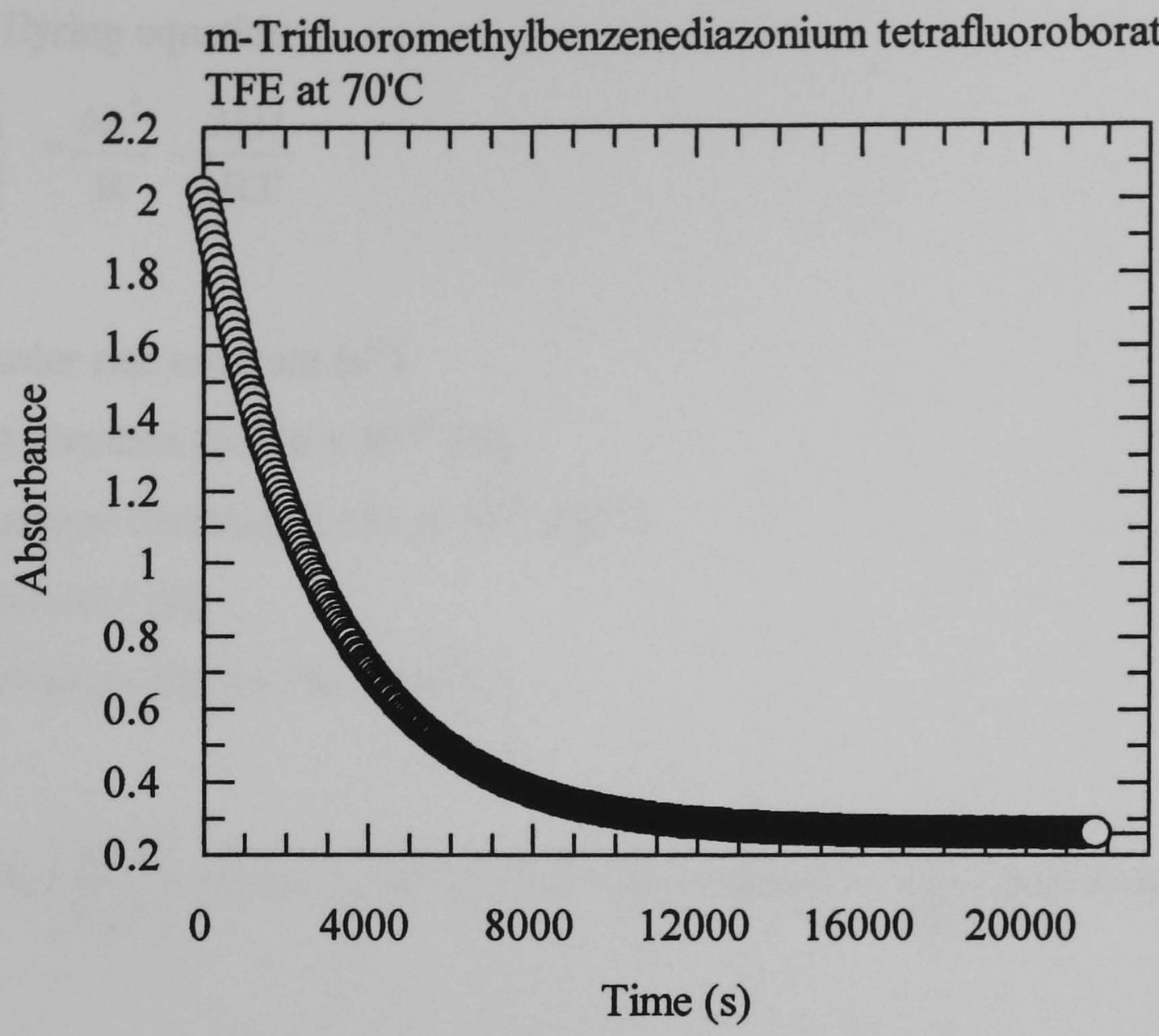
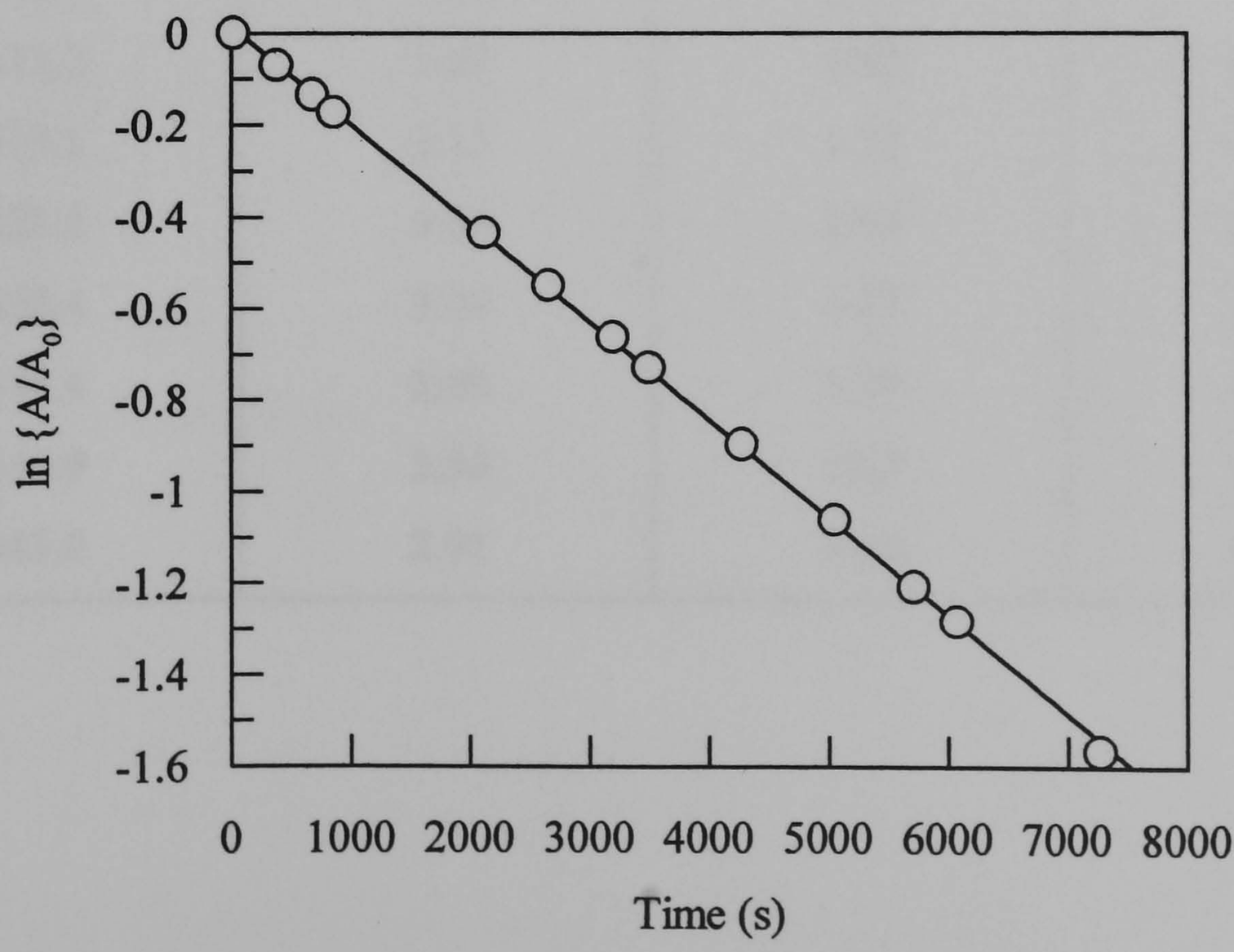


Figure 2.1

The first order rate law for the decrease in absorption of the arenediazonium salt is

$$[A] = [A_0]e^{-kt}.$$

A plot of ln $\{[A]/[A_0]\}$ versus time gives a straight line with gradient = -k



gradient = -2.65×10^{-4} s^{-1} (standard error 2.28×10^{-6} s^{-1})

therefore k = 2.65×10^{-4} s^{-1}

From the Eyring equation

$$\ln\left\{\frac{k.h}{k_B T}\right\} = \frac{\Delta S^{\ddagger}}{R} - \frac{\Delta H^{\ddagger}}{RT}$$

k = first order rate constant (s^{-1})

h = Planck constant (6.626×10^{-34} J s)

k_B = Boltzmann constant (1.381×10^{-23} J K^{-1})

T = Temperature (K)

R = Gas constant (8.314 J K^{-1} mol^{-1})

a plot of $\ln\left\{\frac{k.h}{k_B T}\right\}$ versus $\frac{1}{T}$ gives a line with gradient = $-\frac{\Delta H^{\ddagger}}{R}$ and intercept = $\frac{\Delta S^{\ddagger}}{R}$

Table 2.0 Rate constant at various temperatures for 3-trifluoromethyl-benzenediazonium tetrafluoroborate in TFE

Temp /K	$10^3 T^{-1}$ /K^{-1}	$10^5 k$ / s^{-1}	$\ln\left\{\frac{k.h}{k_B T}\right\}$
308.3	3.24	0.34	-42.1
312.2	3.20	0.62	-41.5
319.2	3.13	1.72	-40.5
323.1	3.09	2.64	-40.1
328.4	3.04	4.77	-39.5
333.4	2.99	9.19	-38.9
336.9	2.96	15.3	-38.4
343.0	2.91	34.0	-37.6

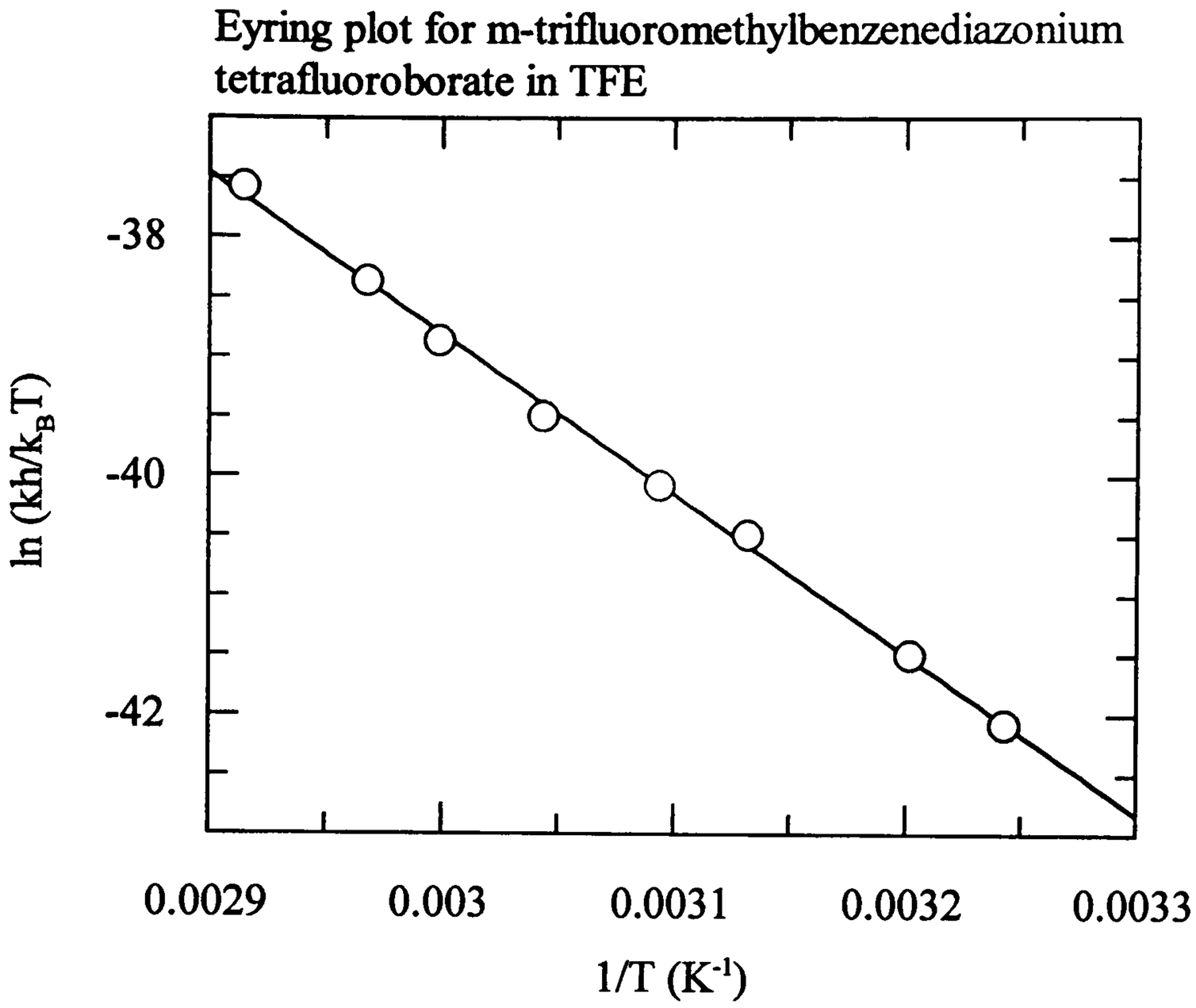


Figure 2.2

gradient= -1.33 x 10^4 K (standard error 1.71 x 10^2 K)

$$= \frac{-\Delta H^{\ddagger}}{R}$$

$\Delta H^{\ddagger}$ = 111 kJ mol^{-1}

Intercept = 1.24 (standard error 0.53)

$$= \frac{\Delta S^{\ddagger}}{R}$$

$\Delta S^{\ddagger}$ = 10.3 J K^{-1} mol^{-1}

Correlation Coefficient -0.999

Table 2.1. Benzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
25.10	0.53
30.93	1.09
40.38	4.50
50.10	15.7
59.20	51.7

Table 2.2. Benzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^4 k / s^{-1}
25.80	1.06
30.02	1.98
35.20	4.44
45.30	18.3
55.04	71.0

Table 2.3. Benzenediazonium chloride in TFE.

Temperature /°C	10^4 k / s^{-1}
25.80	0.98
30.02	1.94
35.20	4.40
45.30	17.5
55.02	71.0

Table 2.4. Benzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^4 k / s^{-1}
25.46	0.97
31.00	1.89
35.75	3.59
40.84	9.73
45.17	17.6
50.40	34.2

Table 2.5. Benzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^4 k / s^{-1}
25.30	2.32
31.80	5.72
37.23	7.25
42.40	15.7
45.32	16.1

Table 2.6. Benzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^4 k / s^{-1}
25.50	0.48
28.65	0.84
35.16	2.19
42.00	5.74
50.16	17.2
58.18	46.7

Table 2.7. 3-Methylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
25.05	2.62
30.85	4.55
40.56	16.6
50.10	46.9
59.70	131

Table 2.8. 3-Methylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^3 k / s^{-1}
25.11	0.52
30.89	1.04
40.53	4.07
51.05	13.1
56.29	21.6

Table 2.9. 3-Methylbenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^3 k / s^{-1}
25.46	0.52
31.00	1.23
35.75	2.50
40.84	5.20
45.17	9.45
50.40	15.7

Table 2.10. 3-Methylbenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}
25.30	0.36
31.80	0.76
37.23	1.71
42.40	3.51
45.28	4.52

Table 2.11. 3-Methylbenzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^3 k / s^{-1}
25.50	0.23
30.49	0.49
31.28	0.64
36.59	1.17
44.24	3.72
49.90	7.29
58.18	18.5

Table 2.12. 3-Methoxybenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^3 k / s^{-1}
25.11	0.24
30.85	0.51
40.56	1.67
50.10	5.53
59.77	16.0

Table 2.13. 3-Methoxybenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^3 k / s^{-1}
25.10	0.87
30.89	1.79
40.53	6.13
50.90	22.7
56.29	46.4

Table 2.14. 3-Methoxybenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^3 k / s^{-1}
25.92	1.73
30.34	3.45
38.45	10.6
44.55	19.8
50.53	36.7

Table 2.15. 3-Methoxybenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}
25.30	0.41
31.80	1.05
37.23	1.86
42.40	3.80
45.28	4.93

Table 2.16. 3-Methoxybenzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^3 k / s^{-1}
25.50	0.51
31.28	1.57
36.59	3.23
44.24	7.94
49.90	15.9
51.14	18.1
56.73	16.7

Table 2.17. 3-Trifluoromethylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
63.92	0.81
70.05	2.07
75.53	4.40
80.11	7.73
85.23	13.8

Table 2.18. 3-Trifluoromethylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^5 k / s^{-1}
35.30	0.34
39.22	0.62
46.19	1.72
50.12	2.64
55.43	4.77
60.43	9.19
63.92	15.3
70.05	34.0

Table 2.19. 3-Trifluoromethylbenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^6 k / s^{-1}
30.03	2.32
34.69	3.68
45.17	4.51
51.67	15.8
55.94	22.7

Table 2.20. 3-Trifluoromethylbenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}
25.37	0.84
31.02	1.82
36.73	2.84
41.15	6.50
45.73	8.42
50.90	12.8

Table 2.21. 3-Cyanobenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
46.57	0.99
50.49	1.38
59.96	3.33
64.45	3.74
70.34	6.93
80.11	17.3
85.23	30.1

Table 2.22. 3-Cyanobenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^5 k / s^{-1}
45.44	0.59
55.43	2.59
59.96	3.82
64.45	8.69
70.47	15.2

Table 2.23. 3-Cyanobenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^6 k / s^{-1}
39.01	0.24
42.45	0.44
48.54	1.42
50.78	2.52
54.98	5.46
58.12	10.2

Table 2.24. 3-Cyanobenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^2 k / s^{-1}
36.72	0.11
43.70	7.21
49.70	1.34
55.32	2.87
60.08	5.39

Table 2.25. 3-Nitrobenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
60.78	3.97
65.37	6.02
70.04	7.71
75.53	15.0
80.17	26.9
85.23	30.3

Table 2.26. 3-Nitrobenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^4 k / s^{-1}
45.26	0.12
46.19	0.26
50.16	0.39
55.20	0.53
59.82	1.57
65.34	2.84
70.49	5.26

Table 2.27. 4-Methylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}
30.01	0.09
39.57	0.40
49.60	1.57
59.59	6.09
65.02	12.1

Table 2.28. 4-Methylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^4 k / s^{-1}
39.56	3.90
45.20	7.26
49.69	12.3
55.21	27.5
59.73	48.5
65.21	89.5
70.11	149

Tables 3.29.1-4. 4-Methylbenzenediazonium tetrafluoroborate in TFE:trifluoromethoxybenzene (TFMOB) at various molar ratios.

Table 2.29.1. TFE:TFMOB 10:1.

Temperature /°C	10^4 k / s^{-1}
35.02	2.43
40.53	5.73
49.49	17.9
59.08	50.9
65.05	127

Table 2.29.2. TFE:TFMOB 5:1.

Temperature /°C	10^4 k / s^{-1}
35.02	2.34
40.53	5.52
49.49	16.3
59.08	52.9
65.05	115

Table 2.29.3. TFE:TFMOB 3:1.

Temperature /°C	10^4 k / s^{-1}
35.02	1.73
40.53	5.85
49.49	18.0
59.08	48.3
65.05	141

Table 2.29.4 TFE:TFMOB 1:0.

Temperature /°C	10^4 k / s^{-1}
35.02	1.82
40.53	3.63
49.49	15.9
59.08	43.4
65.05	89.4

Table 2.30 Rate constants at 25°C and activation parameters for substituted benzenediazonium tetrafluoroborates in water.

Substituent	$10^6 k^{25}$ / s^{-1}	$\Delta H^{\#}$ / kJ mol^{-1}	$\Delta S^{\#}$ / J K^{-1} mol^{-1}
H	53.0	109	37.4
3-Me	263	93.0	-2.42
4-Me	4.35	114.4	36.5
3-MeO	240	98.5	15.8
3-CF_3	0.27	128	55.7
3-NO_2	9.69	99.1	-16.9
3-CN	11.3	79.3	-74.7

Table 2.31 Rate constants at 25°C and activation parameters for substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	$10^5 k^{25}$ / s^{-1}	$\Delta H^{\#}$ / kJ mol^{-1}	$\Delta S^{\#}$ /J K^{-1} mol^{-1}
H	9.21	115	62.1
3-Me	53.0	99.3	24.8
4-Me	3.93	108	34.0
3-MeO	87.3	103	42.3
3-CF_3	0.07	111	10.3
3-NO_2	0.06	124	53.6
3-CN	0.03	116	19.7

Table 2.32 Rate constants at 25°C and activation parameters for substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol.

Substituent	$10^5 k^{25} / s^{-1}$	$\Delta H^{\#} / kJ\ mol^{-1}$	$\Delta S^{\#} / J\ K^{-1}\ mol^{-1}$
H	9.72	116	66.2
3-Me	51.9	108	55.6
3-MeO	173	98.4	31.6
3-CF_3	0.17	72.6	-123
3-CN	0.001	172	178

Table 2.33 Rate constants at 25°C and activation parameters for substituted arenediazonium tetrafluoroborates in ethanol.

Substituent	$10^4 k^{25} / s^{-1}$	$\Delta H^{\#} / kJ\ mol^{-1}$	$\Delta S^{\#} / J\ K^{-1}\ mol^{-1}$
H	2.32	74.7	-63.5
3-Me	3.63	100	26.4
3-MeO	4.09	96.5	13.9
3-CF_3	8.44	84.7	-19.7
3-CN	2.62	132	128

Table 2.34 Rate constants at 25°C and activation parameters for substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid.

Substituent	$10^4 k / s^{-1}$	$\Delta H^{\#} / kJ\ mol^{-1}$	$\Delta S^{\#} / J\ K^{-1}\ mol^{-1}$
H	0.47	111	45.0
3-Me	2.25	110	54.1
3-MeO	5.15	108	54.7

2.3 Product Analysis.

The products of the solvolysis reactions were identified by analytical gas liquid chromatography (comparison of retention times with authentic samples) and by ^{1}H and ^{13}C NMR (the products were isolated by preparative gas chromatography). The trifluoroethyl aryl ether products were not commercially available so they were prepared from the solvolysis reaction of the corresponding arenediazonium salt in trifluoroethanol (TFE).

2.3.1 Quantitative GLC analysis.

All of the thermal arenediazonium solvolysis reactions studied quantitatively by GLC were carried out using the following general procedure. The arenediazonium salt was dissolved in solvent. The reaction mixture was refluxed for a period of time dependent upon the substituted benzenediazonium salt under study. The solution was cooled, quenched with water and neutralised with aqueous sodium carbonate. This aqueous solution was then extracted with ether, and the extracts were combined. A solution of dichloromethane containing a known amount of undecane was added to the extract solution and the reaction mixture was analysed by GLC.

The photolytic solvolysis reactions were studied in a similar manner to the thermal reactions. The source of radiation was an immersion well photochemical reactor which contained the UV lamp. The extent of reaction was monitored by withdrawing small samples of the reaction mixture and analysing them on a uv spectrophotometer. A uv scan between 200-500 nm was carried out to follow the progress of the reaction.

2.3.2 Molar response factor determination (MRF).

The quantitative determination of a component in gas chromatography is based upon the ratio of the measurement of the recorded peak areas of the component with respect to an internal standard, which in the majority of cases was undecane (where undecane was unsuitable, octane was used.). The requirements for an effective internal standard are summarised as follows,

(a) it should give a completely resolved peak, but should be eluted close to the components to be measured,

(b) its peak height or peak area should be similar in magnitude to those of the components to be measured; and
(c) it should be chemically similar to the component under investigation but not present in the original sample.

The procedure involves the addition of a known amount of an internal standard to a known amount of the component to be determined. The resulting mixture is chromatographed and a MRF calculated. The analysis of the unknown mixture is carried out by addition of a similar amount of internal standard to the reaction mixture; from the observed ratio of peak areas the solute concentration is calculated using MRF's (Figure 2.3).

$$\text{MRF} = \frac{\text{Signal of A}}{\text{no. of moles of A}} \times \frac{\text{no. of moles of undecane}}{\text{signal of undecane}}$$

Figure 2.3

The MRFs measured are summarised in Table 2.35 and those calculated are in Table 2.36. The calculated MRF's are obtained by measuring the MRF for *m*-MeArOCH$(CF_3)_2$ and comparing this to the value for *m*-MeArOCH$_2CF_3$. This ratio is then applied to the value for X-ArOCH$_2CF_3$ to obtain the MRF for X-ArOCH$(CF_3)_2$.

Table 2.35. Experimental molar response factors for X-ArF and X-ArOCH$_2CF_3$ relative to undecane.

X	MRF	
	X-ArF	X-ArOCH$_2CF_3$
m-CF_3	0.65	0.41
m-NO_2	0.54	0.44
m-CN	0.62	0.42
H	0.52	0.68
m-MeO	0.58	0.63
m-Me	0.65	0.76
p-MeO	0.59	0.56
p-Me	0.66	0.72

Table 2.36 Calculated MRF's for X-ArOCH(CF_3)$_2$ relative to undecane.

X	MRF X-ArOCH(CF_3)$_2$
m-CF_3	0.28
m-NO_2	0.26
m-CN	0.25
H	0.40
m-MeO	0.37
m-Me	0.44

2.3.3 Solvolysis reactions of benzenediazonium tetrafluoroborate and chloride in TFE.

Table 2.37 illustrates the products obtained from the dediazoniation of benzenediazonium tetrafluoroborate and chloride in TFE. The reaction using benzenediazonium chloride was investigated to establish whether tetrafluoroborate is responsible for the donation of a fluoride anion to the aryl cation to form the aryl fluoride. Chlorobenzene was investigated as a possible product, but it was found to be absent. The presence of fluorobenzene and trifluoroethyl phenyl ether for both benzenediazonium salts can be clearly seen. The actual % recoveries and errors for this reaction and other quantitative work are shown in the appendix.

Table 2.37. Quantitative normalized GLC analysis of products from benzenediazonium tetrafluoroborate and chloride in 100% TFE.

Substrate	PhF / %	$PhOCH_2CF_3$ / %
PhN_2Cl	9.50	90.5
PhN_2BF_4	27.6	72.4

2.3.4 Reactions of arenediazonium tetrafluoroborates in mixed solvent systems.

The solvolysis reactions of benzenediazonium and 4-methylbenzenediazonium tetrafluoroborates in a mixed solvent system of water and TFE (1:1 molar ratio) was investigated and the results are shown in Table 2.38. The presence of 4-cresol and phenol suggests that water reacts with the phenyl cation intermediate. The aryl fluoride

and aryl ether products previously seen in the dediazoniation reaction with TFE are observed again. The yields of the products are calculated on the assumption that the total yield for that individual reaction is 100%.

Table 2.38. GLC analyses of products from substituted benzenediazonium tetrafluoroborates in TFE:H_2O (1:1).

Substituent	ArF / %	$ArOCH_2CF_3$ / %	ArOH / %
H	5.00	40.1	54.9
4-Me	24.3	42.0	33.7

The solvolysis reactions of 4-methylbenzenediazonium tetrafluoroborates in mixed solvent systems of TFE and TFMOB at different molar ratios, are shown in Table 2.39. Trifluoromethoxybenzene was chosen as a co-solvent to investigate, because of the presence of an oxygen lone pair in a favorable position to aid fluoride transfer. Table 2.40 illustrates a similar type of investigation but this time, a mixed solvent system of TFE and difluoromethyl 2,2,2-trifluoroethyl ether was used. Again the choice of co-solvent (difluoromethyl 2,2,2-trifluoroethyl ether) was due to the presence of oxygen in a favorable position to assist in fluoride transfer. These studies of mixed solvent systems are qualitative so it is assumed that the total yield of products is 100%.

Table 2.39. Qualitative product analysis from 4-methylbenzenediazonium tetrafluoroborate in TFE:trifluoromethoxybenzene (TFMOB).

Solvent	Yield of ArF / %	Yield of $ArOCH_2CF_3$ / %
TFE:TFMOB (10:1)	33.5	66.5
TFE:TFMOB (5:1)	39.0	61.0
TFE:TFMOB (2.5:1)	39.5	60.5
TFE	25.3	74.7

Table 2.40. Qualitative product analysis from 4-methylbenzenediazonium tetrafluoroborate in TFE:difluoromethyl 2,2,2-trifluoroethyl ether (DFTFE).

Solvent	Yield of ArF / %	Yield of $ArOCH_2CF_3$ / %
TFE:DFTFE (10:1)	8.90	91.1
TFE:DFTFE (5:1)	14.1	85.9
TFE: DFTFE (2.5:1)	12.7	87.3
TFE	25.3	74.7

2.3.5 Solvolysis reaction of benzenediazonium tetrafluoroborate in TFE with added inorganic fluoride salts.

Table 2.41 illustrates the product yields for the investigation of adding various fluoride salts to the reaction of benzenediazonium tetrafluoroborate in TFE. The salts that were chosen were $NaPF_6$, $NaBF_4$, and $NaSbF_6$. The reason for these choices of salts, was they were viewed as potential fluoride donors that are soluble in TFE. An obvious source of inorganic fluoride is potassium fluoride, unfortunately it is insoluble in a lot of organic solvents (TFE included). It is, however, extremely soluble in water; Table 2.42 illustrates the solvolysis reactions of 4-methoxy- and 4-methyl- benzenediazonium tetrafluoroborates in a saturated potassium fluoride environment. The yields of the substituted phenols were determined quantitatively by comparison of the UV absorbance of the reaction mixture with a standard of known concentration.

A direct comparison of the solvolysis reaction of 4-methoxy- and 4-methyl-benzenediazonium tetrafluoroborates in an aqueous environment devoid of potassium fluoride is shown in Table 2.43.

Table 2.41. Quantitative GLC analysis of products from benzenediazonium tetrafluoroborate in TFE with added inorganic salts.

Salt [mol dm^{-3}]	PhF	$PhOCH_2CF_3$
$NaPF_6$ [1.76]	27.3	72.7
$NaBF_4$ [0.63]	33.9	66.1
$NaSbF_6$ [0.60]	29.5	70.5
0	27.6	72.4

Table 2.42. Quantitative analysis of substituted benzenediazonium tetrafluoroborates in saturated aqueous KF (thermal and photolytic reactions).

Substituent X	Yield of Phenol %	
	Photolytic	Thermal
4-MeO	92.0	96.4
4-Me	92.0	96.5

Concentration of KF = 10.2 mol dm^{-3}.

Table 2.43 Quantitative analysis of the photolysis of *para* substituted benzenediazonium tetrafluoroborates in water.

Substituent	Phenol %
Me	93.0
OMe	89.6

2.3.6 Solvolysis reactions of substituted arenediazonium tetrafluoroborates in TFE.

The GLC quantitative analysis results for the solvolysis of various arenediazonium tetrafluoroborates in pure TFE are shown in Table 2.44 and Table 2.46. A similar study but this time monitoring the photolytic solvolysis of the same substituted arenediazonium tetrafluoroborates is shown in Tables 2.45 and 2.47.

Table 2.44. Normalised quantitative analysis of the thermolysis of *para* substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	ArF / %	$ArOCH_2CF_3$ / %
H	27.6	72.4
Me	33.5	66.5
OMe	—*	—*

* reaction too slow to monitor.

Table 2.45. Normalised quantitative analysis of the photolysis of *para* substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	ArF %	$ArOCH_2CF_3$ %
H	42.6	57.4
Me	45.2	54.8
OMe	48.8	51.2

Table 2.46. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in TFE via thermolysis.

Substituent	ArF / %	$ArOCH_2CF_3$ / %
H	27.6	72.4
Me	42.3	57.7
MeO	29.1	70.9
CF_3	27.2	72.8
CN	37.2	62.8
NO_2	43.7	56.3

Table 2.47. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in TFE via photolysis.

substituent	ArF / %	$ArOCH_2CF_3$ / %
H	42.6	57.4
Me	44.0	56.0
MeO	30.9	69.1
CF_3	32.8	67.2
CN	32.9	67.1
NO_2	43.3	56.7

2.3.7 Solvolysis reactions of substituted arenediazonium tetrafluoroborates in HFIP.

Hexafluoroisopropanol was chosen as a possible fluoride donor solvent. It was felt that the influence of 6 fluorine atoms β to the oxygen, might reduce the nucleophilicity of the oxygen sufficiently to lower the yield of the aryl ether and promote formation of the aryl fluoride. Table 2.48 illustrates the GLC quantitative product yield obtained for the thermal solvolysis reactions of various meta substituted arenediazonium tetrafluoroborates in HFIP. Table 2.49 illustrates the quantitative product distribution for the same arenediazonium tetrafluoroborates in HFIP but via photolysis.

Table 2.48. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol via thermolysis.

Substituent	ArF / %	$ArOCH(CF_3)_2$ / %
H	26.2	73.8
Me	23.5	76.5
MeO	12.4	87.6
CF_3	33.4	66.5

Table 2.49. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol via photolysis.

Substituent	ArF / %	$ArOCH(CF_3)_2$ / %
H	14.7	85.3
Me	14.6	85.4
MeO	13.4	86.6
CF_3	11.3	88.7

2.3.8 Solvolyis reactions of substituted arenediazonium tetrafluoroborates in trifluoroacetic acid.

Trifluoroacetic acid was identified as a possible fluoride donor solvent. The fact that it is a poor nucleophile but yet a highly ionising solvent suggested that aryl cation formation would be supported. Tables 2.50 and 2.51 show the thermal and photolytic solvolysis reactions of various substituted arenediazonium tetrafluoroborates in trifluoroacetic acid.

Table 2.50. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid via thermolysis.

Substituent	ArF / %	CF_3CO_2Ar / %
H	4.00	96.0
Me	15.1	84.9
MeO	10.5	89.5
CF_3	18.2	81.8
CN	13.8	86.2
NO_2	8.70	91.3

Table 2.51. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid via photolysis.

Substituent (X)	ArF / %	CF_3CO_2Ar / %
H	17.9	82.1
Me	19.8	80.2
MeO	14.6	85.4
CF_3	19.2	80.8
CN	20.9	79.1
NO_2	21.5	78.5

2.3.9 Solvolysis of substituted arenediazonium tetrafluoroborates in ethanol.

The work so far led us to believe that TFE was the best organic fluoride donor solvent studied. At this point, it was felt it was worth investigating the dediazoniation reactions (carried out in TFE), in ethanol. It was felt that if the mechanism by which ethanol reacted with the arenediazonium salt could be understood, then an insight into how TFE can react with arenediazonium ions might be gained. Table 2.52 illustrates the product distribution for the thermal dediazoniation of various substituted arenediazonium tetrafluoroborates in ethanol.

Table 2.52. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in ethanol via thermolysis.

Substituent	ArH / %	ArF / %	CH_3CH_2OAr / %
H	<1	3.54	95.4
Me	3.30	15.1	81.6
MeO	4.20	17.3	78.5
NO_2	92.1	<1	7.90

2.3.10 Solvolytic reaction of 3-nitrobenzenediazonium tetrafluoroborate in ethanol (1-1-d_2).

Having established that ethanol acts as a reducing agent, it was decided to investigate which hydrogen is transferred from ethanol to the arenediazonium ion for reduction to occur. Previous work by Melander using methanol as a reducing agent demonstrated that the hydroxy hydrogen is not involved.[92] The hydrogen that is transferred is the one on the α carbon. Subsequent reports in the literature, using Melander's work as the benchmark, cited the proton on the α carbon being the one that is transferred when ethanol is used as the reducing agent. It was decided to investigate the reduction of 3-nitrobenzenediazonium tetrafluoroborate with ethanol in more detail. The product obtained from the thermal dediazoniation reaction of 3-nitrobenzenediazonium tetrafluoborate in ethanol (1,1-d_2) was determined structurally by ^1H and D NMR. Information on coupling constants allowed the position of the deuterium atom transferred to be identified.

Table 2.52. Product analysis of the solvolytic reaction of 3-nitrobenzenediazonium tetrafluoroborate in ethanol (1-1-d_2).

Substrate	Solvent	Product
3-$NO_2C_6H_4N_2BF_4$	CH_3CD_2OH	3-$NO_2C_6H_4D$

δ_H 7.5 (m, 1H, Ar), 7.7 (m,1H, Ar), 8.2 (m, 2H, Ar), δ_D (300 MHz) 7.6 (t, J = 1.2 Hz, 1D, Ar).

m/z (EI) 124 (M^+, 80%), 94, 78, 52.

Chapter 3. Discussion.

The main subject of this thesis has been the study of the product distribution from a range of substituted arenediazonium tetrafluoroborates in possible fluoride donor solvents and cosolvents. We have also investigated the rates of some of these reactions over a temperature range and hence calculated the activation parameters. This study is a continuation of work undertaken by K. McCrudden for her doctorate at the University of Newcastle upon Tyne (1994).[91]

3.1 Kinetics.

The rates of the dediazoniation reactions of arenediazonium tetrafluoroborates were measured in water, trifluoroethanol (TFE), hexafluoroisopropanol (HFIP), ethanol (EtOH) and trifluoroacetic acid (TFA). The rate constants are average values of two experimental rate determinations. In general the standard deviation was always less than 5% and in the majority of cases less than 1%. The rate constants at 25°C were not measured directly but were extrapolated from the Eyring plot constructed for each substrate. From the rate constants at different temperatures the activation parameters $\Delta H^{\#}$ and $\Delta S^{\#}$ were calculated. These parameters can be seen in Tables 3.1-3.5 and in the appendix with their corresponding standard deviation. For the enthalpy of activation, the standard deviation in the majority of cases is less than 5%. The entropy of activation for the dediazoniation reactions is less precise, as it is an extrapolated value. In most cases the Eyring plot covers at least 25°C. Slight errors within this range will result in large errors in the value of the entropy parameter obtained from the extrapolation, so the entropy results should be viewed with caution. Tables 3.1 to 3.5 are shown here for easy reference.

Table 3.1 Rate constants at 25°C and activation parameters for X-substituted benzenediazonium tetrafluoroborates in water.

Substituent	$10^6 k^{25} / s^{-1}$	$\Delta H^{\#} / kJ\ mol^{-1}$	$\Delta S^{\#} / J\ K^{-1}\ mol^{-1}$
H	53.1	109	37.4
3-Me	263	93.0	-2.42
4-Me	4.35	114	36.5
3-MeO	240	98.5	15.8
3-CF_3	0.27	128	55.7
3-NO_2	9.69	99.1	-16.9
3-CN	11.3	79.3	-74.7

Table 3.2 Rate constants at 25°C and activation parameters for X-substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	$10^5 k^{25} / s^{-1}$	$\Delta H^{\#} / kJ\ mol^{-1}$	$\Delta S^{\#} / J\ K^{-1}\ mol^{-1}$
H	9.21	114	62.1
3-Me	53.0	99.3	24.8
4-Me	3.93	108	34.0
3-MeO	87.3	103	42.3
3-CF_3	0.07	111	10.3
3-NO_2	0.06	124	53.6
3-CN	0.03	116	19.7

Table 3.3. Rate constants at 25°C and activation parameters for X-substituted benzenediazonium tetrafluoroborates in HFIP.

Substituent	$10^5 k^{25} / s^{-1}$	$\Delta H^{\#}$ / kJ mol^{-1}	$\Delta S^{\#}$ / J K^{-1} mol^{-1}
H	9.72	116	66.2
3-Me	51.9	108	55.6
3-MeO	173	98.4	31.6
3-CF_3	0.17	72.6	-123
3-CN	0.001	172	178

Table 3.4. Rate constants and activation parameters for X-substituted benzenediazonium tetrafluoroborates in EtOH.

Substituent	$10^4 k^{25} / s^{-1}$	$\Delta H^{\#}$ / kJ mol^{-1}	$\Delta S^{\#}$ / J K^{-1} mol^{-1}
H	2.32	74.7	-63.5
3-Me	3.63	100	26.4
3-MeO	4.09	96.5	13.9
3-CF_3	8.44	84.7	-19.7
3-CN	2.62	132	128

Table 3.5. Rate constants at 25°C and activation parameters for X-substituted benzenediazonium tetrafluoroborates in TFA.

Substituent	$10^4 k / s^{-1}$	$\Delta H^{\#}$ / kJ mol^{-1}	$\Delta S^{\#}$ / J K^{-1} mol^{-1}
H	0.47	111	45.0
3-Me	2.25	110	54.1
3-MeO	5.15	108	54.7

As shown below, the enthalpies and entropies of activation are components of the standard free energy of activation which conveys the same information as the rate constant to which it is directly related by transition state theory.

$$k = \frac{k_B T}{h} e^{-\Delta G^{\#}/RT}$$

The lower $\Delta G^{\#}$ of a reaction the larger the rate constant and the faster the reaction. $\Delta G^{\#}$ can be resolved into enthalpy and entropy contributions by the equation

$$\Delta G^{\#} = \Delta H^{\#} - T\Delta S^{\#}$$

which leads to

$$k = \frac{k_B T}{h} e^{-\frac{\Delta H^{\#}}{RT}} e^{\frac{\Delta S^{\#}}{R}}$$

An individual rate constant or activation free energy carries little mechanistic information. Calculating the enthalpy and entropy terms $\Delta H^{\#}$ and $\Delta S^{\#}$ gives a better insight into the transformation of reactants into products. The chemical reaction can be viewed in terms of stretches and bends of bonds and of collisions between molecules.

$\Delta H^{\#}$ is closely related to the ease of the bond breaking and reforming in the generation of the activated complex. Qualitatively, the lower $\Delta H^{\#}$, the faster the reaction. $\Delta S^{\#}$ is a measure of the change in the degree of organisation or ordering of both the reacting molecules and of the distribution of energy within them. If formation of the transition state requires a high degree of organisation in the way reactant molecules must approach each other, then the attainment of the transition state occurs with a sizeable decrease in entropy and the probability of its formation is decreased.

The following reaction mechanism proposed by Zollinger (Figure 3.1) can be used to interpret our kinetic results. The arenediazonium ion undergoes a reversible cleavage of the carbon-nitrogen bond to form the first intermediate, a cation/molecule pair, within a single solvent shell. This intermediate may then either (1) undergo capture by nucleophiles (or solvent) to form products or (2) dissociate to form the second intermediate, the solvent separated aryl cation and a nitrogen molecule; this will then undergo nucleophilic capture to form products.

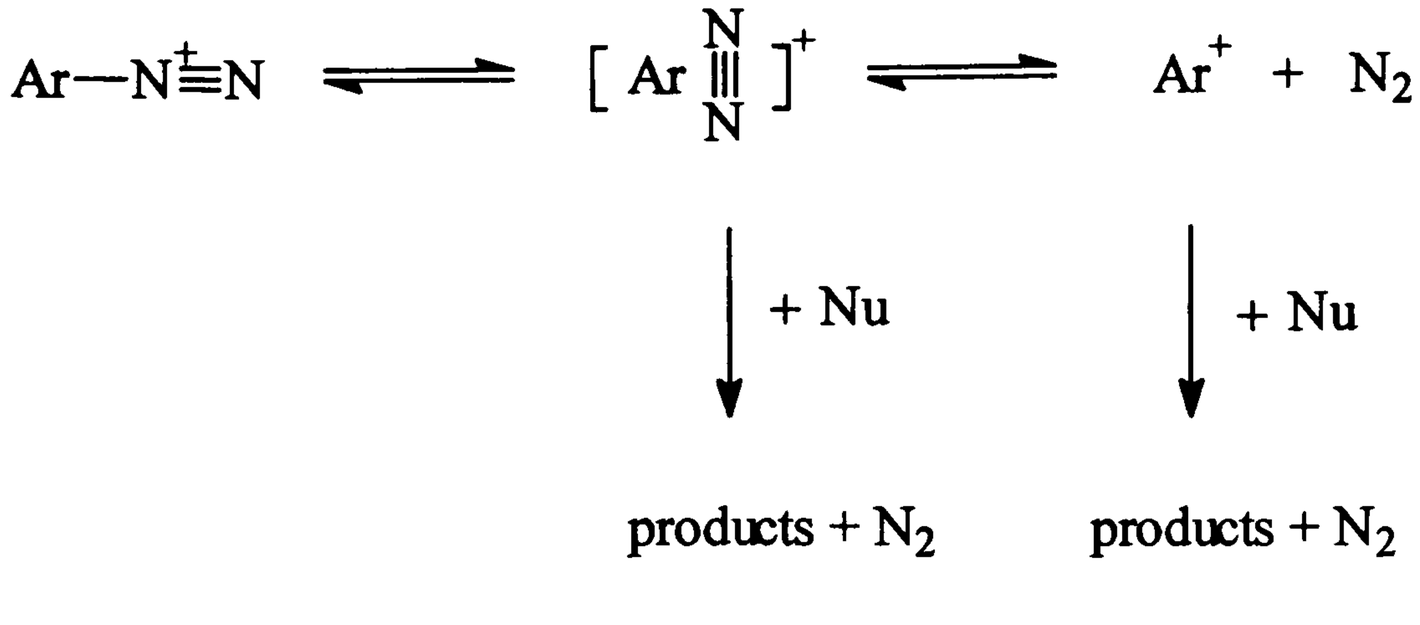


Figure 3.1

The following reaction coordinate diagram (Figure 3.2), which is based upon Zollinger's mechanism can be used to interpret the results. The rate of the reaction is determined by the height of the barrier between the initial diazonium salt and the transition state This barrier can be lowered in which case the rate of reaction is increased. This is achieved on the reaction coordinate diagram by either increasing the free energy level of the starting arenediazonium salt or by decreasing the free energy level of the intermediate.

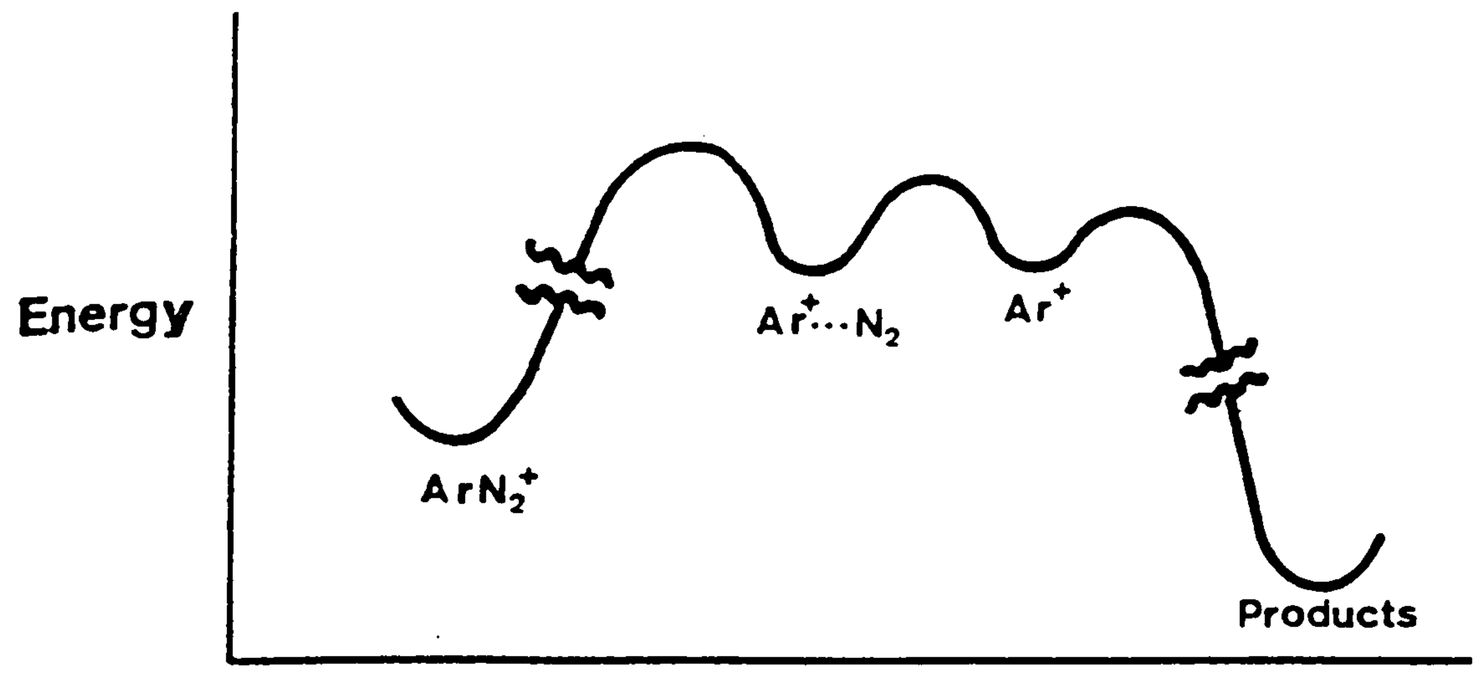


Figure 3.2

Individual parameters carry little mechanistic information; it is more meaningful to examine changes in rate constants and activation parameters while varying a particular feature in the reaction. The features that were chosen to be varied were substituents attached to the arenediazonium ion, and the solvent in which dediazoniation occurred.

3.1.1 Activation parameters.

Activation parameters are a useful indication of mechanistic trends. For bimolecular reactions the enthalpy of activation is small as bond making and bond breaking are concerted so the resultant energy change will be small as the reactant proceeds to the transition state. In contrast, the entropy of activation will be negative and large. This is because two species are coming together to form one so there will be a large loss of rotational and translational entropy.

For unimolecular reactions, the enthalpy and entropy factors are quite different from those of bimolecular reactions. In an S_N1 solvolysis reaction of a neutral substrate, the reactant dissociates to give an ion pair. The energy required to break the bond is partially compensated by the change in the enthalpy of solvation as neutral substrates give dipolar activated complexes. The net result is solvation lowers the enthalpy of activation. The greater the solvation effect, the lower the enthalpy of activation and hence the faster the reaction. For S_N1 reactions, the entropies of activation tend to be close to zero. The compensating effects of the entropy gained due to loosening of the bond in the reactant molecule is counterbalanced by the decrease in entropy due to the more highly ordered arrangement of solvent molecules around the activated complex. An increase in solvation will result in a negative entropy of activation as a result of a greater degree of ordering in the transition state. The more strongly the solvent molecules are bound, the greater the overall loss of entropy. Tables 3.1 to 3.5 illustrate the activation parameters for the dediazoniation reactions in different solvents. For the reactions in water the enthalpies of activation are of a similar magnitude (100 $kJmol^{-1}$). There appears to be no trend for the corresponding entropies of activation. The values range from 36.5 $JK^{-1}mol^{-1}$ for the 4-methylbenzenediazonium salt to -74.7 $JK^{-1}mol^{-1}$ for the 3-cyanobenzenediazonium salt. Similar values for the enthalpies of activation are seen for the dediazoniation reactions in TFE (approximately 100 $kJmol^{-1}$). The entropies of activation for the dediazoniation reactions in TFE are all positive and range from 10.3 $JK^{-1}mol^{-1}$ for the 3-trifluoromethylbenzenediazonium ion to 62.1 $JK^{-1}mol^{-1}$ for the parent ion. For the dediazoniation reactions in hexafluoroisopropanol the enthalpies of activation are again of a similar magnitude (100 $kJmol^{-1}$) except for the 3-cyanobenzenzenediazonium ion (172 $kJmol^{-1}$). The entropies of activation for these

reactions in hexafluoroisopropanol vary from -123 $JK^{-1}mol^{-1}$ for the 3-trifluoromethylbenzenediazonium ion to 178 $JK^{-1}mol^{-1}$ for the 3-cyanobenzendiazonium ion. As both of these substituents have extemely small rate constants, hence long reaction times, it is felt these results reflect a large degree of error. Similar values are observed for the enthalpies of activation for the reactions in ethanol and trifluoroacetic acid. The enthalpies of activation are approximately 100 $kJmol^{-1}$. The entropies of activation for the dediazoniation reactions in ethanol vary considerably (from -63.5 $JK^{-1}mol^{-1}$ to 128 $JK^{-1}mol^{-1}$) whilst the entropies of activation for the dediazoniation reactions in trifluoroacetic acid for the parent, 3-methyl and 3-methoxy tend to be approximately 50 $JK^{-1}mol^{-1}$.

The enthalpy value is relatively low compared with normal S_N1 values due to the stability of the nucleofuge i.e. dinitrogen. However, heterolytic dediazoniation is further different from a typical S_N1 reaction because the reactant (arenediazonium ion) and the intermediate are both charged species. The effect of this is that in the transition state there will not be a change in overall charge, instead it will be merely be redistributed. A consequence of this effect is the enthalpy of activation will not be affected to the extent that it is by solvent polarity in a typical S_N1 reaction, hence the reason why the majority of enthalpies of activation are of a similar magnitude irrespective of the solvent.

3.1.2 Effect of substituents.

Examining the rate constant for different arenediazonium tetrafluoroborates in water, indicates the nature of the substituent and its position affects the rate of dediazoniation. The effect of *meta* and *para* substituents on the rate of dediazoniation is considerable. The ratio in the rate constant for the *meta* methyl and *meta* trifluoromethyl benzenediazonium dediazoniation reactions in water is approximately 1000 fold. Viewing the ratio in rate constant for the *para* methyl substituent and the *meta* methyl substituent we see a ratio in rate constant of sixty times. These effects arise since the starting arenediazonium ion or aryl cation can be stabilised or destabilised by the substituent group. Similar effects are observed for the dediazoniation reactions in TFE, hexafluoroisopropanol and trifluoroacetic acid (Table 3.6).

Table 3.6 to show the factors in rate constant for substituents with respect to the parent benzenediazonium tetrafluoroboraten at 25°C.

Substituent	Solvent (k) (*10^2k)				
	Water	TFE	HFIP	EtOH	TFA
H	1.0	1	1	1	1
3-Me	5.0	5.8	5.3	1.6	4.8
3-MeO	4.5	9.5	17.8	1.8	11.0
3-CF_3	*0.5	*0.8	*1.7	3.6	—
3-NO_2	*18.1	*0.6	—	—	—
3-CN	*21.2	*0.3	*0.01	+1.1	—
4-Me	*8.2	0.4	—	—	—

Any attempt to intrepret this data indiviually in a Hammett equation results in a scatter (see Appendix A, p.145). This is due to the starting arenediazonium ion and aryl cation being resonance stabilised by electron donation to different degrees.

Comparing the rates for the dediazoniation reactions of arenediazonium salts with electron donating substituents to the unsubstituted salt, we observe that for the reaction in TFE an increase in the rate by a factor of 9.5 and 5.8 times occurs for the 3-methoxy and 3-methyl substituents. For the dediazoniation reactions in trifluoroacetic acid a similar rate enhancement is observed for the 3-methoxy and 3-methyl substituents. In this case the effect is 11 and 4.8 times greater respectively than the unsubstituted analogue. The rate enhancement effect is similar in hexafluoroisopropanol, 3-methoxy and 3-methyl substituents increase the rate by a factor of 17.8 and 5.3 respectively to the unsubstituted benzenediazonium salt. For the dediazoniation reactions in water the effect is less pronounced, the increase is 4.5 and 5 times greater than the unsubstituted salt. With ethanol as the solvent, the dediazoniation rate increase is negligible for arenediazonium salts containing 3-methyl and 3-methoxy substituents.

The results for the dediazoniation reaction in water are in good agreement with those observed by Swain and co-workers who also studied the effects of substituents on the reaction of benzenediazonium tetrafluoroborates in water. In order to explain the effect of substituents on the rate of dediazoniation we should consider a reaction coordinate

diagram (Figure 3.2) which is based upon Zollinger's mechanism. The rate of the reaction is reflected by the height of the barrier from the initial state and the transition state (TS). Introducing a substituent that increases the rate of dediazoniation relative to the parent compound decreases the barrier from the initial state and the transition state. This can occur by a decrease in the stability of the arenediazonium salt or a decrease in the free energy of the transition state leading to the aryl cation intermediate. Similarly a substituent that decreases the rate of dediazoniation relative to the parent compound, increases the barrier between the initial state and the transition state. This occurs by either stabilisation of the substrate or destabilisation of the rate-determining transition state.

Substituents in the *meta* position affect the stability of the intermediate. They have little effect on the arenediazonium salt. Substituents that can donate electrons, stabilise the intermediate aryl cation by providing negative charge to the ortho carbons. A methyl substituent in the *meta* position releases electrons to the electron deficient site. This effect (known as the inductive effect) occurs as a result of the electron deficient site being able to attract electron density from the polarisable alkyl group through the σ bonded system. The *meta* methoxy group stabilises the aryl cation by electron donation from its lone pair. Electron withdrawing groups (nitro, cyano and trifluoromethyl) destabilise the aryl cation by withdrawing electrons from it.

Viewing the results in Table 3.6, it can be seen that an electron donating *para* substituent, is rate retarding. This is in direct contrast to electron donating groups in the *meta* position. This suggests that electron donating substituents in the *para* position stabilise the arenediazonium salt by resonance considerably more than the aryl cation. Although no work was carried out in this study with electron withdrawing *para* substituents, previous work has shown them to be rate retarding as well.[91] It is believed that these substituents decrease the stability of the aryl cation thereby increasing the energy barrier of the reaction.

For electron donating *para* groups Swain proposed that the double bond character of the C-N bond is increased, consequently the bond is strengthened thus the rate constant for dediazoniation is reduced.[59] However it must also be noted that *para* electron donating substituents do have an effect on the stability of the intermediate aryl cation. Kemp and

Ambroz observed that *para* substituents with a lone pair (NMe_2) stabilise the triplet form of the intermediate to such an extent that it is preferred to the singlet form. In view of the fact electron donating *para* substituents reduce the rate constant of dediazoniation reactions, then stabilisation of the diazonium substrate must be greater than the intermediate state stabilisation.[103]

In conclusion stabilisation of the cation is most important for *meta* substituents while for *para* electron donating substituents the most important mechanism is stabilisation of the starting benzenediazonium ion.

3.1.3 Effect of solvent.

Listing the dediazoniation rate constants in order of increasing solvent polarity (Table 3.7), no significant change in rate constant is observed. The slowest and fastest rate constants only differ by a factor of 5.

Table 3.7 to show the rate constant in solvents of different polarity for benzenediazonium tetrafluoroborate at 25°C.

Solvent	$k\,10^4$	ε
TFA	0.47	8.20
HFIP	0.97	16.7
TFE	0.92	26.6
EtOH	2.32	24.3
H_2O	0.53	80.1

Changing the solvent in which a reaction is carried out often exerts a profound effect on its rate. Thus for an alkyl halide that undergoes hydrolysis by the S_N1 mode an increase in the polarity of the solvent (increase in ε, the dielectric constant) is found to result in a very marked increase in reaction rate. The rate of solvolysis of the tertiary halide Me_3CBr is found to be 1500 times faster in water than ethanol. This occurs because, in the S_N1 mode, charge is developed and concentrated in the T.S. compared with the starting material. The energy required to effect such a process decreases as ε rises; the

process is also facilitated by increasing solvation, and consequent stabilisation, of the developing ion pair compared with the starting material.

Table 3.7 indicates that increasing solvent polarity has little effect on the rate constant for heterolytic dediazoniation reactions. The reason for this is that the initial reactant is already charged, so in the T.S. no new charge is developed. Thus the change in solvation upon formation of the T.S. state for the dediazoniation reaction is less than for the formation of the T.S. for the tertiary alkyl halide where the initial starting reagent is uncharged.

Viewing the rate constants for TFE and water it can be seen that they differ by a factor of 2 (Table 3.7). This is rather a small change considering the difference in nucleophilicity of the solvents. The decrease in rate as the solvent changes from TFE to water was previously noted by Zollinger when studying the kinetics of the benzenediazonium ion. Zollinger suggested that the difference in rate constants is due to the different solvating abilities of the two solvents. Water is able to solvate aryl cations better than TFE, so the free energy level of the aryl cation is lower in water. However, this medium also solvates the arenediazonium cation better than TFE, so this free energy level is also lower in water. The overall effect is an increase in the difference in free energy between the ground state and the transition state (i.e. the activation energy $\Delta G^{\#}$) for the reaction in water compared to TFE (Figure 3.3). In general for heterolytic dediazoniations, increasing the solvating properties leads to a decrease in rate. This observation is consistent with the Hughes-Ingold rules for S_N1 reactions, which state that in the case of species that are charged in the initial state, in the transition state their charge is more spread out so increasing the solvent polarity slows the reaction down. It should be noted that the rate changes are small considering the difference between the solvent systems.

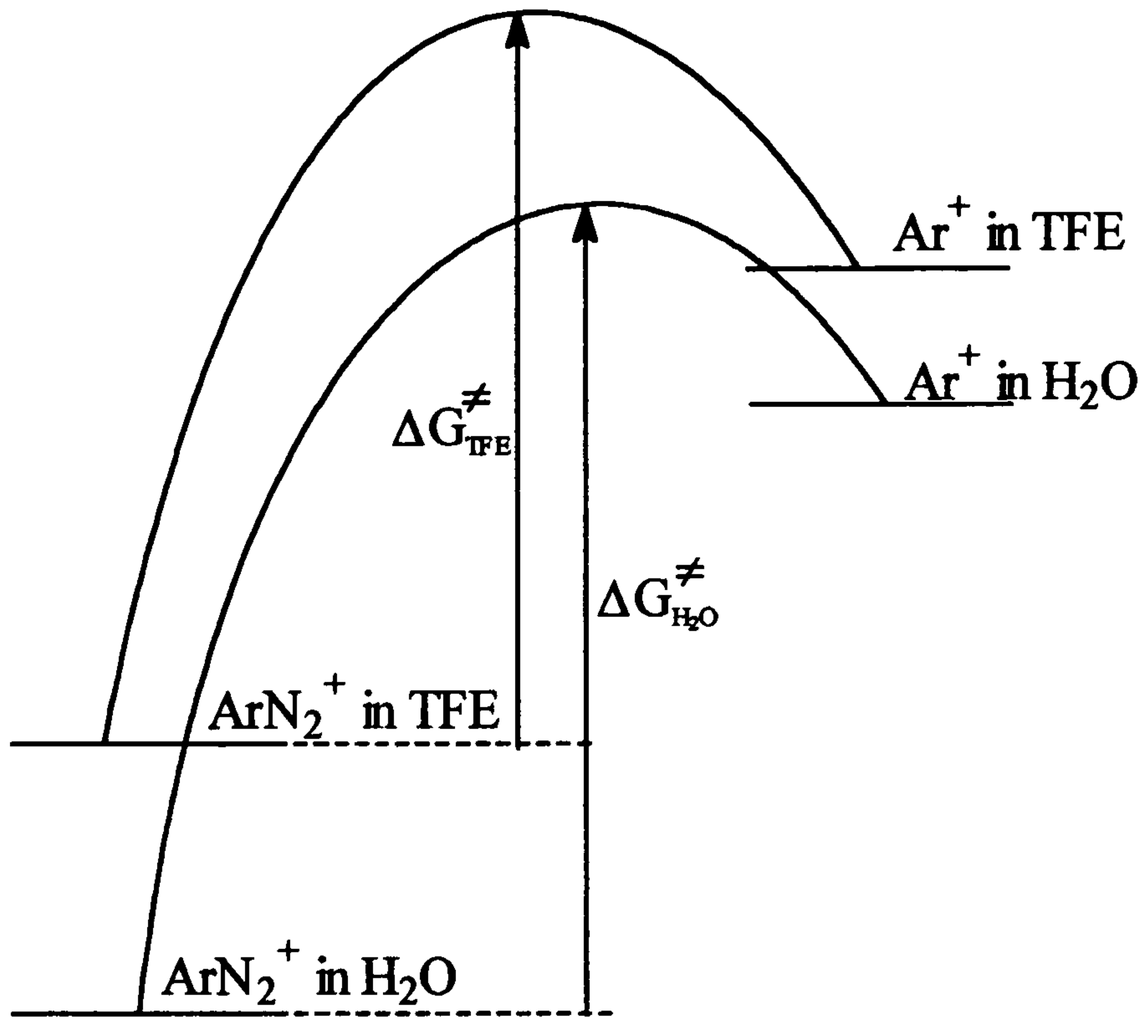


Figure 3.3

3.2 Product Analysis.

3.2.1 Analysis of products from benzenediazonium tetrafluoroborate and chloride.

The classic Balz-Schiemann reaction where solid benzenediazonium tetrafluoroborate decomposes to aryl fluoride was studied by Swain and co-workers to see whether the source of fluoride is BF_4^- or F^- (Figure 3.4).[118] By demonstrating that the product distribution was not affected by BF_3 concentration they were able to disprove the fluoride source as F^- and show it to be tetrafluoroborate.

$$Ar^+ + BF_4^- \longrightarrow ArF + BF_3$$

$$BF_4^- \rightleftharpoons BF_3 + F^-$$

$$Ar^+ + F^- \longrightarrow ArF$$

Figure 3.4

Swain studied the reaction of t-butylbenzenediazonium tetrafluoroborate in methylene chloride.[118] The only products present were ArF and ArCl. The presence of aryl chloride suggested to the authors that Ar^+ is sufficiently electrophilic to be capable of attacking neutral CH_2Cl_2 and abstracting a chloride. The aryl fluoride was accounted for by the reaction of Ar^+ with BF_4^-.

Previous work by K. McCrudden suggested that the dediazoniation reaction in TFE afforded a higher yield of fluorobenzene than expected.[91] It was suggested that TFE may be a source of fluoride as well as BF_4^-. To test this idea we decided to eliminate BF_4^- as a source of fluoride. Using chloride as a counter anion in TFE we were able to determine whether TFE is a fluoride source.

Table 3.8. Quantitative analysis of products from benzenediazonium tetrafluoroborate and chloride in 100% TFE.

Substrate	PhF / %	$PhOCH_2CF_3$ / %
PhN_2Cl	9.50	90.5
PhN_2BF_4	27.6	72.4

The results in Table 3.8 show that, using chloride as the counter ion, approximately 10% of the product is ArF. The corresponding dediazoniation reaction in TFE with BF_4^- as counter ion produced fluorobenzene in 27% yield. These results would suggest that the solvent (TFE) can donate 10% of the fluoride in the product while BF_4^- contributes 17%. For the dediazoniation reactions using benzenediazonium chloride, chlorobenzene was not observed as a product. Work by McClelland and Steenken has shown the lifetime of the aryl cation to very short.[119] As TFE supports the formation of free ions and solvent separated ion pairs, and it is present in a large excess over the chloride ion, the aryl cation will react with the first species it encounters which is the solvent.

3.2.2 Analyses of products from substituted benzenediazonium tetrafluoroborates in mixed solvent systems.

Table 3.9 shows the results of the dediazoniation of benzenediazonium tetrafluoroborate and 4-methylbenzenediazonium tetrafluoroborate in a mixed solvent system of TFE and water (1:1 molar ratios). Benzenediazonium tetrafluoroborate produces fluorobenzene, phenol and trifluoroethyl phenyl ether whilst the 4-methyl analogue produces 4-methylfluorobenzene, 4-methylphenol and trifluoroethyl 4-methylphenyl ether.

Table 3.9. Normalized GLC analyses of products from substituted benzenediazonium tetrafluoroborates in TFE:H_2O (1:1).

Substituent	ArF / %	$ArOCH_2CF_3$ / %	ArOH / %
H	5.00	40.1	54.9
4-Me	24.3	42.0	33.7

Allowing for experimental error, the yields of the trifluoroethyl phenyl ethers and phenol products are not too dissimilar. This suggests that the phenyl cation shows very little selectivity between water and TFE. As water is a stronger nucleophile than TFE it would be expected to predominate as the main nucleophile but this is not reflected in the product distribution. The combination of the two solvents must affect the individual nucleophilicities. Previous work on the selectivity of vinyl carbocations in TFE:H_2O mixtures demonstrated that TFE had a similar nucleophilicity to water.[91] The reason for this is hydrogen bonding interactions which reduce the nucleophilicity of oxygen in water while at the same time increasing the nucleophilicity of oxygen in TFE. These interactions are shown in Figure 3.5

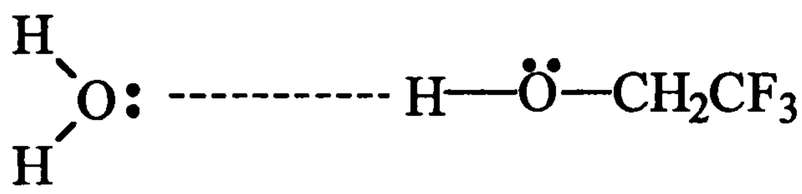


Figure 3.5

The differences in yields of the aryl fluorides from the 4-methyl and parent benzenediazonium salts may be a consequence of the different stabilities of the respective aryl cations. The methyl group although *para* will be able to stabilise the aryl cation thereby increasing its lifetime. This would increase the probability of encounters with BF_4^- ions. It would also increase the number of correct orientations of TFE with the aryl cation for fluoride transfer to occur.

Having established it is possible for an organic solvent to act as a fluoride donor it was decided to investigate other potential fluoride donor solvents. Two cases examined were trifluoromethoxybenzene (TFMOB) and difluoromethyl 2,2,2 trifluoroethyl ether (DFTFE). Both solvents have an oxygen in a favourable position to assist in fluoride expulsion (Figure 3.6).

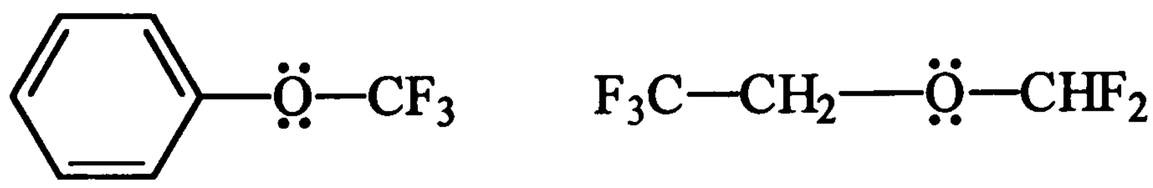


Figure 3.6

Each of the solvents was used in conjunction with TFE in a mixed solvent system for the dediazoniation reaction of 4-methylbenzenediazonium tetrafluoroborate. Table 3.10 shows the yields of aryl fluorides observed using the mixed solvent systems TFE:TFMOB and TFE:DFTFE.

Table 3.10. Normalised product analysis from 4-methylbenzenediazonium tetrafluoroborate in mixed solvent systems.

Solvent	Yield of ArF / %	Yield of $ArOCH_2CF_3$ / %
TFE:TFMOB (10:1)	33.5	66.5
TFE:TFMOB (5:1)	39.0	61.0
TFE:TFMOB (2.5:1)	39.5	60.5
TFE:DFTFE (10:1)	8.90	91.1
TFE:DFTFE (5:1)	14.1	85.9
TFE: DFTFE (2.5:1)	12.7	87.3

Although this determination is only qualitative it gives an indication that larger yields of aryl fluorides are obtained in mixed solvent systems with TFE:TFMOB (40%) than with the solvent system TFE:DFTFE (12%). These results should be contrasted with the aryl fluoride yield in pure TFE (25%). These results would seem to suggest that the addition of TFMOB increases the formation of aryl fluoride. Whether this increase is due to changing the properties of the solvents i.e. more ion pairs are favoured than free ions or TFMOB is able to act as a fluorine donor is difficult to determine. What is evident, however, is that by changing the composition of the solvent system, the product distribution is affected.

3.2.3 Quantitative analysis with added inorganic salts.

The effects of adding inorganic salts to the solvolysis reaction of benzenediazonium tetrafluoroborate in TFE were studied by quantitative GLC. The results (Table 3.11) indicate that addition of hexafluorophosphate, tetrafluoroborate and hexafluoroantimonate had little effect on product distribution. No increase in the yield of fluorobenzene was observed. If TFE promoted formation of ion pairs to any extent, increasing the number of ion pairs would increase the yield but as this is not observed the free aryl cation must predominate. As this species is a short lived intermediate it will react with whatever is closest to it, which will be TFE. These results seem to suggest that fluorobenzene formation occurs by the electrophilic aryl cation abstracting a fluoride from TFE. An interesting follow up to this set of reactions would be to study the effects of doing the dediazoniation reactions in a media that promotes formation of ion pairs. In this medium, increasing the concentration of the anion should lead to an increase in the yield of aryl fluoride. A possible solvent to use would be dichloroethanol which has a low dielectric constant hence ion pairs would be favoured. Complications would occur with the inclusion of aryl chloride in the product distribution.

Table 3.11. Quantitative GLC analysis of products from benzenediazonium tetrafluoroborate in TFE with added inorganic salts.

Salt [mol dm^{-3}]	PhF	$PhOCH_2CF_3$
$NaPF_6$ [1.76]	27.3	72.7
$NaBF_4$ [0.63]	33.9	66.1
$NaSbF_6$ [0.60]	29.5	70.5

3.2.4 Analysis of substituted benzenediazonium tetrafluoroborates in a saturated aqueous KF solution.

The rationalisation behind this investigation was to provide an environment in which the aryl cation is surrounded by fluoride ions. Choosing potassium fluoride due to its low cost and its effectiveness as a fluorinating agent restricted the solvent system to being aqueous. Unfortunately the vast majority of metal fluorides are insoluble in organic solvents suitable for dediazoniation so our preferred solvent system, TFE was

inappropriate for KF. The objective was to saturate the solvent system with KF so hopefully the aryl cation would experience a sufficient concentration of fluoride ions. Table 3.12 illustrates the dediazoniation reactions of 4-methyl- and 4-methoxy-benzenediazonium tetrafluoroborates in saturated aqueous KF system. The results clearly show substituted phenols to be the main product. This would suggest that our attempts to create an environment in which the aryl cation is surrounded by fluoride ions has been unsuccessful. The aryl cation is surrounded by a shell of tightly bound water molecules. These water molecules far outweigh the number of fluoride ions. Since aryl cations are exceedingly short lived, they cannot diffuse through the water, hence water is the reaction partner.

Table 3.12. Quantitative analysis of substituted benzenediazonium tetrafluoroborates in saturated aqueous KF (thermal and photolytic reactions).

Substituent X	Yield of Phenol %	
	Photolytic	Thermal
4-MeO	92.0	96.4
4-Me	92.0	96.5

Concentration of KF = 10.2 mol dm^{-3}.

3.2.5 Photolytic reactions.

It is well known that solid benzenediazonium salts decompose under the influence of light. The mechanism of decomposition is not fully understood but it would appear that it is largely determined by the environment and substituents of the benzenediazonium salt. The dediazoniation reactions of 4-methyl- and 4-methoxybenzenediazonium tetrafluoroborates in saturated KF solutions had demonstrated that the reaction occurred faster photolytically than thermally. Both arenediazonium salts had decomposed within 2 hours photolytically whereas the thermal reactions took days. Hence it was decided to investigate the product distribution of the photolytic dediazoniation of several substituted benzenediazonium salts in TFE and compare this to their corresponding thermal reactions. Tables 3.13 and 3.14 provide an indication that the yields of substituted

fluorobenzenes obtained by photolytic dediazoniations are slightly better than the corresponding thermal dediazoniations. The 4-methoxybenzenediazonium tetrafluoroborate dediazoniation occurs so slowly in TFE thermally, that a reliable product distribution was not attained. The corresponding photolytic reaction is faster and a good yield of *p*-methoxyfluorobenzene is obtained. The photolytic reaction mechanism is different from that of the thermal reaction mechanism, and this is reflected in the large differences in the rates. It is unlikely that the photolytic reaction operates via a radical mechanism as there are no signs of a reductive product. It is likely that similar cationic intermediates exist as the end products are the same. More work needs to be done on the photolytic route to gain an understanding of the mechanism involved. The rate enhancement that is observed by photolytic dediazoniation suggest this method may have industrial possibilities.

Table 3.13. Quantitative analysis of the thermolysis of *para* substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	ArF / %	$ArOCH_2CF_3$ / %
H	27.6	72.4
Me	33.5	66.5
OMe	——*	——*

* reaction too slow to monitor.

Table 3.14. Quantitative analysis of the photolysis of *para* substituted benzenediazonium tetrafluoroborates in TFE.

Substituent	ArF %	$ArOCH_2CF_3$ %
H	42.6	57.4
Me	45.2	54.8
OMe	48.8	51.2

Tables 3.15 and 3.16 display the product yields obtained for six substituted benzenediazonium tetrafluoroborates for thermal and photolytic dediazoniations in TFE. In both cases, similar yields are obtained but the rates photolytically are much faster.

Table 3.15. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in TFE via thermolysis.

substituent	ArF / %	$ArOCH_2CF_3$ / %
H	27.6	72.4
Me	42.3	57.7
MeO	29.1	70.9
CF_3	27.2	72.8
CN	37.2	62.8
NO_2	43.7	56.3

Table 3.16. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in TFE via photolysis.

substituent	ArF / %	$ArOCH_2CF_3$ / %
H	42.6	57.4
Me	44.0	56.0
MeO	30.9	69.1
CF_3	32.8	67.2
CN	32.9	67.1
NO_2	43.3	56.7

In all the dediazoniation reactions in TFE, a large yield of the aryl ether is obtained as the main product. The reason for this is the nucleophilic oxygen of TFE reacts with the aryl cation preferentially to fluoride abstraction from TFE by the aryl cation. It was proposed that if the nucleophilicity of oxygen in an organic fluoride donor solvent could be reduced, then an increase in the ratio of fluoroaromatic to aryl ether would be observed. Hexafluoroisopropanol was identified as a possible fluoride donor solvent. It is a highly ionising solvent which allows the formation of aryl cations. The oxygen of HFIP is surrounded by 6 fluorine atoms on the β carbons. The effect of these fluorines is to reduce the nucleophilicity of this oxygen via an inductive effect. Viewing the results in Tables 3.17 and 3.18, it can be seen that the yields of the aryl fluoride are lower than in the corresponding reactions in TFE.

Table 3.17. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol via thermolysis.

substituent	ArF / %	$ArOCH(CF_3)_2$ / %
H	26.2	73.8
Me	23.5	76.5
MeO	12.4	87.6
CF_3	33.4	66.5

Table 3.18. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol via photolysis.

substituent	ArF / %	$ArOCH(CF_3)_2$ / %
H	14.7	85.3
Me	14.6	85.4
MeO	13.4	86.6
CF_3	11.3	88.7

The reason for this is unclear; it would be expected that by reducing the nucleophilicity of oxygen in hexafluoroisopropanol, less of the aryl ether product would be obtained but, as can be seen, this is clearly not the case. One possible explanation is that for elimination (or abstraction) of fluoride to occur, a neighbouring group needs to participate. This may occur in TFE by a nucleophilic oxygen attacking an electropositive carbon β to it, resulting in an epoxide intermediate being formed. At the same time that this happens, a fluoride ion is expelled. Reducing the nucleophilicity of the oxygen involved reduces the ability of the molecule to expel fluoride. This may explain the decrease in fluoroaromatic product observed in hexafluoroisopropanol. A possible mechanism for fluoride donation from TFE is shown in Figure 3.7.

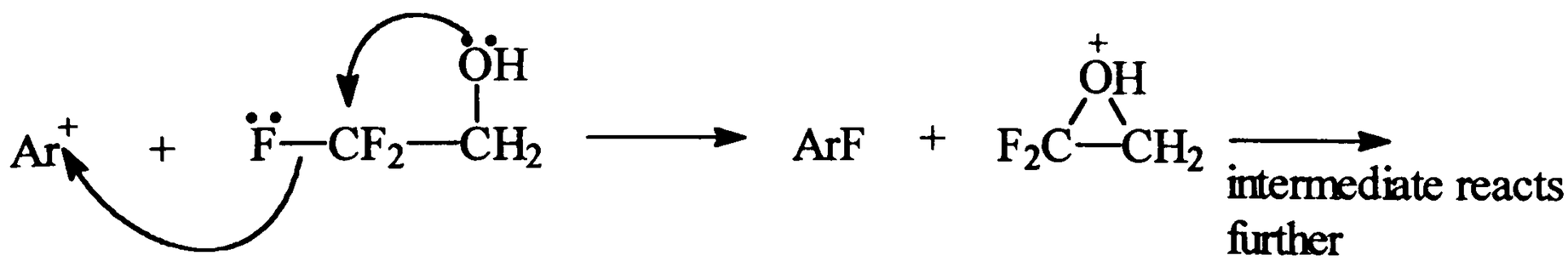


Figure 3.7

In the case of hexafluoroisopropanol, it appears, that nucleophilic attack by the solvent is favoured relative to fluoride abstraction by the aryl cation. The low yield of fluoroaromatic product suggests, that hexafluoroisopropanol is not a source of fluoride hence the fluoride source is from ion pairs. The aryl cation is sufficiently close to a tetrafluoroborate ion to be able to abstract a fluoride from it (Figure 3.8).

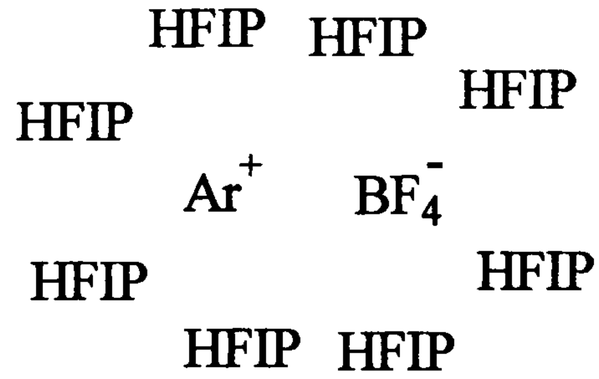


Figure 3.8 A solvated ion pair.

Another organic solvent that was viewed as a potential fluoride donor was trifluoroacetic acid. Trifluoroacetic acid is a weakly nucleophilic but highly ionising solvent. It was hoped this would provide an environment which would support aryl cation formation. Tables 3.19 and 3.20 show the thermal and photolytic yields for the dediazoniation of six substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid.

Table 3.19. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid via thermolysis.

substituent	ArF / %	CF_3CO_2Ar / %
H	4.00	96.0
Me	15.1	84.9
MeO	10.5	89.5
CF_3	18.2	81.8
CN	13.8	86.2
NO_2	8.70	91.3

Table 3.20. Quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in trifluoroacetic acid via photolysis.

substituent (X)	ArF / %	CF_3CO_2Ar / %
H	17.9	82.1
Me	19.8	80.2
MeO	14.6	85.4
CF_3	19.2	80.8
CN	20.9	79.1
NO_2	21.5	78.5

In both types of reactions, the yield of the fluoroaromatic is less than that in the corresponding dediazoniation reactions in TFE. The product distributions thermally and photolytically in trifluoroacetic acid are similar. A similar effect to that suggested in HFIP is postulated. The presence of the carbonyl group in trifluoroacetic acid will reduce the nucleophilicity of the hydroxyl oxygen. It will also sterically hinder the hydroxyl oxygen from attacking a β carbon. As a result of these effects it is unlikely fluoride will be expelled from trifluoroacetic acid so the source of fluoride, is likely to be ion pairs.

3.2.6 Dediazoniation with ethanol.

Having established that TFE was the best organic fluoride donor solvent examined so far, it was decided to carry out the corresponding reactions in ethanol to investigate the product distribution. A literature search revealed that previous work in this field by various authors had established that the product distribution (which depended on whether the reaction proceeded heterolytically or homolytically) depended on the substituents present in the benzenediazonium salt and the atmosphere under which it was carried out (oxygen or nitrogen). Strongly electron withdrawing groups favoured reduction products whereas electron donating substituents favoured the formation of aryl ethers. The literature revealed that in the case of protodediazoniation, the only work examining hydrogen atom transfer was by Melander and Bunnett and was mainly concerned with eliminating hydroxyl as a source of the hydrogen atom.[92, 93] The solvent

used for this study was methanol and the authors had concluded that the hydroxyl hydrogen atom was not involved, but the hydrogen atom on the α carbon was involved. Subsequent reports in the literature reported the α carbon hydrogen atom to be involved in transfer for protodediazoniation reactions in alcohol. We decided to investigate the mechanism for hydrogen atom transfer in ethanol to establish whether the mechanism in ethanol is the same as that for methanol.

Table 3.21 illustrates the thermal dediazoniation of six substituted benzenediazonium tetrafluoroborates in ethanol. With electron donating substituents such as methyl and methoxy the product that predominates for these salts is the aryl ether. The product distribution for the 3-methylbenzenediazonium salt is 3-methylbenzene (3%), 3-methylfluorobenzene (15%) and ethyl 3-methylphenyl ether (82%). A similar product distribution is observed with the 3-methoxybenzenediazonium salt; the yields are 3-methoxybenzene (4%), 3-methoxyfluorobenzene (17%) and ethyl 3-methoxyphenyl ether (79%). In contrast to electron donating substituents, electron withdrawing substituents (nitro and cyano) favour reduction products for the dediazoniation reactions. For 3-nitrobenzenediazonium tetrafluoroborate, the product distribution is nitrobenzene (92%), ethyl 3-nitrophenyl ether (8%), and 3-nitrofluorobenzene in only a trace amount.

Table 3.21. Normalised quantitative analysis of *meta* substituted benzenediazonium tetrafluoroborates in ethanol via thermolysis.

substituent	ArH / %	ArF / %	CH_3CH_2OAr / %
H	<1	4	96
Me	3	15	82
MeO	4	17	79
NO_2	92	<1	8

The product distributions are rationalised by electron donating groups favouring a heterolytic mechanism In this case the C-N bond cleaves to form an aryl cation and nitrogen. This process is favoured as the aryl cation is stabilised by electron donating groups and dinitrogen is a stable product. Hence the aryl cation is attacked by the nucleophilic oxygen of ethanol to form the aryl ether. The aryl fluoride that occurs is as

a result of the aryl cation reacting with the tetrafluoroborate anion. In contrast, with electron withdrawing groups the aryl cation is less favoured as electron withdrawing groups will destabilise it. Homolytic cleavage of the C-N bond occurs to give radical species. An aryl radical is able to abstract a hydrogen atom from ethanol to produce the corresponding benzene species.

Having established that ethanol acts as a reducing agent for arenediazoinium salts with electron withdrawing groups, it was decided to investigate which hydrogen enters the aromatic nucleus. The possible hydrogen atoms available are the methyl hydrogen, methylene hydrogen or the hydroxyl hydrogen. It can be seen that for the dediazoniation reaction of 3-nitrobenzenediazonium tetrafluoroborate in ethanol 1,1-d_2, nitrobenzene deuterated in the 3 position is obtained (Table 3.22).

Table 3.22. Product analysis of the solvolytic reaction of 3-nitrobenzenediazonium tetrafluoroborate in ethanol (1-1-d_2).

Substrate	Solvent	Product
$3\text{-}NO_2C_6H_4N_2BF_4$	CH_3CD_2OH	$3\text{-}NO_2C_6H_4D$

δ_H 7.5 (m, 1H, Ar), 7.7 (m,1H, Ar), 8.2 (m, 2H, Ar), δ_D (300 MHz) 7.6 (t, J = 1.2 Hz, 1D, Ar); *m/z* (EI) 124 (M^+, 80%), 94, 78, 52.

This result shows that the deuterium atom on the α carbon of ethanol (methylene hydrogen) is transferred to the aryl radical to give deuterated nitrobenzene (Figure 3.9).

$$m\text{-}NO_2C_6H_4N_2BF_4 + CH_3CD_2OH \longrightarrow m\text{-}NO_2C_6H_4D + CH_3COD + HBF_4$$

Figure 3.9

This observation is in agreement with the work carried out by Bunnett and Melander using methanol.[92,93] They demonstrated that the hydroxyl hydrogen is not involved in the hydrogen transfer but instead the hydrogen in the α position of methanol. A possible mechanism for the dediazoniation in ethanol is shown in Figure 3.10.

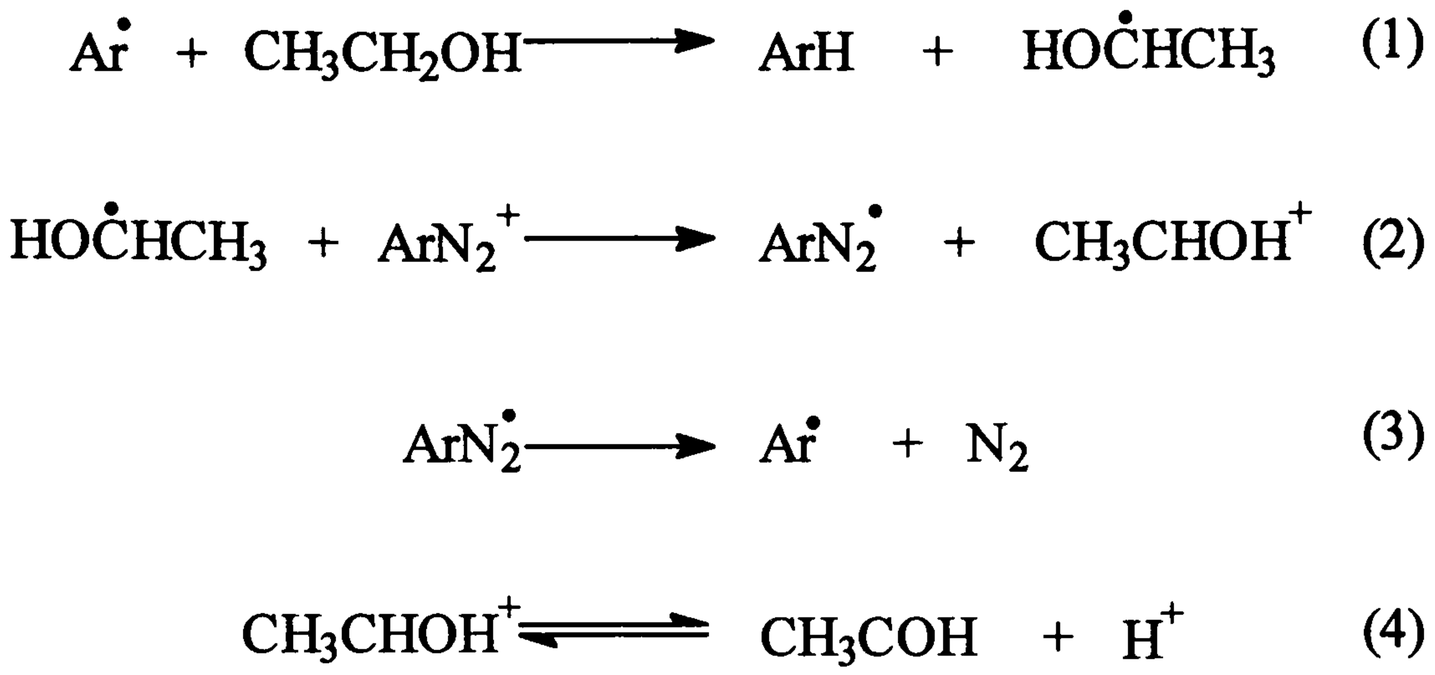


Figure 3.10

Initiation involves electron transfer from ethanol to the diazonium ion to form a diazenyl radical that enters the propagation cycle as step 3.

Chapter 4. Experimental.

4.1 General.

All of the starting materials were purchased from either Aldrich or Fluorochem and were of reagent grade purity. Trifluoroethanol (TFE) purchased from Fluorochem Ltd was distilled and 4 Å molecular sieves were added to keep it anhydrous. The solvents used were standard laboratory grade, purified using the methods outlined in the Newcastle University Department of Chemistry research guide. Nitrogen was supplied from BOC and was obtained in the laboratory via a gas line. TLC was performed on aluminium backed kieselgel 60 F_{254} plates of 0.2 mm thickness. ^{1}H spectra were recorded on a Bruker WP200 (200 MHz) spectrometer. The solvent used for NMR was $CDCl_3$ unless otherwise stated. The melting points of the products were determined using a Gallenkamp melting point apparatus.

4.2 Preparations.

General.

The arenediazonium salts are all prepared using the same general method (see benzenediazonium tetrafluoroborate). Due to the reactive nature of the salts, they were stored in the dark at -5°C.

4.2.1 Benzenediazonium tetrafluoroborate.

Aniline (7.2 g, 76mmol) was added to a stirred solution of tetrafluoroboric acid (20 cm^3, 48% wt) and water (20 cm^3). The solution was placed in an ice bath and stirred as a cold aqueous solution of sodium nitrite (5.34 g, 76 mmol in water (5 cm^3)) was added dropwise. The reaction mixture was stirred for a few minutes at room temperature and then filtered under reduced pressure. The precipitate was washed with dilute aqueous tetrafluoroboric acid, ethanol and diethyl ether, then dried under vacuum. The product was purified by dissolving in acetone followed by reprecipitation with ether. This was carried out three times to remove any colouration present (5.95 g, 41%, m.p. (decomp) = 105-110 °C, lit.,[94] 108-110°C).

4.2.2 4-Methoxybenzenediazonium tetrafluoroborate.

Addition of the aqueous sodium nitrite caused the reaction mixture to turn from yellow/brown to purple. The crude precipitate was a purple solid which was purified by dissolution in acetonitrile followed by reprecipitation using diethyl ether (57%, m.p. (decomp) = 140 - 141 C, lit.,[94] 142 °C).

4.2.3 4-Methylbenzenediazonium tetrafluoroborate.

Addition of the aqueous sodium nitrite caused the reaction mixture to turn from brown to cream in colour. Recrystallisation of the product was from a methanol/water mixture to give a white solid (28%, m.p. (decomp) = 109 - 111°C, lit.,[94] 112°C).

4.2.4 Isoamyl nitrite.

To a solution of water (2.5 ml), concentrated sulphuric acid (3.1 ml) and isoamyl alcohol (10.0g) cooled in ice, was added a solution of sodium nitrite (8.3 g, water (34.1 ml)). The rate of addition was controlled so the temperature was maintained at 1°C. The reaction mixture was allowed to stand for 1.5 hours at room temperature after which the precipated sodium sulphate was removed by filtration. The upper yellow isoamyl nitrite layer was separated and washed with a solution containing sodium hydrogen carbonate (0.1 g), sodium chloride (1.3 g) and water (5 ml). The resulting solution was dried with magnesium sulphate (0.6 g) filtered from the ^{1}H NMR, the crude isoamyl nitrite was deemed to be satisfactory for use in the preparation of benzenediazonium chloride (10.6 g, 80 %; δ_H 1.0 (d, 6H, $(CH_3)_2$-CH), 1.6 (m, 1H, CH), 1.7, (m, 2H, $CHCH_2$), 4.6, (t, 2H, CH_2CH_2ONO)).

4.2.5 Benzenediazonium chloride.

A solution of saturated hydrogen chloride in ethanol (kindly supplied by Mr I.D. Menneer) was added to aniline hydrochloride (2.63 g) in ethanol (20 cm^3). This solution was cooled in ice and isoamyl nitrite (3.00 g) was added. The mixture was allowed to stand for 5-10 minutes at room temperature. Benzenediazonium chloride was precipitated by the gradual addition of ether. The crystals were filtered under reduced pressure and washed with a 1:1 mixture of alcohol/ether followed by ether (10 ml). Care

was taken to ensure the crystals were kept moist with ether (δ_H (d_6-DMSO): 8.0 (t, 2H), 8.4 (t, 1H), 8.7 (d, 2H);

λ_m (ethanol), 267 nm). The experimental 1H NMR spectrum agrees with that of the literature.[95]

4.2.6 3-Nitrobenzenediazonium tetrafluoroborate.

The crude product was a light brown solid which was purified by recrystallisation from acetone/ether (89%, m.p. (decomp) = 168-170°C, lit.,[96] 165°C).

4.2.7 3-Trifluoromethylbenzenediazonium tetrafluoroborate.

The product was a white powder which was purified by dissolution in acetonitrile followed by reprecipitation using diethyl ether (58.2%, m.p. (decomp) = 146-147°C, lit.,[97]142°C).

4.2.8 3-Cyanobenzenediazonium tetrafluoroborate.

The crude product which was slightly off-whitish was recrystallised from acetonitrile/ether (twice) to give a white powder (82%, m.p. (decomp) = 152-157°C, lit.,[98] 148°C).

4.2.9 3-Methoxybenzenediazonium tetrafluoroborate.

The crude precipate was a dark red solid which was purified by recrystallisation from acetonitrile/ether (repeated 3 times). This gave a white/yellow fluffy powder (83%, m.p. (decomp) = 85-86°C, lit.,[94] 87-88°C).

4.2.10 3-Methylbenzenediazonium tetrafluoroborate.

The crude product was a red solid which was purified by recrystalisation from acetonitrile/ether (repeated 3 times). The final recrystallisation gave a product which was a white powder (78%, m.p. (decomp) = 101-102°C, lit.,[94] 97-101°C).

4.2.11 Attempted preparation of 3-(dimethylamino)benzenediazonium tetrafluoroborate.

N,N-Dimethyl-1,3-phenylenediamine dihydrochloride (Aldrich, 1.00 g) was added to tetrafluoroboric acid (6 ml, 48%) stirred at -5°C. A solution of sodium nitrite (0.87 g) in

H_2O (3 ml) was added slowly to avoid effervescence. The initial addition turned the colour of the reaction mixture dark red/brown which proceeded to brown upon complete addition. No precipitate was observed to be present in the reaction mixture unlike other diazotisation reactions. Adding ethanol and cooling the solution overnight caused a small amount of precipitate to form. The solution was filtered and the solid product dried under vacuum. Recrystallisation in acetone/ether afforded a brown/green product, the ^1H NMR spectrum of which indicated it was not the required compound. The procedure was repeated with the amine added to an excess of nitrous acid at -5°C. A red precipitate formed in the effervescent solution. The reaction mixture was filtered to give red crystals which decomposed on the filter paper to give a brown oil.

4.2.12 Preparation of 4-(dimethylamino)benzenediazonium tetrafluoroborate.

N,N-Dimethyl-1,4-phenylenediamine (Aldrich, 0.50 g) was added to a solution of tetrafluoroboric acid (2.7 ml, 48%) cooled at -5°C. A solution of sodium nitrite (0.37 g) was added slowly over a period of 30 minutes. Addition of sodium nitrite caused a greenish precipitate to separate out. Upon completion, the reaction mixture was filtered to give a green solid. The crude product was recrystallised from acetonitrile/ether to give a metallic green solid (0.44 g, 52%, m.p. (decomp) = 152-153°C, lit.,[96] 153-156°C; δ_H 3.31 (s, 6H, N-CH_3), 6.97 (d, J = 10 Hz, 2H, Ar), 8.03 (d, J = 10 Hz, 2H, Ar)).

4.2.13 Attempted preparation of *m*-phenylenebisdiazonium bistetrafluoroborate.

(I) Recrystallisation of *m*-phenylenediamine dihydrochloride.

Phenylenediamine dihydrochloride (1.4g) was dissolved in concentrated hydrochloric acid (50 ml). The solution was warmed and charcoal added. A solution of dilute hydrochloric acid (30 ml concentrated HCl, 20 ml water and 1g of stannous chloride) was added to the initial solution. The charcoal was removed by filtration. Recrystallisation was achieved by cooling in an ice/water salt mixture. The crystals were washed with a small amount of concentrated HCl and dried in a vacuum desiccator overnight (1.2 g, 86%, m.p. = 64-65°C, lit.,[99] 64-66°C).

(II) Preparation.

The phenylenediamine dihydrochloride (500 mg, 2.76 mmol) was dissolved in tetrafluoroboric acid (10 ml, 48%) and cooled. A solution of sodium nitrite (430 mg, 6.3 mmol) in water (5ml) was cooled in an ice/salt water bath. The diamine was added dropwise slowly to the aqueous solution of sodium nitrite which was continuously stirred. After standing for 15 minutes, filtration gave a yellow/brown powder. Characterisation of this compound proved difficult; ^{1}H and ^{13}C NMR and elemental analysis proved unsatisfactory analytical techniques for this compound so it is unclear whether this is the correct compound or not (283 mg, m.p. (decomp.) = 212°C, lit.,[100] 206°C; IR (KBr): 3300 br (NH), 3000 s (CH), 2300 s (N≡N), 1500 s (C=C), 1000, 900, 820, 650 cm^{-1}).

4.3 Preparation of trifluoroethyl aryl ethers.

The trifluoroethyl aryl ethers were prepared using the same general method (see trifluoroethyl phenyl ether). Preparative GLC was carried out using a Varian Aerograph, series 2700, fitted with an OV17 glass column and attached to a perkin Elmer S6 recorder.

4.3.1 Trifluoroethyl phenyl ether.[101]

Benzenediazonium tetrafluoroborate (3.00 g, 15 mmol) was dissolved slowly in TFE (6.00 cm^3). The reaction mixture was heated under reflux for three hours during which the solution turned from colourless through orange to brown. The reaction mixture was cooled, quenched with water (20 cm^3) and neutralised with aqueous sodium carbonate solution. The aqueous solution was extracted three times with ether (20 cm^3) and dried over magnesium sulphate. A GLC of the ether extract confirmed the presence of two products. The first was identified as fluorobenzene from a known authentic sample (Aldrich). The second product was isolated by preparative GLC. Trifluoroethyl phenyl ether was collected (ca. 90 mg; δ_H 4.4 (q, J = 8.1 Hz, 2H, $-CH_2CF_3$), 7.0 (d, 2H Ar), 7.1 (m, 1H, Ar), 7.3 (m, 2H, Ar).

4.3.2 Trifluoroethyl 4-methylphenyl ether.[106]

A solution of 4-methylbenzenediazonium tetrafluoroborate (3.0 g, 14 mmol) in TFE (6 ml) was heated under reflux for three hours during which the solution turned from colourless to red. The product was isolated by preparative GLC (δ_H 2.3 (s, 3H, CH_3-Ar), 4.3 (q, J = 8.1 Hz, 2H, -CH_2CF_3), 6.8 (d, 2H, Ar), 7.1 (d, 2H, Ar)).

4.3.3 Trifluoroethyl 3-methylphenyl ether.[104]

3-Methylbenzenediazonium tetrafluoroborate (5.2 g, 25 mmol) was dissolved in TFE (25 ml). The reaction mixture was heated under reflux for 24 hours causing it to change from colourless to dark brown. The product was isolated by preparative GLC (δ_H 2.3 (s, 3H, CH_3-Ar), 4.7 (q, J = 8.1 Hz, 2H, -CH_2CF_3), 6.9 (m, 3H, Ar), 7.2 (m, 1H, Ar)).

4.3.4 Trifluoroethyl 3-nitrophenyl ether.[105]

A solution of 3-nitrobenzenediazonium tetrafluoroborate (6.9 g, 29 mmol) in TFE (20 ml) was heated under reflux for 48 hours. During this time the solution changed from colourless to dark brown. The product was isolated and purified by preparative GLC (ca. 100 mg; δ_H 4.4 (q, J = 7.9 Hz, 2H, -CH_2CF_3), 7.4 (m, 3H Ar), 7.9 (m, 1 H, Ar)).

4.3.5 Trifluoroethyl 3-trifluoromethylphenyl ether.[106]

3-Trifluoromethylbenzenediazonium tetrafluoroborate (6.2 g, 23 mmol) in TFE (20 ml) was heated under reflux for 48 hours causing the solution to turn from colourless to dark red. The product was isolated by preparative GLC (δ_H 4.6 (q, J = 8.3 Hz, 2H, -CH_2CF_3), 7.3 (m, 1H, Ar), 7.4 (m, 1H, Ar), 7.7 (m, 1H, Ar), 7.8 (m, 1H, Ar)).

4.3.6 Trifluoroethyl 3-cyanophenyl ether.[107]

The reaction mixture which contained 3-cyanobenzenediazonium tetrafluoroborate (7.0g, 32 mmol) in TFE (20 ml) was heated under reflux for 24 hours, during which time it changed from colourless to dark red. The product was isolated by preparative GLC (δ_H 4.6 (q, J = 8.0 Hz, 2H, -CH_2CF_3), 7.4 (m, 2H, Ar), 7.7 (m, 1H, Ar), 8.9 (m, 1H, Ar)).

4.3.7 2-Hexafluoroisopropyl 3-methylphenyl ether.[108]

3-Methylbenzenediazonium tetrafluoroborate (3.7 g, 18 mmol) was added to hexafluoroisopropanol (10 ml) and this was heated at 60°C for 24 hours. The reaction mixture was initially colourless but it proceeded to turn dark brown/red after heating. The product was separated and purified by preparative GLC (δ_H 2.3 (s, 3H, CH_3-Ar), 4.7 (sept., J = 5.7 Hz, 1H, $(CF_3)_2$-CH), 6.9 (m, 3H, Ar), 7.2 (m, 1H, Ar)).

Preparation of ethyl aryl ethers.

Ethyl aryl ethers were prepared using the general method outlined in 4.3.1. The main modification to this method is the use of ethanol as solvent instead of TFE.

4.3.8 Ethyl phenyl ether.[109]

Benzenediazonium tetrafluoroborate (6g, 31 mmol) was dissolved in ethanol (40 ml). The reaction mixture was heated under reflux at 80°C for 72 hours to give a brown oil. The product was separated and purified by preparative GLC (δ_H 1.4 (t, J = 7.0 Hz, 3H, CH_2CH_3), 4.0 (q, J = 7Hz, 2H, CH_2CH_3), 6.9 (m, 3H, Ar), 7.2 (m, 2H, Ar)).

4.3.9 Ethyl 3-methylphenyl ether.[111]

3-Methylbenzenediazonium tetrafluoroborate (3.2 g, 16 mmol) was added to ethanol (45 ml) and this solution was refluxed at 80°C for 24 hours to give a crude product which was a brown oil. The product was isolated by preparative GLC (δ_H 1.3 (t, J = 6.9 Hz, 3H, CH_3CH_2), 2.3 (s, 3H, CH_3-Ar) 3.9 (q, J = 7.0 Hz, 2H, CH_2CH_3), 6.7 (m, 3H, Ar), 7.2 (m, 1H, Ar)).

4.3.10 Ethyl 3-methoxyphenyl ether.[110]

3-Methoxybenzenediazonium tetrafluoroborate (3.1 g, 14 mmol) was dissolved in ethanol (45 ml). The reaction mixture was heated under reflux for 24 hours during which time it changed from colourless to red. The product was isolated by preparative GLC (δ_H 1.3 (t, J = 7.0 Hz, 3H, CH_3CH_2), 3.7 (s, 3H, CH_3O), 3.9 (q, J = 7.0 Hz, 2H, CH_2CH_3), 6.4 (m, 3H, Ar), 7.2 (m, 1H, Ar)).

4.3.11 Ethyl 3-cyanophenyl ether.[112]

A solution of 3-cyanobenzenediazonium tetrafluoroborate (2.4 g, 11 mmol) in ethanol (25 ml) was heated under reflux at 80°C for 48 hours. Analysis of the reaction mixture by GLC showed that it contained more of the reduced compound (cyanobenzene) than normal. The required product (ethyl 3-cyanophenyl ether) was isolated by preparative GLC (δ_H 1.3 (t, J = 7.1 Hz, 3H, CH_2CH_3), 4.4 (q, J = 7.1 Hz, 2H, CH_2CH_3), 7.6 (m,3H, Ar), 8.0 (m, 1H, Ar)).

4.3.12 Attempted preparation of ethyl 3-nitrophenyl ether.[113]

The reaction mixture which contained 3-nitrobenzenediazonium tetrafluoroborate (3.0 g, 13 mmol) in ethanol (25 ml) was heated under reflux at 80°C for 72 hours to give a crude product which was a red / brown oil. The product was separated and purified by preparative GLC and found to be nitrobenzene, by comparison with a known authentic standard (δ_H 7.5 (m, 2H,Ar), 7.7 (m,1H,Ar), 8.2 (m, 2H, Ar)).

4.3.13 Nitrobenzene-d_1

3-Nitrobenzenediazonium tetrafluoroborate (0.25 g, 1.1 mmol) was dissolved in ethanol (1,1-d_2) (2 ml, 99 % pure). The reaction mixture was heated under reflux at 80°C for 48 hours to give a brown oil. The product was purified by prep. GLC (δ_H 7.5 (m, 1H, Ar), 7.7 (m,1H, Ar), 8.2 (m, 2H, Ar), δ_D (300 MHz) 7.6 (t, J = 1.2 Hz, 1D, Ar)). *m/z* (EI) 124 (M^+, 80%), 94, 78, 52.

4.4 Kinetics.

General.

UV spectral analysis was carried out on a Cecil 5000 series (5502 model) UV/VIS spectrophotometer. Quartz cells of pathlength 1 cm^3 were used.

4.4.1 A typical kinetic run.

To determine the peak of maximum absorbance (λ_{max}) of the arenediazonium salt being studied, a solution was made up and diluted so that the absorbance fell within the range 0.8-2.0 at λ_{max}. The concentration of this solution was noted and subsequent stock solutions of this concentration were made. In each case the solutions were made up using a Gilson Pipetman (models P5000 and P1000) which were regularly calibrated. The absorbance change with respect to time at λ_{max} was followed with the aid of a computer program (Logger).[114] Before commencing the run, the UV quartz cells were allowed to come to thermal equilibrium with the cell block. In the faster reactions, 25-50µl of the substrate solution was injected into the UV cell containing the appropriate solvent once it had reached the desired temperature. After recording the UV spectrum, the logger software was run to collect absorbance at λ_{max}. The decrease in absorbance was measured for at least 3 half lives. Depending on the rate of reaction, up to four cells could be studied at one time. Each reaction was studied twice at any given temperature. In each case, the decomposition of a particular arenediazonium salt covered a range of 25-30°C. The data obtained were fitted to a single exponential decay equation with offset obtained from Grafit.[115]

$$A = A_0 e^{-kt} + \text{Offset}$$

where A is the absorbance at time t, A_0 is the initial absorbance at t=0, k is the observed reaction rate constant and the offset is A_∞. The half life of the reaction was calculated from a preliminary rate constant in order to estimate the time required to observe the reaction for 3 half lives.

$$\frac{\ln 2}{k} = t_{1/2}$$

The activation parameters , $\Delta H^{\#}$ and $\Delta S^{\#}$ were calculated from the Eyring equation

$$\ln\left\{\frac{k.h}{k_B T}\right\} = \frac{\Delta S^{\ddagger}}{R} - \frac{\Delta H^{\ddagger}}{RT}$$

k = first order rate constant (s^{-1})

h = Planck constant (6.626×10^{-34} J s)

k_B = Boltzmann constant (1.381×10^{-23} J K^{-1})

T = Temperature (K)

R = Gas constant (8.314 J K^{-1} mol^{-1})

a plot of $\ln\left\{\frac{k.h}{k_B T}\right\}$ versus $\frac{1}{T}$ gives a line with a gradient = $-\frac{\Delta H^{\ddagger}}{R}$ and intercept = $\frac{\Delta S^{\ddagger}}{R}$;

although $\Delta H^{\#}$ and $\Delta S^{\#}$ were determined computationally by linear regression. Good clean first order kinetics were observed for all substrates in each solvent mixture studied.

Table 4.1. Wavelengths used for kinetic measurements.

Substituent	λ_{used} / nm				
	TFE	H_2O	HFIP	TFA	EtOH
m-Me	263	263	260	285	269
m-MeO	263	263	275	285	269
m-NO_2	245	224	----	----	----
m-CN	259	259	258	----	258
m-CF_3	260	255	259	----	249
H	255	263	274	299	269
p-Me	294	280	----	----	----

4.4.2 Reaction media.

The solvents used were as follows; distilled water, anhydrous trifluoroethanol (99% pure, TFE), trifluoromethoxybenzene (99% pure; TFMOB), difluoromethyl 2,2,2-trifluoroethyl ether (97% pure; DFTFE), hexafluoroisopropanol (99 % pure, HFIP) and trifluoroacetic acid (99% pure, TFA). The densities of each solvent were used to calculate the volumes of each solvent that were required to produce the correct mixture. The appropriate volumes of solvent were combined with the aid of a Gilson Pipetman.

The following molar ratios were used for mixed solvent systems

Solvent system	molar ratios
TFE:H_2O	(1:1)
TFE:DFTFE	(10:1), (5:1), (2.5:1)
TFE:TFMOB	(10:1), (5:1), (3:1), (2.5:1)

4.5 Product Analysis.

4.5.1 General.

Analytical gas liquid chromatography (GLC) was carried out on a Pye Unicam machine fitted with a glass packed column (10% Apiezon on Chromosorb W, 60-80 mesh) and also on a Perkin Elmer Sigma 4b capillary machine fitted with a 12 meter (non polar) bonded phase fused silica capillary column. Most of the analyses were carried out on the capillary GLC machine.

The operating conditions for this machine were as follows; the carrier gas was nitrogen and both air and hydrogen were used for the flame ionisation detector, 3-4 μl injections of the sample were made and the attenuation was usually set at 4×10^3. The injection port and detector temperatures were set at 250°C. In the case of the Perkin Elmer Sigma 4b capillary machine, a temperature ramp program was not available so the machine was run at a fixed temperature (100 °C). The different conditions used to separate and analyse products are given in the following table.

Table 4.2 GLC conditions for the Pye Unicam machine.

Substrate	Solvent	GLC conditions
4-Methylbenzenediazonium tetrafluoroborate	TFE, H_2O	Initial temp. 80°C for 2 min., rising to 180°C at 16°C/min.
4-Methoxybenzenediazonium tetrafluoroborate	TFE,H_2O,TFE/TFMOB, TFE/DFTFE	Initial temp. 80°C for 2 min., rising to 220°C at 16°C/min.
Benzenediazonium tetrafluoroborate.	All solvents studied	Initial temp. 80°C for 2 min., rising to 180°C at 12°C min.

The arenediazonium salt solvolysis reactions were carried out under conditions similar to those of the kinetic reactions though on a larger scale and different concentrations.

4.5.2 Qualitative analysis of reactions in mixed solvent systems.

The reactions studied for the mixed solvent systems all involved the *p*-methylbenzenediazonium tetrafluoroborate. Although qualitative analysis does not present the most accurate method of obtaining precise yields, by maintaining the same diazonium salt, and only changing the solvent system, differences in the ratio of aromatic fluoride and aryl ether products are an early indication of trends and whether further work is warranted.

4.5.2.1 General procedure.

The arenediazonium salt (~50 mg) was dissolved in the solvent system chosen. The reaction mixture was heated at a fixed temperature for a predetermined time (based upon kinetic information). The reaction mixture was quenched with water (10 cm^3) and neutralised with aqueous Na_2CO_3. The aqueous solution was then extracted three times with ether (6 cm^3 each time), the extracts were combined and analysed by GLC. At least 5 injections were made, each reaction was carried out twice.

4.5.2.2 Solvolysis of 4-methylbenzenediazonium tetrafluoroborate in trifluoroethanol:trifluoromethoxybenzene (TFE:TFMOB).

The general procedure described in (4.5.2.1) was followed. The reaction was heated at 65°C for 8 hours. The molar ratios of TFE:TFMOB used were 10:1, 5:1, 3:1, and 2.5:1 (See section 4.4.2.)

4.5.2.3 Solvolysis of 4-methylbenzenediazonium tetrafluoroborate in trifluoroethanol:difluoromethyl 2,2,2-trifluoroethyl ether (TFE:DFTFE).

Due to the low boiling point of DFTFE (b.p 30°C) these reactions were carried out in sealed vials. The reaction mixtures were heated for 4 hours at 70°C. During this time the reaction mixture turned from clear to black. The solutions were then worked up as described in section 4.5.2. (For the corresponding molar ratio see section 4.4.2).

4.5.3 Quantitative analysis.

To quantify product yields by GLC a standard must be used. The molar response factors of each of the products are measured against this standard. The compound mainly used as an internal standard was undecane. Occasionally octane was used to monitor product yields when the retention times of the component under investigation and undecane were similar.

4.5.3.1 Measurement of molar response factors (MRF's).

A general procedure was followed for each product; the method for fluorobenzene is described. Undecane (30-60 mg) and fluorobenzene (30-60 mg) were accurately weighed into a 10 cm^3 volumetric flask. This was diluted with ether giving a stock solution. The stock solution was diluted further with more ether and analysed via GLC at least 6 times. This solution was diluted to a different concentration and analysed again at least 6 times. Each injection produces a chromatogram with two peaks, undecane and fluorobenzene. These peak areas allow the calculation of MRF's via the equation shown.

$$\frac{\text{Signal of A}}{\text{no. of moles of A}} \times \frac{\text{no. of moles of undecane}}{\text{signal of undecane}} = \text{MRF}$$

This procedure was done twice when measuring the MRF for each product. The MRF's measured are summarised in Table 4.3. The full experimental MRF's are shown in appendix B with their corresponding standard deviation. In the majority of cases the standard deviation is less than 2%.

Table 4.3 Experimental molar response factors for X-ArF and X-$ArOCH_2CF_3$ versus undecane ($C_{11}H_{24}$).

X	MRF	
	X-ArF	X-$ArOCH_2CF_3$
m-CF_3	0.65	0.41
m-NO_2	0.54	0.44
m-CN	0.62	0.42
H	0.52	0.68
m-MeO	0.58	0.63
m-Me	0.65	0.76
p-MeO	0.59	0.56
p-Me	0.66	0.72

Table 4.4. Experimental molar response factors for X-ArF, X-$ArOCH_2CH_3$ and ArH versus octane (C_8H_{18}).

X	X-ArF	X-$ArOCH_2CH_3$	X-ArH
m-Me	0.95	1.02	0.92
H	0.84	0.91	0.81
m-MeO	0.87	0.95	0.85
m-NO_2	----------	----------	0.48

4.5.3.2 Solvolysis of arenediazonium salts in TFE.

The procedure outlined below is the general method for the quantitative analysis of arenediazonium salts in trifluoroethanol.

The arenediazonium salt (40-80 mg) was dissolved in trifluoroethanol (2.5 cm^3) and undecane (40 mg) with stirring. The reaction mixture was heated under reflux for a

period of time dependent on the particular substituted benzenediazonium salt under study. For benzenediazonium chloride, 3-methylbenzenediazonium, and 3-methoxybenzenediazonium tetrafluoroborates the length of reflux was for 3-5 hours. In the case of 3-trifluoromethylbenzenediazonium, 3-cyanobenzenediazonium and 3-nitrobenzenediazonium the reaction mixtures were heated under reflux for 1-2 days. The solution was cooled, quenched with water (10 cm^3) and neutralised with aqueous sodium carbonate. This aqueous solution was then extracted three times with ether (6 cm^3). The extracts were combined and analysed by GLC. The reaction was repeated. Knowing the MRF's for the products in the reaction mixture allows the calculation of the number of moles present of these compounds. Hence yields of products can be calculated.

4.5.3.3 Solvolysis of arenediazonium tetrafluoroborates in HFIP.

General procedure.

The arenediazonium tetrafluoroborate (40-80 mg) was dissolved in hexafluoroisopropanol (2.5 cm^3) and undecane (40 mg) with stirring. The reaction mixture was heated under reflux at 60°C. In the case of benzene, 3-methylbenzene and 3-methoxybenzene diazonium tetrafluoroborates the reaction mixture was heated for a period of 8 hours. For the less reactive arenediazonium tetrafluoroborates (3-trifluoro, 3-cyano and 3-nitro) the reaction mixture was heated under reflux for 48 hours. The reaction mixture was cooled, quenched with water (10 cm^3) and neutralised with aqueous sodium carbonate. This aqueous solution was then extracted three times with ether (6 cm^3). The extracts were combined and analysed by GLC. The reaction was repeated.

4.5.3.4 Solvolysis of arenediazonium tetrafluoroborates in trifluoroacetic acid.

General procedure.

The arenediazonium tetrafluoroborate (80-100 mg) was dissolved in trifluoroacetic acid (3 ml). The reaction mixture was heated under reflux at 60°C for 14 hours. The reaction mixture was cooled, quenched with water (4 cm^3) and neutralised with aqueous sodium carbonate. The aqueous solution was then extracted three times with dichloromethane (6 cm^3). A solution of dichloromethane (10 ml) containing undecane

(29 mg) was added and the resultant solution was analysed by GLC. This reaction was repeated. The solvolysis reactions of benzenediazonium, 3-methylbenzenediazonium, 3-cyanobenzenediazonium and 3-nitrobenzenediazonium tetrafluoroborates in trifluoroacetic acid were investigated.

4.5.3.5 Solvolysis of arenediazonium tetrafluoroborates in ethanol.

General procedure.

The arenediazonium tetrafluoroborate (70-100 mg) was dissolved in ethanol (5 ml) and undecane (~ 40 mg). For benzene, 3-methylbenzene and 3-methoxybenzene diazonium tetrafluoroborates, reaction mixtures were heated under reflux for 24 hours. The time period for the solvolysis of 3-nitrobenzenediazonium tetrafluoroborates was 48 hours. The reaction mixture was then worked up and analysed as described in 4.5.3.2.

4.5.3.6 Addition of inorganic fluorides.

Solvolysis of benzenediazonium tetrafluoroborate with added sodium tetrafluoroborate.

Benzenediazonium tetrafluoroborate (60 mg), sodium tetrafluoroborate (577 mg) and undecane (38 mg) were dissolved in TFE (3 ml). The reaction mixture was heated at 65°C for 8 hours with constant stirring. The reaction mixture was quenched with ice cold water (10 ml), neutralised with aqueous sodium bicarbonate and extracted with ether (2 x 5 ml). The product mixture was analysed by GLC.

Solvolysis of benzenediazonium tetrafluoroborate with added sodium hexafluorophosphate.

Procedure as for 4.5.3.6 except benzenediazonium tetrafluoroborate (65 mg), sodium hexafluorophosphate (320 mg) and undecane (36 mg) were added to TFE (3ml).

Solvolysis of benzenediazonium tetrafluoroborate with added sodium hexafluoroantimonate.

Procedure as for 4.5.3.6 except benzenediazonium tetrafluoroborate (70 mg), sodium hexafluoroantimonate (464 mg) and undecane (46 mg) were added to TFE (3ml).

Solvolysis of 4-methoxy and 4-methyl benzenediazonium tetrafluoroborates in saturated aqueous potassium fluoride.

4-Methoxybenzenediazonium tetrafluoroborate (877 mg) was dissolved in water (200 ml) containing potassium fluoride (120 g). The reaction mixture was heated under reflux for 12 hours with constant stirring. The reaction mixture was cooled and quenched with water (50 ml). The products were extracted with ether (4 x 50 ml), the extracts were combined and the volume of ether was reduced to 2 ml on the rotary evaporator. The reaction mixture was then diluted in methanol (500 ml). Analytical GLC showed 4-methoxyphenol to be the only product (96.4 %). The concentration of the phenol product in this solution was calculated by comparison of its absorbance at 292.5 nm with that of a standard solution of 4-methoxyphenol (829 mg) in methanol (500 ml).

This procedure was repeated for 4-methylbenzenedizonium tetrafluoroborate (729 mg). In this case, the yield of 4-methylphenol (96.5 %) was calculated by comparison with a known amount of 4-methylphenol in methanol at 281.5 nm.

4.5.4 Photolysis Reactions.

General.

Photolytic work was carried out using either a semi-micro photochemical reactor for small scale reactions or an immersion-well photochemical reactor for larger work. In both cases the apparatus was made by Photochemical Reactors Ltd. The semi-micro photochemical reactor consisted of one six inch four watt UV lamp with a peak emission at 254nm. This was operated via a built in electronic timer. The immersion-well photochemical reactor (model RQ125) could be operated either with a 6 watt low pressure mercury lamp or a 125 watt medium pressure lamp. The apparatus was used in conjunction with a 150ml standard reaction flask.

4.5.4.1 Photolytic solvolysis reactions of arenediazonium tetrafluoroborates in TFE.

General procedure.

Benzenediazonium tetrafluoroborate (60 mg) was dissolved in TFE (3 cm^3) and transferred to a UV cell. The reaction was carried out using an immersion-well photochemical reactor. The sample was irradiated with UV light of 6 watt intensity for 4 hours. Small samples (30 µl) were extracted every 5 minutes. These were diluted in a

UV cell (3ml) and a UV scan between 200-500 nm was carried out. Hence the change from arenediazonium salt to product could be followed. After 20 minutes, the solution was yellow. The reaction was monitored for approximately 4 hours. Upon completion, the products were neutralised (sodium bicarbonate), extracted with ether (2 x 5cm^3) and a known amount of undecane added. The solution was analysed by GLC. For 3-cyano and 3-nitrobenzenediazonium tetrafluoroborates, a UV lamp of 125 watt intensity was used for time periods of 2 hours and 9 hours respectively.

4.5.4.2 Photolysis of arenediazonium tetrafluoroborates in hexafluoroisopropanol.

General procedure.

The arenediazonium salt (40 mg) was dissolved in hexafluoroisopropanol (3 ml) in a quartz UV cell. This solution was irradiated with a 6 watt UV lamp for 8 hours. The reaction was quenched with cold water (2 ml) extracted with ether (2 x 5 ml) and a known amount of undecane added (~ 50 mg). The reaction mixture was analysed by GLC.

This was the procedure that was followed for the photolysis of benzenediazonium, 3-methylbenzenediazonium, 3-methoxybenzenediazonium and 3-trifluoromethylbenzenediazonium tetrafluoroborates in hexafluoroisopropanol. For nitrobenzenediazonium tetrafluoroborate, the period of irradition was 2 days, whilst for cyanobenzenediazonium tetrafluoroborate it was 24 hours.

4.5.4.3 Photolysis of arenediazonium tetrafluoroborates in trifluoroacetic acid.

General procedure.

The arenediazonium salt (80-100 mg) was dissolved in trifluoroacetic acid (3ml) in a UV cell. The reaction mixture was irradiated with a 6 watt UV lamp for 8 hours. The reaction was then quenched with ice cold water (4 cm^3) and extracted with ether (2 x 5ml). A known amount of undecane (30 mg) was added and the reaction mixture was analysed by GLC.

The arenediazonium salts studied were, benzene, 3-methylbenzene, 3-methoxybenzene, 3-trifluoromethylbenzene, 3-cyanobenzene and 3-nitrobenzene diazonium tetrafluoroborates.

4.5.4.4 Photolysis of arenediazonium tetrafluoroborates in saturated aqueous potassium fluoride.

4-Methoxybenzenediazonium tetrafluoroborate (730 mg) was dissolved in a saturated aqueous potassium fluoride solution (10.2 mol dm^{-3}, 200 ml) and transferred to a photolysis cell. The UV lamp was turned on and the reaction mixture was stirred. Small samples (40 μl) were extracted every 5 minutes, these were diluted in a UV cell (3ml) and a UV scan between 200-500 nm was carried out so the change from arenediazonium salt to product could be followed. After fifteen minutes, the solution was yellow. The reaction was stirred for approximately 2 hours and was monitored in this way by UV. Upon completion the products were extracted with ether (4 x 50cm^3) and this extract was dried over magnesium sulphate and filtered. The ether was reduced to 2 cm^3. This solution was analysed by GLC which showed 4-methoxyphenol to be the only product present. The reaction mixture was then diluted in methanol (500 ml). The concentration of the phenol product in this solution was calculated by comparison of its absorbance at 292.5 nm with that of a standard solution of 4-methoxyphenol (829 mg) in methanol (500 ml). 4-Methoxyphenol was found to be present in 92.0 % yield.

The photolytic solvolysis reaction of 4-methylbenzenediazonium tetrafluoroborate in a saturated aqueous potassium fluoride solution was followed in a similar way to that described above. 4-Methylbenzenediazonium tetrafluoroborate (830 mg) was dissolved in a saturated aqueous potassium fluoride solution (10.2 mol dm^{-3}, 200 ml). In this case the yield of 4-methylphenol (92.0 %) was calculated by comparison of its absorbance at 281.5 nm with that of a known amount of 4-methylphenol in methanol at 281.5 nm.

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Table 6.1 Benzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}	10^7 standard deviation
25.10 (± 0.20)	0.54	1.36
25.10 (± 0.20)	0.52	1.32
30.93 (± 0.10)	1.06	3.67
30.93 (± 0.10)	1.12	3.24
40.38 (± 0.15)	4.46	11.5
40.38 (± 0.15)	4.54	11.2
50.10 (± 0.11)	15.6	67.7
50.10 (± 0.11)	15.8	62.4
59.70 (± 0.10)	51.3	223
59.70 (± 0.10)	52.0	214

Table 6.2 Benzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^4 k / s^{-1}	10^7 standard deviation
25.80 (± 0.12)	1.05	0.83
25.80 (± 0.12)	1.07	0.88
30.02 (± 0.10)	1.98	0.83
30.02 (± 0.10)	1.97	0.84
35.16 (± 0.15)	4.43	1.37
35.16 (± 0.15)	4.45	2.17
45.30 (± 0.11)	18.6	21.2
45.30 (± 0.11)	18.0	37.6
55.04 (± 0.10)	71.1	6.01
55.04 (± 0.10)	71.1	7.23

Table 6.3 Benzenediazonium chloride in TFE.

Temperature /°C	10^4 k / s^{-1}	10^7 standard deviation
25.80 (± 0.12)	0.91	3.59
25.80 (± 0.12)	1.05	0.84
30.02 (± 0.10)	1.92	2.31
30.02 (± 0.10)	1.96	3.45
35.20 (± 0.15)	4.41	1.64
35.20 (± 0.15)	4.39	1.86
45.30 (± 0.11)	17.5	49.7
45.30 (± 0.11)	17.4	23.8
55.02 (± 0.10)	71.0	34.5
55.02 (± 0.10)	71.1	23.4

Table 6.4 Benzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
25.46 (± 0.05)	0.97	0.24
31.00 (± 0.04)	1.89	1.10
35.75 (± 0.05)	3.59	8.47
40.84 (± 0.04)	9.73	2.60
45.17 (± 0.03)	17.5	9.95
50.40 (± 0.04)	34.3	14.2

Table 6.5 Benzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
25.30 (± 0.10)	2.22	1.11
25.30 (± 0.10)	2.42	1.23
31.80 (± 0.09)	5.68	1.79
31.80 (± 0.09)	5.76	1.34
37.23 (± 0.06)	6.22	9.39
37.23 (± 0.06)	8.29	8.89
42.40 (± 0.08)	15.6	11.9
42.40 (± 0.08)	15.8	10.8
45.32 (± 0.11)	16.2	12.0
45.32 (± 0.11)	16.0	11.2

Table 6.6 Benzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
25.50 (± 0.11)	0.42	0.08
25.50 (± 0.11)	0.53	0.05
28.65 (± 0.12)	0.80	0.05
28.65 (± 0.12)	0.88	0.06
35.16 (± 0.11)	2.15	0.06
35.16 (± 0.11)	2.21	0.08
42.00 (± 0.10)	5.85	0.96
42.00 (± 0.10)	5.63	1.52
50.16 (± 0.15)	16.5	23.2
50.16 (± 0.15)	17.8	21.7
58.18 (± 0.11)	48.2	60.5
58.18 (± 0.11)	45.2	58.2

Table 6.7 3-Methylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.05 (± 0.10)	0.24	0.45
25.05 (± 0.10)	0.28	0.51
30.85 (± 0.11)	0.42	0.96
30.85 (± 0.11)	0.48	0.88
40.56 (± 0.10)	1.66	4.75
40.56 (± 0.10)	1.65	4.32
50.10 (± 0.14)	6.01	4.52
50.10 (± 0.14)	3.35	6.28
59.70 (± 0.10)	11.1	94.5
59.70 (± 0.10)	15.1	92.3

Table 6.8 3-Methylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^3 k / s^{-1}	10^5 standard deviation
25.11 (± 0.15)	0.60	0.06
25.11 (± 0.15)	0.44	0.05
30.89 (± 0.16)	0.88	0.23
30.89 (± 0.16)	1.20	0.77
40.53 (± 0.12)	3.94	2.01
40.53 (± 0.12)	4.20	1.81
51.05 (± 0.14)	14.4	14.1
51.05 (± 0.14)	11.8	10.1
56.29 (± 0.11)	21.2	14.5
56.29 (± 0.11)	22.0	15.7

Table 6.9 3-Methylbenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^3 k / s^{-1}	10^5 standard deviation
25.46 (± 0.05)	0.52	0.48
31.00 (± 0.04)	1.23	0.15
35.75 (± 0.05)	2.50	2.21
40.84 (± 0.04)	5.08	2.99
45.17 (± 0.03)	9.45	12.5
50.40 (± 0.04)	15.7	25.1

Table 6.10 3-Methylbenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.30 (± 0.10)	0.30	0.35
25.30 (± 0.10)	0.42	0.44
31.80 (± 0.09)	0.46	1.81
31.80 (± 0.09)	1.06	1.54
37.23 (± 0.06)	1.69	3.37
37.23 (± 0.06)	1.73	3.22
42.40 (± 0.08)	3.46	4.80
42.40 (± 0.08)	3.57	3.88
45.28 (± 0.12)	4.48	29.8
45.28 (± 0.12)	4.56	11.3

Table 6.11 3-Methylbenzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.50 (± 0.10)	0.21	0.40
25.50 (± 0.10)	0.25	0.23
30.49 (± 0.11)	0.44	1.04
30.49 (± 0.11)	0.54	1.09
31.28 (± 0.11)	0.61	2.11
31.28 (± 0.11)	0.67	3.58
36.59 (± 0.10)	1.10	10.1
36.59 (± 0.10)	1.24	9.89
44.24 (± 0.11)	3.68	7.26
44.24 (± 0.11)	3.76	8.56
49.90 (± 0.10)	7.01	23.7
49.90 (± 0.10)	7.57	17.6
58.18 (± 0.12)	18.3	10.73
58.18 (± 0.12)	18.8	11.23

Table 6.12 3-Methoxybenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.11 (± 0.10)	0.22	0.24
25.11 (± 0.10)	0.26	0.41
30.85 (± 0.11)	0.49	0.54
30.85 (± 0.11)	0.53	0.73
40.56 (± 0.10)	1.60	4.65
40.56 (± 0.10)	1.74	3.72
50.10 (± 0.14)	5.50	2.09
50.10 (± 0.14)	5.56	3.11
59.77 (± 0.10)	16.2	6.53
59.77 (± 0.10)	15.8	6.88

Table 6.13 3-Methoxybenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.10 (± 0.10)	0.85	1.10
25.10 (± 0.10)	0.89	0.98
30.89 (± 0.11)	1.83	7.73
30.89 (± 0.11)	1.74	10.9
40.53 (± 0.10)	6.04	40.8
40.53 (± 0.10)	6.22	32.6
50.90 (± 0.14)	22.4	101
50.90 (± 0.14)	22.8	141
56.29 (± 0.10)	51.2	210
56.29 (± 0.10)	41.5	187

Table 6.14 3-Methoxybenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^3 k / s^{-1}	10^5 standard deviation
25.92 (± 0.06)	1.73	0.88
30.34 (± 0.08)	3.45	0.96
38.45 (± 0.04)	10.6	7.88
44.55 (± 0.05)	19.8	10.2
50.53 (± 0.04)	36.7	41.8

Table 6.15 3-Methoxybenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}	10^6 standard deviation
25.30 (± 0.10)	0.31	0.56
25.30 (± 0.10)	0.51	0.65
31.80 (± 0.09)	1.01	2.20
31.80 (± 0.09)	1.09	1.80
37.23 (± 0.06)	1.80	6.10
37.23 (± 0.06)	1.92	4.98
42.40 (± 0.08)	3.78	4.80
42.40 (± 0.08)	3.82	3.88
45.28 (± 0.12)	4.88	12.5
45.28 (± 0.12)	4.98	11.2

Table 6.16 3-Methoxybenzenediazonium tetrafluoroborate in trifluoroacetic acid.

Temperature /°C	10^3 k / s^{-1}	10^5 standard deviation
25.50 (± 0.10)	0.25	0.05
25.50 (± 0.10)	0.76	0.10
31.28 (± 0.10)	1.55	1.10
31.28 (± 0.10)	1.59	1.25
36.59 (± 0.10)	3.06	2.10
36.59 (± 0.10)	3.40	2.06
44.24 (± 0.10)	7.74	2.69
44.24 (± 0.10)	8.14	2.56
49.90 (± 0.12)	15.1	7.81
49.90 (± 0.12)	16.7	6.89
51.14 (± 0.12)	18.0	17.4
51.14 (± 0.12)	18.4	16.8
56.73 (± 0.10)	16.2	17.6
56.73 (± 0.10)	17.2	14.5

Table 6.17 3-Trifluoromethylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
63.92 (± 0.02)	0.82	0.72
63.92 (± 0.02)	0.80	1.03
70.05 (± 0.15)	2.06	0.61
70.05 (± 0.15)	2.07	0.44
75.53 (± 0.03)	4.39	3.53
75.53 (± 0.03)	4.41	2.88
80.11 (± 0.05)	7.50	2.04
80.11 (± 0.05)	7.96	1.63
85.23 (± 0.04)	13.8	7.89
85.23 (± 0.04)	13.7	7.65

Table 6.18 3-Trifluoromethylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^5 k / s^{-1}	10^8 standard deviation
35.30 (± 0.01)	0.35	2.54
35.30 (± 0.01)	0.33	2.45
39.22 (± 0.10)	0.58	0.55
39.22 (± 0.10)	0.64	0.56
46.19 (± 0.06)	1.80	1.68
46.19 (± 0.06)	1.64	1.69
50.12 (± 0.02)	2.60	0.78
50.12 (± 0.02)	2.68	0.68
55.43 (± 0.04)	4.83	3.51
55.43 (± 0.04)	4.71	7.84
60.43 (± 0.04)	8.39	25.5
60.43 (± 0.04)	10.0	9.13
63.92 (± 0.02)	15.9	5.26
63.92 (± 0.02)	14.8	18.8
70.05 (± 0.04)	34.0	22.3
70.05 (± 0.04)	34.0	41.4

Table 6.19 3-Trifluoromethylbenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^6 k / s^{-1}	10^8 standard deviation
30.03 (± 0.05)	2.31	3.43
34.69 (± 0.04)	3.68	2.34
45.17 (± 0.06)	4.51	6.48
51.67 (± 0.05)	15.8	12.7
55.94 (± 0.08)	22.7	12.7

Table 6.20 3-Trifluoromethylbenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^3 k / s^{-1}	10^4 standard deviation
25.37 (± 0.10)	0.80	0.17
25.37 (± 0.10)	0.88	0.21
31.02 (± 0.12)	1.78	0.58
31.02 (± 0.12)	1.86	0.34
36.73 (± 0.10)	2.76	0.97
36.73 (± 0.10)	2.92	0.88
41.15 (± 0.12)	6.42	3.01
41.15 (± 0.12)	6.58	2.88
45.73 (± 0.10)	8.38	1.00
45.73 (± 0.10)	8.45	1.34
50.90 (± 0.11)	10.5	1.47
50.90 (± 0.11)	15.1	1.33

Table 6.21 3-Cyanobenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
46.57 (± 0.04)	1.03	2.40
46.57 (± 0.04)	0.96	2.60
50.49 (± 0.02)	1.43	1.89
50.49 (± 0.02)	1.32	1.89
59.96 (± 0.04)	3.32	4.44
59.96 (± 0.04)	3.31	4.23
64.45 (± 0.04)	3.66	7.98
64.45 (± 0.04)	3.81	8.54
70.34 (± 0.10)	6.87	12.6
70.34 (± 0.10)	6.98	12.4
80.10 (± 0.05)	16.8	42.6
80.10 (± 0.05)	17.8	42.5
85.23 (± 0.04)	30.5	13.9
85.23 (± 0.04)	29.7	24.3

Table 6.22 3-Cyanobenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^5 k / s^{-1}	10^7 standard deviation
45.44 (± 0.04)	0.57	1.47
45.44 (± 0.04)	0.61	1.64
55.43 (± 0.04)	2.87	2.49
55.43 (± 0.04)	2.31	1.76
59.96 (± 0.06)	3.71	1.40
59.96 (± 0.06)	3.95	1.74
64.45 (± 0.20)	9.19	5.94
64.45 (± 0.20)	8.20	4.65
70.47 (± 0.05)	15.2	9.58
70.47 (± 0.05)	15.3	9.54

Table 6.23 3-Cyanobenzenediazonium tetrafluoroborate in hexafluoroisopropanol.

Temperature /°C	10^6 k / s^{-1}	10^8 standard deviation
39.01 (± 0.11)	0.24	0.34
42.45 (± 0.10)	0.44	0.54
48.54 (± 0.11)	1.42	6.78
50.78 (± 0.12)	2.52	3.23
54.98 (± 0.10)	5.46	4.56
58.12 (± 0.10)	10.3	9.65

Table 6.24 3-Cyanobenzenediazonium tetrafluoroborate in ethanol.

Temperature /°C	10^2 k / s^{-1}	10^4 standard deviation
36.72 (± 0.02)	0.12	0.50
36.72 (± 0.02)	0.10	0.50
43.70 (± 0.02)	8.16	1.55
43.70 (± 0.02)	6.26	1.23
49.70 (± 0.05)	1.33	1.79
49.70 (± 0.05)	1.35	4.00
55.32 (± 0.02)	3.09	7.48
55.32 (± 0.02)	2.66	7.07
60.08 (± 0.07)	6.44	20.1
60.08 (± 0.07)	4.34	6.39

Table 6.25 3-Nitrobenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}	10^6 standard deviation
60.78 (± 0.02)	4.48	8.28
60.78 (± 0.02)	3.45	6.68
65.37 (± 0.02)	6.54	1.76
65.37 (± 0.02)	5.50	2.16
70.04 (± 0.04)	7.71	8.89
70.04 (± 0.04)	7.70	8.68
75.53 (± 0.04)	12.1	22.0
75.53 (± 0.04)	12.8	41.6
80.17 (± 0.02)	26.8	34.9
80.17 (± 0.02)	27.0	23.5
85.23 (± 0.02)	30.2	22.1
85.23 (± 0.02)	30.4	24.8

Table 6.26 3-Nitrobenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^5 k / s^{-1}	10^7 standard deviation
45.26 (± 0.02)	1.34	1.33
45.26 (± 0.02)	1.00	2.13
46.19 (± 0.06)	2.02	2.31
46.19 (± 0.06)	3.13	4.12
50.16 (± 0.02)	3.96	7.65
50.16 (± 0.02)	3.90	5.03
55.20 (± 0.05)	5.20	3.49
55.20 (± 0.05)	5.41	2.56
59.82 (± 0.27)	14.4	28.4
59.82 (± 0.27)	17.0	27.4
65.34 (± 0.31)	28.6	4.34
65.34 (± 0.31)	28.3	5.27
70.49 (± 0.15)	48.4	32.7
70.49 (± 0.15)	56.9	20.6

Table 6.27 4-Methylbenzenediazonium tetrafluoroborate in water.

Temperature /°C	10^4 k / s^{-1}	10^7 standard deviation
30.01 (± 0.04)	0.09	0.08
30.01 (± 0.04)	0.10	0.10
39.57 (± 0.02)	0.41	0.30
39.57 (± 0.02)	0.38	0.72
49.59 (± 0.02)	1.48	9.57
49.59 (± 0.02)	1.66	2.41
59.59 (± 0.02)	6.22	21.5
59.59 (± 0.02)	5.96	18.0
65.02 (± 0.05)	12.1	8.67
65.02 (± 0.05)	12.1	7.46

Table 6.28 4-Methylbenzenediazonium tetrafluoroborate in TFE.

Temperature /°C	10^3 k / s^{-1}	10^4 standard deviation
39.57 (± 0.02)	0.39	0.15
39.57 (± 0.02)	0.39	0.11
45.20 (± 0.05)	0.73	0.21
45.20 (± 0.05)	0.72	0.21
49.69 (± 0.02)	1.08	0.40
49.69 (± 0.02)	1.38	0.38
55.21 (± 0.06)	2.68	0.82
55.21 (± 0.06)	2.82	0.80
59.73 (± 0.02)	4.68	4.13
59.73 (± 0.02)	5.02	3.40
65.23 (± 0.05)	8.91	6.10
65.23 (± 0.05)	8.98	5.82
70.11 (± 0.04)	14.1	5.72
70.11 (± 0.04)	15.7	4.86

Tables 6.29-32. 4-Methylbenzenediazonium tetrafluoroborate in TFE:trifluoromethoxybenzene (TFMOB) at various molar ratios.

Table 6.29 TFE:TFMOB 10:1.

Temperature /°C	10^4 k / s^{-1}	10^5 standard deviation
35.02 (± 0.23)	2.24	0.62
35.02 (± 0.23)	2.62	0.53
40.53 (± 0.27)	5.63	0.48
40.53 (± 0.27)	5.83	0.61
49.49 (± 0.16)	17.2	4.29
49.49 (± 0.16)	18.5	4.21
59.08 (± 0.25)	41.1	12.1
59.08 (± 0.25)	60.7	3.44
65.05 (± 0.18)	106	5.34
65.05 (± 0.18)	138	6.23

Table 6.30 TFE:TFMOB 5:1.

Temperature /°C	10^4 k / s^{-1}	10^5 standard deviation
35.02 (± 0.23)	1.32	0.49
35.02 (± 0.23)	3.36	0.53
40.53 (± 0.27)	5.26	0.74
40.53 (± 0.27)	5.78	0.56
49.49 (± 0.16)	18.9	4.52
49.49 (± 0.16)	13.6	3.53
59.08 (± 0.25)	40.4	10.8
59.08 (± 0.25)	65.3	30.1
65.05 (± 0.18)	105	4.31
65.05 (± 0.18)	125	2.37

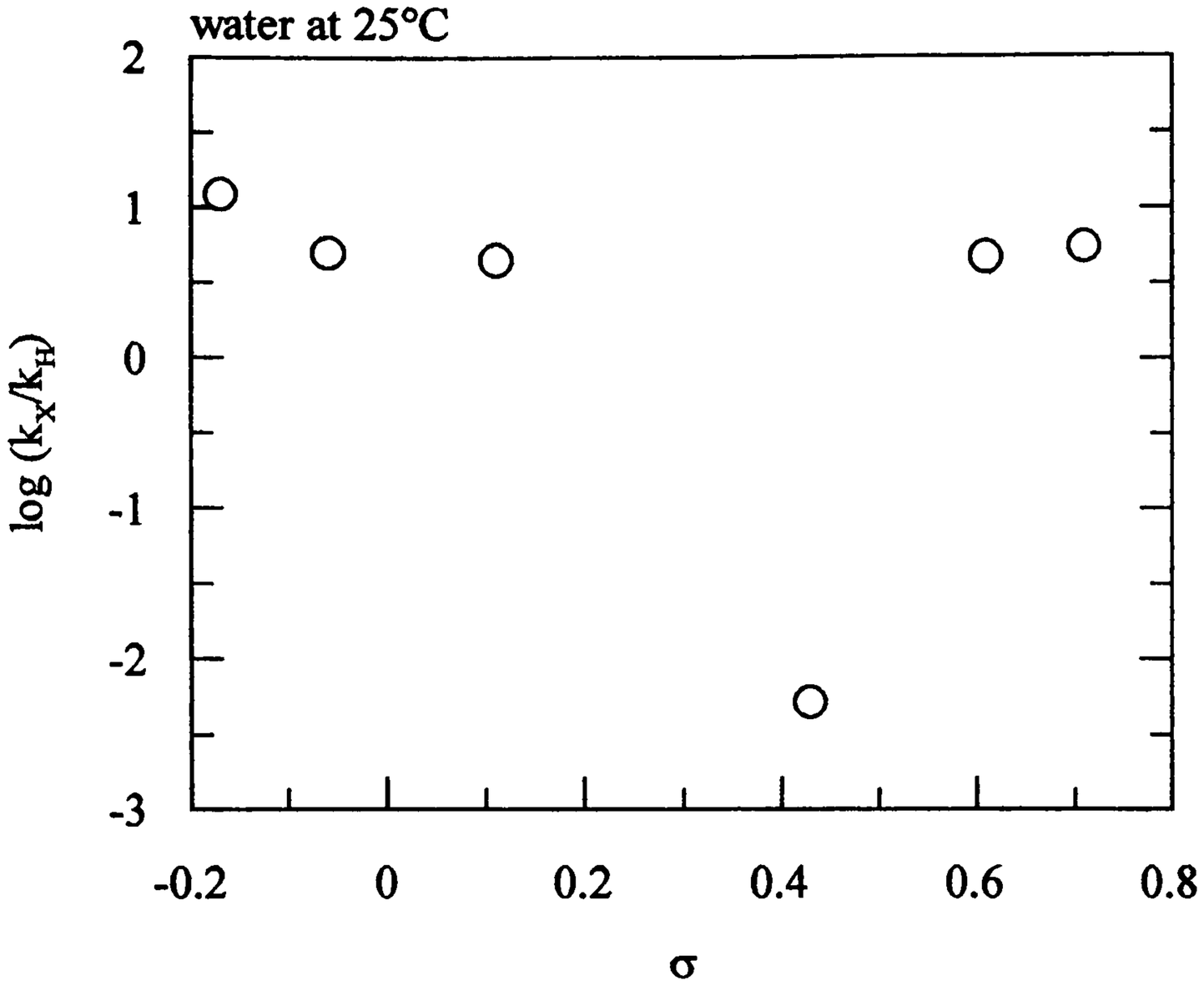
Table 6.31 TFE:TFMOB 3:1.

Temperature /°C	10^4 k / s^{-1}	10^5 standard deviation
35.02 (± 0.23)	1.63	0.23
35.02 (± 0.23)	1.81	0.25
40.53 (± 0.27)	6.09	0.65
40.53 (± 0.27)	5.60	0.58
49.49 (± 0.16)	20.1	4.67
49.49 (± 0.16)	15.3	3.15
59.08 (± 0.25)	42.2	11.2
59.08 (± 0.25)	54.2	21.8
65.05 (± 0.18)	142	7.81
65.05 (± 0.18)	139	8.32

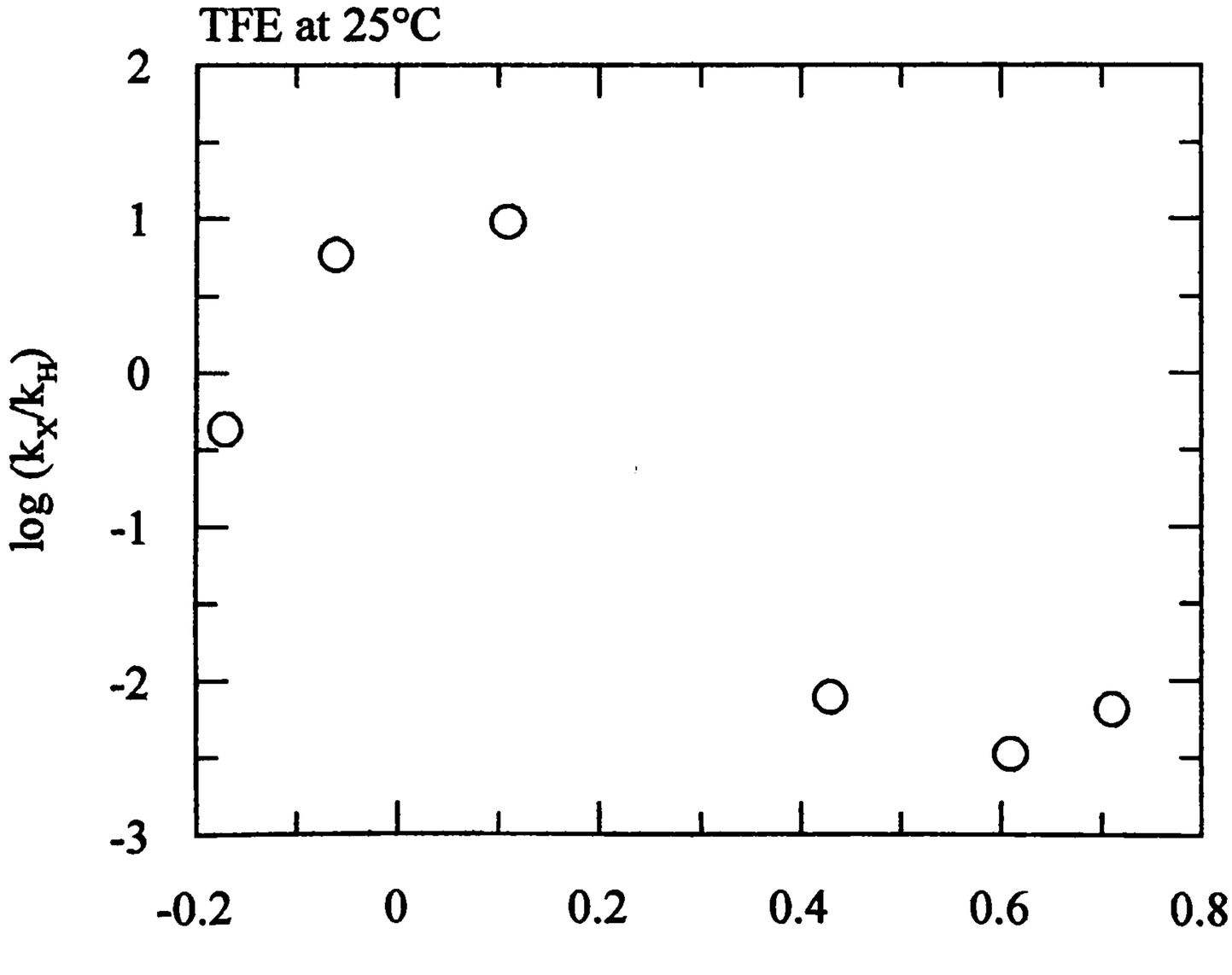
Table 6.32 TFE:TFMOB 1:0.

Temperature /°C	10^4 k / s^{-1}	10^5 standard deviation
35.02 (± 0.23)	1.71	0.23
35.02 (± 0.23)	1.93	0.41
40.53 (± 0.27)	3.74	0.43
40.53 (± 0.27)	3.52	0.51
49.49 (± 0.16)	18.5	4.31
49.49 (± 0.16)	13.2	3.47
59.08 (± 0.25)	41.6	11.0
59.08 (± 0.25)	45.2	18.7
65.05 (± 0.18)	128	54.3
65.05 (± 0.18)	149	62.2

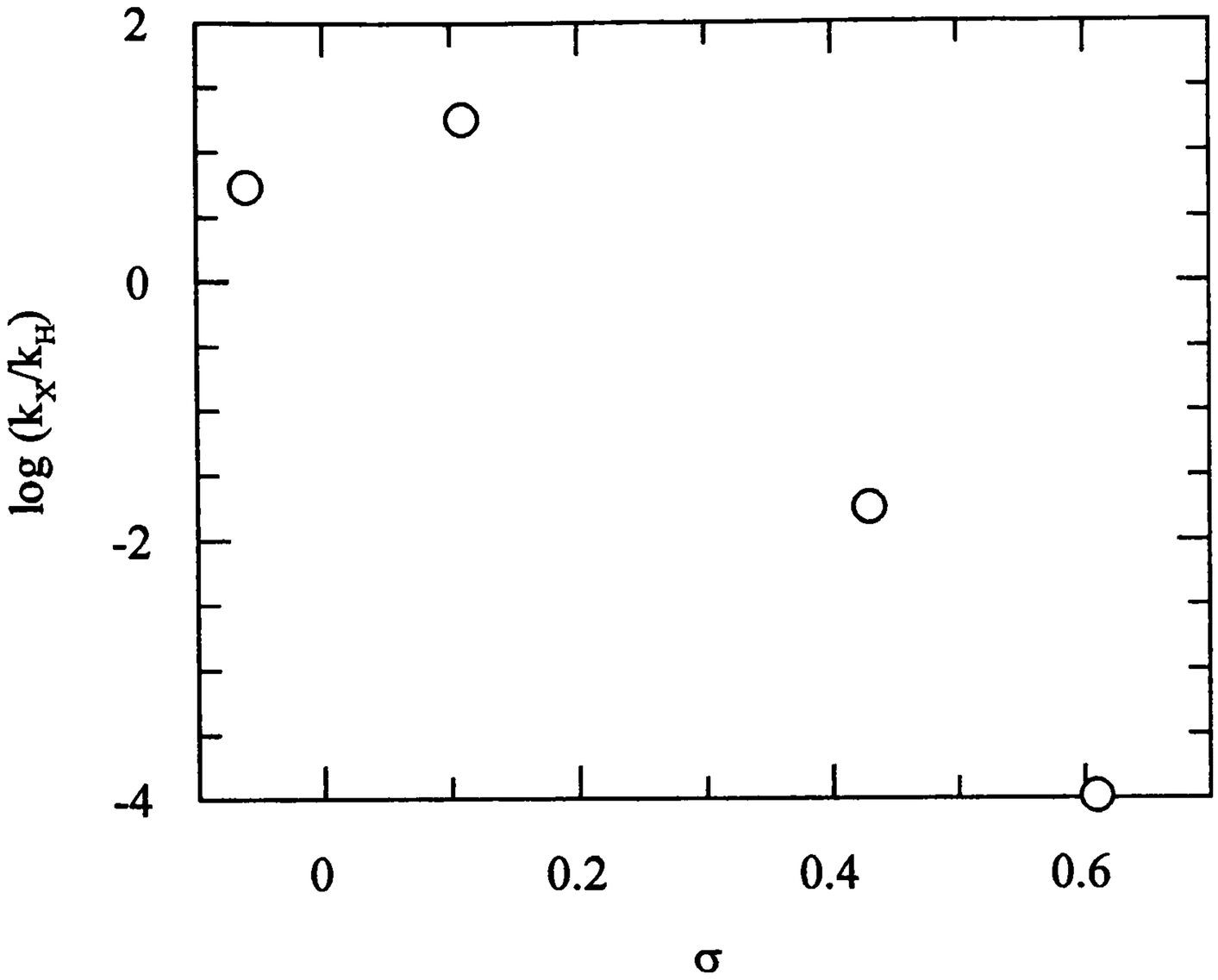
Hammett plot of substituent effects on rate of substituted benzenediazonium tetrafluoroborates in water at 25°C



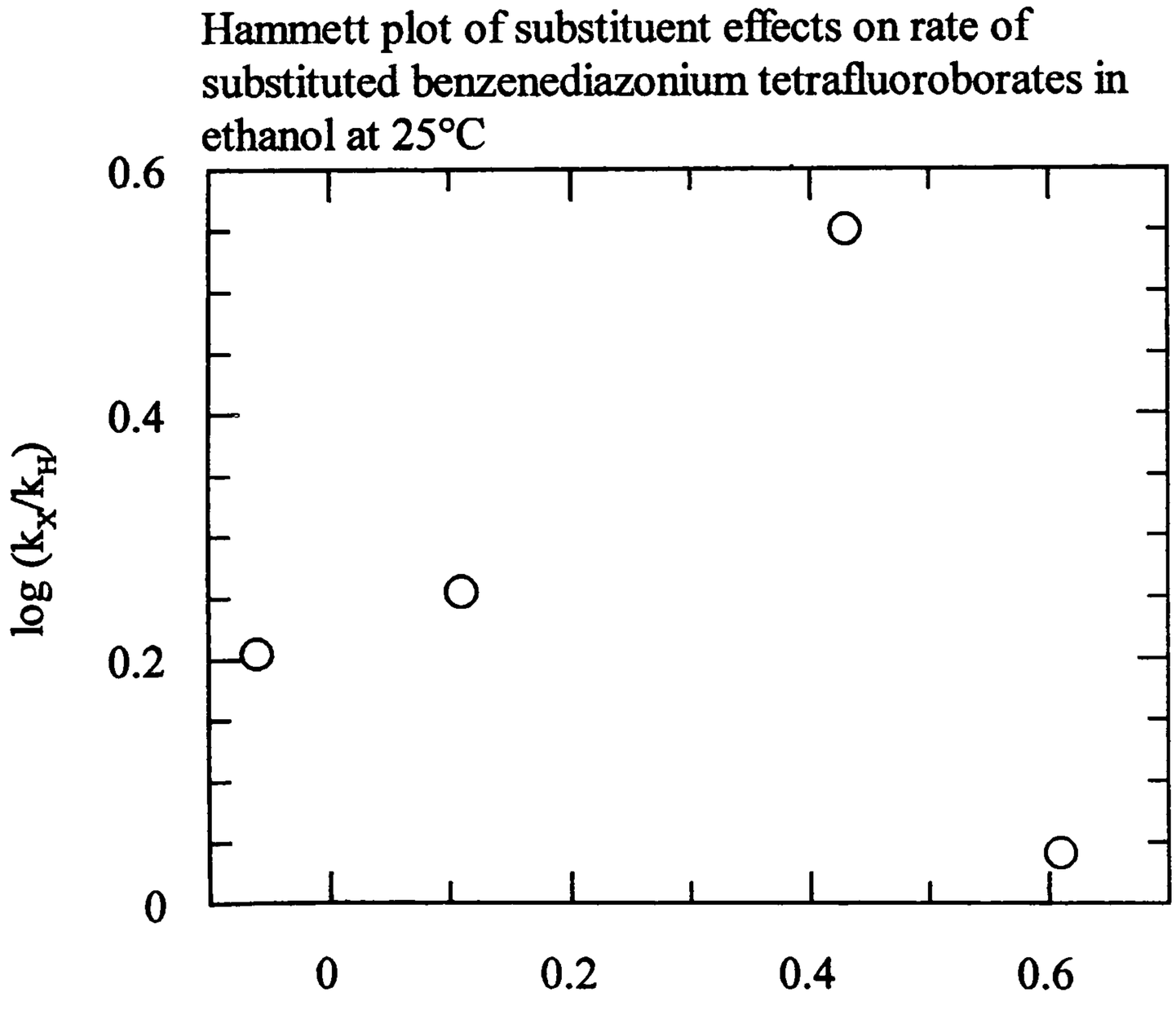
Hammett plot of substituent effects on rate of substituted benzenediazonium tetrafluoroborates in TFE at 25°C



Hammett plot of substituent effects on rate of substituted benzenediazonium tetrafluoroborates in hexafluoroisopropanol at 25°C



Hammett plot of substituent effects on rate of substituted benzenediazonium tetrafluoroborates in ethanol at 25°C



Appendix B Product Analysis.

Table 6.33 Quantitative analysis of benzenediazonium chloride (64.5 mg) in TFE with undecane (36.4 mg).

Injection Number	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
1	11.5	98.8
2	11.6	99.3
3	11.3	93.7
4	11.3	99.8
5	11.5	97.9
6	11.3	95.9
mean (standard dev.)	**11.4 (0.12)**	**97.6 (2.13)**

Table 6.34 Quantitative Analysis of benzenediazonium chloride (64.3 mg) in TFE with undecane (34.6 mg).

Injection Number	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
1	8.44	91.1
2	8.38	91.1
3	8.21	89.3
4	8.16	89.3
5	7.94	88.8
6	8.38	90.3
mean (standard dev.)	**8.25 (0.17)**	**89.9 (0.91)**

Table 6.35 Quantitative Analysis of benzenediazonium tetrafluoroborate (182.3 mg) in TFE with undecane (75.9 mg).

Injection Number	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
1	32.5	67.5
2	31.0	67.0
3	39.5	67.3
4	31.5	66.7
5	30.8	66.0
6	30.7	67.0
7	30.8	66.6
mean (standard dev.)	**32.4 (2.97)**	**66.9 (0.44)**

Table 6.36 Quantitative Analysis of benzenediazonium tetrafluoroborate (182.1 mg) in TFE with undecane (78.9 mg).

Injection Number	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
1	21.0	69.2
2	20.6	71.7
3	19.7	70.0
4	19.0	69.1
5	19.4	69.8
6	18.6	69.2
mean (standard dev.)	**19.7 (0.86)**	**69.8 (0.89)**

Tables 6.37-6.40 4-Methylbenzenediazonium tetrafluoroborate in TFE:trifluoromethoxybenzene TFMOB at various molar ratio concentrations.

Table 6.37 TFE:TFMOB (10:1).

substrate 10^4 mol dm^{-3}	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.40	30.6	69.4
2.40	30.9	69.1
2.40	30.9	69.1
2.38	36.2	63.8
2.38	36.3	63.7
2.38	36.2	63.8
mean (standard dev.)	**33.5 (2.73)**	**66.5 (2.73)**

Table 6.38 4-Methylbenzenediazonium tetrafluoroborate in TFE:TFMOB (5:1).

substrate 10^4 mol dm^{-3}	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.43	38.6	61.4
2.43	37.9	62.1
2.43	38.0	62.0
2.41	39.3	60.6
2.41	40.3	59.7
2.41	40.2	59.8
mean (standard dev.)	**39.0 (0.95)**	**61.0 (0.95)**

Table 6.39 4-Methylbenzenediazonium tetrafluoroborate in TFE:TFMOB (5:2).

substrate 10^4 mol dm $^{-3}$	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.42	39.5	60.5
2.42	39.4	60.6
2.42	39.4	60.6
2.57	39.1	60.9
2.57	40.3	59.7
2.57	39.1	60.9
mean (standard dev.)	**39.5**	**60.6**

Table 6.40 4-Methylbenzenediazonium tetrafluoroborate in TFE:TFMOB (1:0).

substrate 10^4 mol dm $^{-3}$	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.42	26.4	73.6
2.42	26.5	73.5
2.42	26.9	73.1
2.47	23.8	76.2
2.47	24.3	75.7
2.47	23.8	76.2
mean (standard dev.)	**25.3 (1.33)**	**74.7 (1.33)**

Tables 6.41-6.43 4-Methylbenzenediazonium tetrafluoroborate in TFE:difluoro-2,2,2-trifluoroethyl ether DFTFE at various molar ratio concentrations.

Table 6.41 TFE:DFTFE(10:1).

substrate 10^4 mol dm $^{-3}$	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.43	9.53	90.5
2.43	8.34	91.7
2.43	8.93	91.1
2.43	8.95	91.1
2.46	8.93	91.1
2.46	8.97	91.0
2.46	8.45	91.6
2.46	9.41	90.6
mean (standard dev.)	**8.93**	**91.1**

Table 6.42 4-Methylbenzenediazonium tetrafluoroborate in TFE:DFTFE (5:1).

substrate 10^4 mol dm $^{-3}$	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.43	13.1	86.9
2.43	14.9	85.1
2.43	14.0	86.0
2.43	14.3	85.8
2.46	14.1	85.9
2.46	14.2	85.8
2.46	13.6	86.4
2.46	14.5	85.5
mean (standard dev.)	**14.1 (0.52)**	**85.9 (0.52)**

Table 6.43 4-Methylbenzenediazonium tetrafluoroborate in TFE:DFTFE (5:2).

substrate 10^4 mol dm $^{-3}$	Yield of ArF /%	Yield of $ArOCH_2CF_3$ / %
2.43	12.4	87.6
2.43	13.0	87.0
2.43	12.7	87.3
2.43	12.7	87.3
2.46	12.7	87.3
2.46	13.1	87.0
2.46	12.3	87.7
2.46	12.7	87.3
mean (standard dev.)	**12.7 (0.24)**	**87.3 (0.24)**

Table 6.44 Quantitative analysis of products from benzenediazonium tetrafluoroborate (60 mg) in TFE with undecane (38 mg) and added sodium tetrafluoroborate (577 mg).

Injection Number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	27.8	59.8	87.7
2	32.8	58.3	91.1
3	30.2	58.3	88.5
4	30.1	58.6	88.7
mean (standard dev.)	**30.2 (1.74)**	**58.7 (0.65)**	

Table 6.45 Quantitative analysis of products from benzenediazonium tetrafluoroborate (65 mg) in TFE with undecane (36 mg) and added sodium hexafluorophosphate (320 mg).

Injection Number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	26.4	69.3	95.8
2	24.7	63.5	88.1
3	25.3	68.8	94.1
4	25.2	69.6	94.9
mean (standard dev.)	**25.4 (0.63)**	**67.8 (2.52)**	

Table 6.46 Quantitative analysis of products from benzenediazonium tetrafluoroborate (70.0 mg) in TFE with undecane (46.0 mg) and added sodium hexafluoroantimonate (464 mg).

Injection Number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	30.8	65.2	96.0
2	23.8	68.5	92.3
3	28.2	67.5	95.7
4	29.3	67.9	97.2
mean (standard dev.)	**28.0 (2.61)**	**67.3 (1.25)**	

Table 6.47 Quantitative analysis of 4-methoxybenzenediazonium tetrafluoroborate in saturated aqueous KF (200 ml, 10.2 mol dm^{-3}).

substrate 10^3 mol dm^{-3}	Yield of Phenol %	
	UV	Thermal
3.95	94.4	96.5
3.75	89.6	96.2
mean (standard dev.)	**92.0 (2.40)**	**96.4 (0.15)**

Table 6.48 Quantitative analysis of 4-methylbenzenediazonium tetrafluoroborate in saturated aqueous KF (200 ml, 10.2 mol dm^{-3}).

substrate 10^3 mol dm^{-3}	Yield of Phenol %	
	UV	thermal
3.64	91.9	96.2
	92.1	96.7
mean (standard dev.)	**92.0 (0.10)**	**96.5 (0.25)**

Table 6.49 Quantitative analysis of 4-methyl and 4-methoxybenzenediazonium tetrafluoroborates in H_2O via photolysis.

substrate 10^3 mol dm^{-3}	Yield of Phenol %	**mean (standard dev.)**
4-Me (3.55)	92.9	**93.0 (0.05)**
	93.0	
4-MeO (3.75)	89.5	**89.6 (0.10)**
	89.7	

Table 6.50 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (84.9 mg) in TFE with undecane (33.1 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	35.3	51.1	86.4
2	36.9	50.6	87.5
3	32.8	50.8	83.7
4	33.3	50.9	84.2
mean (standard dev.)	**34.6 (1.64)**	**50.9 (0.18)**	

Table 6.51 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (95.8 mg) in TFE with undecane (35.5 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	43.5	46.9	90.3
2	39.7	52.0	91.7
3	41.5	53.8	95.3
4	41.5	53.1	94.6
mean (standard dev.)	**41.6 (1.34)**	**51.5 (2.70)**	

Table 6.52 Quantitative analysis of the thermolysis of 4-methylbenzenediazonium tetrafluoroborate (92.0 mg) in TFE with undecane (45.0 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	27.7	56.9	84.6
2	28.5	56.7	85.2
3	29.5	56.4	85.9
4	28.8	56.8	85.5
mean (standard dev.)	**28.6 (0.65)**	**56.7 (0.18)**	

Table 6.53 Quantitative analysis of the photolysis of 4-methylbenzenediazonium tetrafluoroborate (81.6 mg) in TFE with undecane (33.6 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	49.6	54.6	104
2	49.0	53.4	102
3	48.8	53.6	102
4	48.9	53.8	103
mean (standard dev.)	**49.1 (0.31)**	**53.9 (0.46)**	

Table 6.54 Quantitative analysis of the photolysis of 4-methylbenzenediazonium tetrafluoroborate (95.7 mg) in TFE with undecane (30.4 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	39.2	52.7	91.9
2	39.0	52.0	91.0
3	39.2	54.3	93.6
4	39.8	53.5	93.2
mean (standard dev.)	**39.3 (0.30)**	**53.1 (0.86)**	

Table 6.55 Quantitative analysis of the photolysis of 4-methoxybenzenediazonium tetrafluoroborate (75.2 mg) in TFE with undecane (34.5 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	43.2	44.7	87.9
2	44.4	45.8	90.2
3	42.6	45.9	88.5
4	43.4	45.5	88.9
mean (standard dev.)	**43.4 (0.65)**	**45.5 (0.47)**	

Table 6.56 Quantitative analysis of the photolysis of 4-methoxybenzenediazonium tetrafluoroborate (110 mg) in TFE with undecane (32.2 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	45.2	42.5	87.7
2	46.3	47.1	93.4
3	44.6	47.3	91.9
4	37.4	46.6	84.0
mean (standard dev.)	**43.4 (3.50)**	**45.9 (1.97)**	

Table 6.57 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (97.8 mg) in TFE with undecane (44.8 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	37.9	51.4	89.3
2	41.5	51.8	93.4
3	41.9	52.2	94.1
4	42.1	51.6	93.7
5	46.3	52.0	98.3
mean (standard dev.)	**41.9 (2.67)**	**51.8 (0.28)**	

Table 6.58 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (86.9 mg) in TFE with undecane (44.8 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	35.2	50.2	85.4
2	34.9	51.9	86.8
3	32.3	51.7	84.0
4	33.7	52.4	86.1
5	33.3	53.1	86.3
6	40.1	53.8	93.9
mean (standard dev.)	**34.9 (2.51)**	**52.2 (1.14)**	

Table 6.59 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (72.0 mg) in TFE with undecane (44.8 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	32.5	49.8	82.3
2	42.0	52.1	94.1
3	36.4	52.4	88.8
4	41.3	52.7	94.0
5	37.0	53.8	90.8
mean (standard dev.)	**37.8 (3.48)**	**52.2 (1.31)**	

Table 6.60 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (115 mg) in TFE with undecane (44.8 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	44.3	49.8	94.1
2	34.3	49.5	83.8
3	45.0	47.7	92.7
4	42.0	49.9	91.9
5	41.8	50.0	91.7
6	41.8	49.8	91.6
mean (standard dev.)	**41.5 (3.47)**	**49.5 (0.80)**	

Table 6.61 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (88.8 mg) in TFE with undecane (55.1 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	27.3	67.4	94.7
2	33.8	66.0	99.8
3	28.3	67.7	96.0
4	25.9	67.4	93.4
5	29.0	67.1	96.1
mean (standard dev.)	**28.9 (2.68)**	**67.1 (0.59)**	

Table 6.62 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (86.0 mg) in TFE with undecane (55.1 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	24.9	67.0	92.0
2	25.4	67.1	92.5
3	26.0	64.5	90.5
4	28.0	68.6	96.6
5	26.8	67.8	94.5
mean (standard dev.)	**26.2 (1.09)**	**67.0 (1.38)**	

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Table 6.66 Quantitative analysis of the thermolysis of 3-nitrobenzenediazonium tetrafluoroborate (88.0 mg) in TFE with undecane (57.7 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	40.8	49.9	90.6
2	40.8	51.2	92.0
3	40.8	55.8	96.6
4	40.5	51.2	91.7
5	40.2	50.4	90.6
mean (standard dev.)	**40.6 (0.24)**	**51.7 (2.11)**	

Table 6.67 Quantitative analysis of the photolysis of 3-nitrobenzenediazonium tetrafluoroborate in (118 mg) TFE with undecane (41.4 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	39.9	51.6	91.4
2	39.7	52.0	91.8
3	39.9	52.1	92.0
4	39.4	52.9	92.3
5	38.8	52.5	91.2
mean (standard dev.)	**39.5 (0.41)**	**52.2 (0.44)**	

Table 6.68 Quantitative analysis of the photolysis of 3-nitrobenzenediazonium tetrafluoroborate in (86.0 mg) TFE with undecane (55.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	40.1	52.0	92.2
2	40.3	52.8	93.1
3	41.0	51.7	92.6
4	39.9	52.4	92.3
5	40.4	52.4	92.8
mean (standard dev.)	**40.3 (0.37)**	**52.3 (0.38)**	

Table 6.69 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (117 mg) in TFE with undecane (55.9 mg)

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	25.0	75.1	100
2	25.3	68.5	93.7
3	25.3	73.6	98.8
4	25.6	73.1	98.7
5	25.2	73.5	98.7
mean (standard dev.)	**25.3 (0.19)**	**72.8 (2.24)**	

Table 6.70 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (158 mg) in TFE with undecane (55.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	28.7	71.1	99.8
2	28.6	71.4	99.9
3	28.7	71.4	100
4	28.6	71.4	100
5	28.6	71.6	100
mean (standard dev.)	**28.6 (0.05)**	**71.4 (0.16)**	

Table 6.71 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (81.5 mg) in TFE with undecane (55.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	36.2	73.4	110
2	35.1	71.8	107
3	37.3	73.4	111
4	36.4	72.1	109
5	35.1	71.6	107
mean (standard dev.)	**36.0 (0.84)**	**72.5 (0.78)**	

Table 6.72 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (81.5 mg) in TFE with undecane (55.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	32.4	73.3	106
2	35.8	73.0	109
3	36.3	73.0	109
4	35.2	73.4	109
5	35.4	72.3	108
mean (standard dev.)	**35.0 (1.36)**	**73.0 (0.38)**	

Table 6.73 Quantitative analysis of the thermolysis of 3-cyanobenzenediazonium tetrafluoroborate (76.0 mg) in TFE with undecane (52.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	30.2	60.0	90.2
2	30.5	60.3	90.8
3	27.3	58.3	85.7
4	27.6	57.5	85.2
5	27.9	59.2	87.1
mean (standard dev.)	**28.7 (1.36)**	**59.1 (1.04)**	

Table 6.74 Quantitative analysis of the thermolysis of 3-cyanobenzenediazonium tetrafluoroborate (65.3 mg) in TFE with undecane (52.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	41.7	66.8	109
2	39.4	41.7	81.0
3	39.7	55.6	95.3
4	40.0	60.2	100
5	39.3	60.0	99.4
mean (standard dev.)	**40.0 (0.87)**	**56.9 (8.38)**	

Table 6.75 Quantitative analysis of the photolysis of 3-cyanobenzenediazonium tetrafluoroborate (73.3 mg) in TFE with undecane (52.9 mg).

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
3.39	14.7	39.2	53.9
	16.2	41.8	58.0
	23.0	36.2	59.2
	14.7	41.3	56.0
	22.1	42.7	64.8
mean (standard dev.)	**18.1 (3.65)**	**40.2 (2.32)**	

Table 6.76 Quantitative analysis of the photolysis of 3-cyanobenzenediazonium tetrafluoroborate (104 mg) in TFE with undecane (52.9 mg)

Injection number	PhF (%)	$PhOCH_2CF_3$ (%)	% Recovery
1	24.6	45.8	70.4
2	25.4	50.6	76.0
3	25.2	44.5	69.7
4	24.6	50.2	74.8
5	25.2	48.3	73.5
6	24.6	46.6	71.2
mean (standard dev.)	**24.9 (0.34)**	**47.7 (2.24)**	

Table 6.77 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (98.0 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	27.4	71.8	99.2
2	20.5	77.4	97.9
3	20.1	75.5	95.6
4	25.7	74.5	100
5	23.4	74.5	97.9
mean (standard dev.)	**23.4 (2.85)**	**74.7 (1.81)**	

Table 6.78 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (99.9 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	18.7	73.3	92.0
2	21.5	71.0	92.5
3	23.4	71.4	94.8
4	22.8	72.2	95.0
5	22.1	74.2	96.3
mean (standard dev.)	**21.7 (1.63)**	**72.4 (1.19)**	

Table 6.79 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (101 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	15.3	103	118
2	15.3	101	116
3	15.3	107	122
4	15.3	107	122
mean (standard dev.)	**15.3 (0.00)**	**105 (2.60)**	

Table 6.80 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (101 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	13.1	91.9	105
2	13.1	98.5	112
3	12.9	96.3	109
4	13.1	91.9	105
mean (standard dev.)	**13.1 (0.09)**	**94.7 (2.85)**	

Table 6.81 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (114 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	19.9	58.5	78.4
2	19.1	59.8	78.9
3	21.3	62.2	83.5
4	20.6	58.3	78.9
5	20.6	60.3	80.9
mean (standard dev.)	**20.3 (0.75)**	**59.8 (1.41)**	

Table 6.82 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (107 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	25.7	66.8	92.5
2	23.4	67.1	90.5
3	24.8	66.8	91.6
4	24.3	63.0	87.3
mean (standard dev.)	**24.6 (0.83)**	**65.9 (1.69)**	

Table 6.83 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (144 mg) in HFIP with undecane (43.3 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	25.8	58.2	84.0
2	25.8	55.5	81.3
3	26.1	58.5	84.5
4	25.8	54.1	79.9
mean (standard dev.)	**25.9 (0.13)**	**56.6 (1.85)**	

Table 6.84 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (84.2 mg) in HFIP with undecane (43.3 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	22.7	50.3	73.0
2	22.0	53.7	75.7
3	21.3	59.0	80.3
4	21.7	55.3	77.0
mean (standard dev.)	**21.9 (0.51)**	**38.3 (1.65)**	

Table 6.85 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (53.5 mg) in HFIP with undecane (43.2).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	14.0	87.8	102
2	13.8	82.8	96.6
3	12.9	81.3	94.2
4	13.5	84.1	97.6
5	13.6	84.1	97.7
mean (standard dev.)	**13.6 (0.37)**	**84.0 (2.15)**	

Table 6.86 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (88.8 mg) in HFIP with undecane (43.2 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	14.2	83.7	97.7
2	18.3	89.3	108
3	13.8	79.6	93.4
4	15.4	84.2	99.6
5	15.4	84.2	99.6
mean (standard dev.)	15.4 (1.58)	84.2 (3.07)	

Table 6.87 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (129 mg) in HFIP with undecane (43.2 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	15.5	78.8	94.3
2	14.6	79.0	93.6
3	15.9	80.4	96.3
4	15.3	79.4	94.7
5	15.3	79.4	94.7
mean (standard dev.)	**15.3 (0.42)**	**79.4 (0.55)**	

Table 6.88 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (141 mg) in HFIP with undecane (43.2 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	13.9	90.4	104
2	12.8	79.1	91.8
3	13.5	81.4	94.9
4	11.7	89.8	102
5	13.0	86.0	99.0
mean (standard dev.)	**13.0 (0.75)**	**85.3 (4.48)**	

Table 6.89 Quantitative analysis of the photolysis of 3-methoxybenzenediazonium tetrafluoroborate (68.0 mg) in HFIP with undecane (51.0mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	8.75	70.9	79.7
2	9.10	72.8	81.9
3	9.20	71.6	80.8
4	9.14	71.5	80.6
5	9.18	71.7	80.9
mean (standard dev.)	9.07 (0.17)	71.7 (0.62)	

Table 6.90 Quantitative analysis of the photolysis of 3-methoxybenzenediazonium tetrafluoroborate (75.0 mg) in HFIP with undecane (51.0mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	13.8	74.0	87.8
2	13.2	73.4	86.6
3	13.5	73.6	87.1
4	13.6	73.7	87.3
5	13.2	73.2	86.4
mean (standard dev.)	**13.5 (0.23)**	**73.6 (0.27)**	

Table 6.91 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (144 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	9.60	91.5	101
2	9.54	91.6	101
3	10.2	91.8	102
4	9.76	91.3	101
mean (standard dev.)	**9.78 (0.26)**	**91.6 (0.18)**	

Table 6.92 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (84.2 mg) in HFIP with undecane (51.0 mg).

Injection number	PhF (%)	$PhOCH(CF_3)_2$ (%)	% Recovery
1	13.3	84.3	97.6
2	12.0	84.6	96.6
3	12.9	84.0	96.9
4	12.2	84.2	96.4
mean (standard dev.)	**12.6 (0.52)**	**84.3 (0.22)**	

Table 6.93 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (104 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	2.82	97.2
2	4.55	95.5
3	3.27	96.7
4	3.41	96.6
5	5.67	94.3
6	2.84	97.2
mean (standard dev.)	**3.76 (1.03)**	**96.3 (1.03)**

Table 6.94 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (100 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	3.56	96.4
2	5.62	94.4
3	4.88	95.1
4	3.36	96.6
mean (standard dev.)	**4.36 (0.94)**	**95.6 (0.91)**

Table 6.95 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (97.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	14.9	85.1
2	15.3	84.7
3	14.6	85.4
4	14.6	85.4
5	14.4	85.6
mean (standard dev.)	**14.8 (0.31)**	**85.2 (0.31)**

Table 6.96 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (100 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	14.7	85.3
2	15.1	84.9
3	15.5	84.5
4	15.8	84.2
5	15.1	84.5
mean (standard dev.)	**15.2 (0.38)**	**84.7 (0.38)**

Table 6.97 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (81.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	9.76	90.2
2	11.2	88.8
3	10.9	89.1
4	10.3	89.7
5	10.5	89.5
mean (standard dev.)	**10.5 (0.50)**	**89.5 (0.48)**

Table 6.98 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (85.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	10.6	89.4
2	10.6	89.4
3	10.8	89.2
4	10.2	89.8
5	10.6	89.4
mean (standard dev.)	**10.6 (0.20)**	**89.4 (0.20)**

Table 6.99 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (76.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	20.3	79.7
2	17.6	82.4
3	17.5	82.5
4	17.5	82.5
5	18.2	81.8
mean (standard dev.)	**18.2 (1.07)**	**81.8 (1.07)**

Table 6.100 Quantitative analysis of the thermolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (80.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
	18.0	82.0
	18.4	81.6
	17.8	82.2
	18.7	81.3
	18.3	81.7
mean (standard dev.)	**18.2 (0.31)**	**81.8 (0.31)**

Table 6.101 Quantitative analysis of the thermolysis of 3-cyanobenzenediazonium tetrafluoroborate (58.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	12.7	87.3
2	14.3	85.7
3	13.7	86.3
4	14.1	85.9
5	14.2	85.8
mean (standard dev.)	**13.8 (0.59)**	**86.2 (0.59)**

Table 6.102 Quantitative analysis of the thermolysis of 3-cyanobenzenediazonium tetrafluoroborate (62.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	13.8	86.2
2	13.7	86.3
3	13.8	86.2
4	13.9	86.1
5	13.7	86.3
mean (standard dev.)	**13.8 (0.07)**	**86.2 (0.07)**

Table 6.103 Quantitative analysis of the thermolysis of 3-nitrobenzenediazonium tetrafluoroborate (72.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	9.21	90.8
2	8.35	91.7
3	8.55	91.5
4	8.73	91.3
5	8.67	91.3
mean (standard dev.)	**8.70 (0.29)**	**91.3 (0.29)**

Table 6.104 Quantitative analysis of the thermolysis of 3-nitrobenzenediazonium tetrafluoroborate (75.0 mg) in TFA with undecane (29.9 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	8.41	91.6
2	9.01	91.0
3	8.42	91.6
4	8.88	91.2
5	8.91	91.1
mean (standard dev.)	**8.73 (0.26)**	**91.3 (0.25)**

Table 6.105 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (102 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	17.9	82.1
2	18.5	81.5
3	17.3	82.7
4	17.9	82.1
5	18.0	82.0
mean (standard dev.)	**17.9 (0.38)**	**82.1 (0.38)**

Table 6.106 Quantitative analysis of the photolysis of benzenediazonium tetrafluoroborate (110 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	18.0	82.0
2	18.1	81.9
3	17.8	82.2
4	18.0	82.0
5	17.9	82.1
mean (standard dev.)	**18.0 (0.10)**	**82.0 (0.10)**

Table 6.107 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (181 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	19.8	80.2
2	19.9	80.1
3	19.7	80.3
4	19.4	80.6
5	20.1	79.9
mean (standard dev.)	**19.8 (0.23)**	**80.2 (0.23)**

Table 6.108 Quantitative analysis of the photolysis of 3-methylbenzenediazonium tetrafluoroborate (168 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	19.8	80.2
2	20.4	79.6
3	20.2	79.8
4	19.8	80.2
5	19.7	80.3
mean (standard dev.)	**20.0 (0.27)**	**80.0 (0.27)**

Table 6.109 Quantitative analysis of the photolysis of 3-methoxybenzenediazonium tetrafluoroborate (98.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	17.7	82.3
2	12.8	87.2
3	13.0	87.0
4	15.0	85.0
5	14.6	85.4
mean (standard dev.)	**14.6 (1.76)**	**85.4 (1.76)**

Table 6.110 Quantitative analysis of the photolysis of 3-methoxybenzenediazonium tetrafluoroborate (101 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	14.4	85.6
2	14.9	85.1
3	14.8	85.2
4	15.2	84.8
5	14.2	85.8
mean (standard dev.)	**14.7 (0.36)**	**85.3 (0.36)**

Table 6.111 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (78.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	21.0	79.0
2	17.3	82.7
3	17.0	83.0
4	21.0	79.0
5	19.1	80.9
mean (standard dev.)	**19.1 (1.72)**	**80.9 (1.72)**

Table 6.112 Quantitative analysis of the photolysis of 3-trifluoromethylbenzenediazonium tetrafluoroborate (84.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	19.4	80.6
2	19.4	80.6
3	19.9	80.1
4	18.9	81.1
5	19.0	81.0
mean (standard dev.)	**19.3 (0.35)**	**80.7 (0.35)**

Table 6.113 Quantitative analysis of the photolysis of 3-cyanobenzenediazonium tetrafluoroborate (84.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	18.6	81.4
2	23.6	76.4
3	20.1	79.9
4	21.1	78.9
5	20.2	79.8
mean (standard dev.)	**20.7 (1.65)**	**79.3 (1.65)**

Table 6.114 Quantitative analysis of the photolysis of 3-cyanobenzenediazonium tetrafluoroborate (90.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	20.4	79.6
2	21.2	78.8
3	21.6	78.4
4	20.7	79.3
5	21.9	78.1
mean (standard dev.)	**21.2 (0.55)**	**78.8 (0.55)**

Table 6.115 Quantitative analysis of the photolysis of 3-nitrobenzenediazonium tetrafluoroborate (23.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	20.9	79.1
2	22.0	78.0
3	21.6	78.4
4	21.5	78.5
5	21.0	79.0
mean (standard dev.)	**21.4 (0.40)**	**78.6 (0.40)**

Table 6.116 Quantitative analysis of the photolysis of 3-nitrobenzenediazonium tetrafluoroborate (28.0 mg) in TFA with undecane (29.4 mg).

Injection number	PhF (%)	$PhOCOCF_3$ (%)
1	21.8	78.2
2	22.0	78.0
3	21.1	78.9
4	21.0	79.0
5	21.5	78.5
mean (standard dev.)	**21.5 (0.39)**	**78.5 (0.39)**

Table 6.117 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (67.7 mg) in EtOH with octane (118 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	2.82	96.5	0.68
2	3.72	95.3	1.01
3	5.50	93.2	1.26
4	4.21	94.8	0.96
5	3.10	95.7	1.24
mean (standard dev.)	**3.87 (0.95)**	**95.1 (1.10)**	**1.03 (0.21)**

Table 6.118 Quantitative analysis of the thermolysis of benzenediazonium tetrafluoroborate (67.7 mg) in EtOH with octane (118 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	2.98	95.9	1.11
2	3.45	95.3	1.28
3	3.12	96.1	0.78
4	3.42	95.4	1.14
5	3.14	95.8	1.05
mean (standard dev.)	**3.22 (0.18)**	**95.7 (0.30)**	**1.07 (0.16)**

Table 6.119 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (154 mg) in EtOH with octane (29.6 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	16.5	75.6	3.46
2	11.4	72.5	2.79
3	12.6	77.5	3.32
4	14.5	78.4	3.14
mean (standard dev.)	**13.8 (1.93)**	**76.0 (2.26)**	**3.17 (0.25)**

Table 6.120 Quantitative analysis of the thermolysis of 3-methylbenzenediazonium tetrafluoroborate (148 mg) in EtOH with octane (29.6 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	15.0	82.9	3.06
2	15.6	80.5	3.06
3	14.6	81.1	3.19
4	15.6	82.1	3.19
mean (standard dev.)	**15.2 (0.42)**	**81.7 (0.92)**	**3.13 (0.07)**

Table 6.121 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (46.6 mg) in EtOH with octane (29.6 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	17.1	78.7	4.26
2	17.5	78.2	4.22
3	16.7	78.5	4.24
4	17.8	77.9	4.29
mean (standard dev.)	**17.3 (0.41)**	**78.3 (0.30)**	**4.25 (0.02)**

Table 6.122 Quantitative analysis of the thermolysis of 3-methoxybenzenediazonium tetrafluoroborate (48.2 mg) in EtOH with octane (29.6 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	17.1	79.0	4.39
2	17.4	78.3	4.19
3	17.0	78.7	4.10
4	17.6	78.5	4.23
mean (standard dev.)	**17.3 (0.23)**	**78.6 (0.26)**	**4.23 (0.10)**

Table 6.123 Quantitative analysis of the themolysis of 3-nitrobenzenediazonium tetrafluoroborate (51.0 mg) in EtOH with undecane (44.0 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	------	4.70	95.3
2	------	8.20	91.8
3	------	10.9	89.1
4	------	7.94	92.3
5	------	7.68	92.1
mean (standard dev.)	------	**7.88 (1.97)**	**92.1 (1.97)**

Table 6.124 Quantitative analysis of the themolysis of 3-nitrobenzenediazonium tetrafluoroborate (51.0 mg) in EtOH with undecane (44.0 mg).

Injection number	PhF (%)	PhOEt (%)	Ph (%)
1	------	8.20	92.5
2	------	7.71	92.2
3	------	8.17	92.4
4	------	7.94	94.9
mean (standard dev.)	------	**8.05 (0.20)**	**93.0 (1.10)**

Experimental molar response factors (MRF's).

Table 6.125 Experimental molar response factor for 3-trifluoromethylfluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.65	0.68
2	0.69	0.67
3	0.60	0.67
4	0.61	0.63
5	0.66	0.64
mean (standard dev.)	**0.64 (0.03)**	**0.66 (0.02)**

MRF 1, 3-trifluoromethylfluorobenzene (43.6 mg) and undecane (43.0 mg).
MRF 2, 3-trifluoromethylfluorobenzene (59.8 mg) and undecane (47.2 mg).

Table 6.126 Experimental molar response factor for trifluoroethyl 3-trifluoromethylphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.49	0.42
2	0.49	0.40
3	0.40	0.33
4	0.42	0.38
mean (standard dev.)	**0.45 (0.04)**	**0.38 (0.03)**

MRF 1, trifluoroethyl 3-trifluoromethylphenyl ether (69.5 mg) and undecane (30.2 mg).
MRF 2, trifluoroethyl 3-trifluoromethylphenyl ether (60.8 mg) and undecane (36.1 mg).

Table 6.127 Experimental molar response factor for 3-nitrofluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.55	0.54
2	0.56	0.55
3	0.54	0.55
4	0.53	0.53
mean (standard dev.)	**0.54 (0.01)**	**0.54 (0.01)**

MRF 1, 3-nitrofluorobenzene (58.7 mg) and undecane (58.3 mg).
MRF 2, 3-nitrofluorobenzene (29.2 mg) and undecane (24.8 mg).

Table 6.128 Experimental molar response factor for trifluoroethyl 3-nitrophenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.41	0.42
2	0.48	0.42
3	0.46	0.47
4	0.44	0.46
mean (standard dev.)	**0.44 (0.03)**	**0.44 (0.02)**

MRF 1, trifluoroethyl 3-nitrophenyl ether (59.5 mg) and undecane (54.7 mg).
MRF 2, trifluoroethyl 3-nitrophenyl ether (73.2 mg) and undecane (75.7 mg).

Table 6.129 Experimental molar response factor for 3-cyanofluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.62	0.63
2	0.62	0.62
3	0.61	0.63
4	0.61	0.63
	0.62	0.62
mean (standard dev.)	**0.62 (0.01)**	**0.63 (0.01)**

MRF 1, 3-cyanofluorobenzene (48.9 mg) and undecane (28.5 mg).
MRF 2, 3-cyanofluorobenzene (47.2 mg) and undecane (26.3 mg).

Table 6.130 Experimental molar response factor for trifluoroethyl 3-cyanophenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.41	0.40
2	0.43	0.41
3	0.42	0.43
4	0.42	0.41
mean (standard dev.)	**0.42 (0.01)**	**0.41 (0.01)**

MRF 1, trifluoroethyl 3-cyanophenyl ether (85.0 mg) and undecane (28.5 mg).
MRF 2, trifluoroethyl 3-cyanophenyl ether (23.3 mg) and undecane (28.5 mg).

Table 6.131 Experimental molar response factor for fluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.56	0.50
2	0.53	0.52
3	0.53	0.51
4	0.53	0.51
mean (standard dev.)	**0.53 (0.01)**	**0.51 (0.01)**

MRF 1, fluorobenzene (37.4 mg) and undecane (45.3 mg).
MRF 2, fluorobenzene (37.3 mg) and undecane (63.8 mg).

Table 6.132 Experimental molar response factor for trifluoroethyl phenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.64	0.70
2	0.67	0.71
3	0.67	0.69
4	0.65	0.70
mean (standard dev.)	**0.66 (0.01)**	**0.70 (0.01)**

MRF 1, trifluoroethyl phenyl ether (27.7 mg) and undecane (33.2 mg).
MRF 2, trifluoroethyl phenyl ether (35.4 mg) and undecane (31.8 mg).

Table 6.133 Experimental molar response factor for 3-methoxyfluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.59	0.57
2	0.56	0.60
3	0.56	0.59
4	0.58	0.60
mean (standard dev.)	**0.57 (0.01)**	**0.59 (0.01)**

MRF 1, 3-methoxyfluorobenzene (69.6 mg) and undecane (30.3 mg).
MRF 2, 3-methoxyfluorobenzene (56.6 mg) and undecane (46.7 mg).

Table 6.134 Experimental molar response factor for trifluoroethyl 3-methoxyphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.62	0.62
2	0.62	0.62
3	0.63	0.64
4	0.64	0.64
mean (standard dev.)	**0.63 (0.01)**	**0.63 (0.01)**

MRF 1, trifluoroethyl 3-methoxyphenyl ether (69.2 mg) and undecane (62.5 mg).
MRF 2, trifluoroethyl 3-methoxyphenyl ether (68.1 mg) and undecane (59.4 mg).

Table 6.135 Experimental molar response factor for 3-methylfluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.68	0.63
2	0.65	0.63
3	0.67	0.60
4	0.69	0.69
mean (standard dev.)	**0.67 (0.01)**	**0.64 (0.03)**

MRF 1, 3-methylfluorobenzene (56.8 mg) and undecane (37.1 mg).
MRF 2, 3-methylfluorobenzene (56.9 mg) and undecane (35.3 mg).

Table 6.136 Experimental molar response factor for trifluoroethyl 3-methylphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.76	0.76
2	0.75	0.75
3	0.75	0.77
4	0.77	0.76
mean (standard dev.)	**0.76 (0.01)**	**0.76 (0.01)**

MRF 1, trifluoroethyl 3-methylphenyl ether (130 mg) and undecane (92.8 mg).
MRF 2, trifluoroethyl 3-methylphenyl ether (126 mg) and undecane (100 mg).

Table 6.137 Experimental molar response factor for 4-methoxyfluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.61	0.59
2	0.60	0.57
3	0.59	0.58
4	0.58	0.58
mean (standard dev.)	**0.60 (0.01)**	**0.58 (0.01)**

MRF 1, 4-methoxyfluorobenzene (29.6 mg) and undecane (31.2 mg).
MRF 2, 4-methoxyfluorobenzene (33.2 mg) and undecane (29.7 mg).

Table 6.138 Experimental molar response factor for trifluoroethyl 4-methoxyphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.56	0.55
2	0.55	0.55
3	0.56	0.57
4	0.57	0.57
mean (standard dev.)	**0.56 (0.01)**	**0.56 (0.01)**

MRF 1, trifluoroethyl 4-methoxyphenyl ether (25.6 mg) and undecane (22.9 mg).
MRF 2, trifluoroethyl 4-methoxyphenyl ether (31.2 mg) and undecane (22.3 mg).

Table 6.139 Experimental molar response factor for 4-methylfluorobenzene in undecane.

Injection number	MRF 1	MRF 2
1	0.65	0.65
2	0.65	0.68
3	0.68	0.67
4	0.66	0.66
mean (standard dev.)	**0.66 (0.01)**	**0.66 (0.01)**

MRF 1, 4-methylfluorobenzene (40.2 mg) and undecane (46.5 mg).
MRF 2, 4-methylfluorobenzene (41.8 mg) and undecane (59.3 mg).

Table 6.140 Experimental molar response factor for trifluoroethyl 4-methylphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.72	0.73
2	0.72	0.72
3	0.71	0.72
4	0.72	0.71
mean (standard dev.)	**0.72 (0.01)**	**0.72 (0.01)**

MRF 1, trifluoroethyl 4-methylphenyl ether (34.7 mg) and undecane (33.0 mg).
MRF 2, trifluoroethyl 4-methylphenyl ether (31.4 mg) and undecane (31.8 mg).

Table 6.141 Experimental molar response factor for 3-methylfluorobenzene in octane.

Injection number	MRF 1	MRF 2
1	0.88	0.88
2	0.89	0.89
3	0.89	0.88
4	0.90	0.88
mean (standard dev.)	**0.89 (0.01)**	**0.89 (0.01)**

MRF 1, 3-methylfluorobenzene (212 mg) and octane (211 mg).
MRF 2, 3-methylfluorobenzene (209 mg) and octane (206 mg).

Table 6.142 Experimental molar response factor for ethyl 3-methylphenyl ether in octane.

Injection number	MRF 1	MRF 2
1	1.02	1.03
2	1.04	1.02
3	1.04	1.02
4	1.02	1.01
mean (standard dev.)	**1.03 (0.01)**	**1.02 (0.01)**

MRF 1, ethyl 3-methylphenyl ether (112 mg) and octane (118 mg).
MRF 2, ethyl 3-methylphenyl ether (110 mg) and octane (95.0 mg).

Table 6.143 Experimental molar response factor for methylbenzene in octane.

Injection number	MRF 1	MRF 2
1	0.86	0.88
2	0.91	0.89
3	0.89	0.88
4	0.89	0.90
mean (standard dev.)	**0.89 (0.02)**	**0.89 (0.01)**

MRF 1, methylbenzene (213 mg) and octane (211 mg).
MRF 2, methylbenzene (205 mg) and octane (206 mg).

Table 6.144 Experimental molar response factor for fluorobenzene in octane.

Injection number	MRF 1	MRF 2
1	0.83	0.83
2	0.85	0.82
3	0.85	0.83
4	0.83	0.81
mean (standard dev.)	**0.84 (0.01)**	**0.83 (0.01)**

MRF 1, fluorobenzene (145 mg) and octane (123 mg).
MRF 2, fluorobenzene (164 mg) and octane (158 mg).

Table 6.145 Experimental molar response factor for ethyl phenyl ether in octane.

Injection number	MRF 1	MRF 2
1	0.92	0.89
2	0.91	0.91
3	0.91	0.90
4	0.90	0.91
mean (standard dev.)	**0.91 (0.01)**	**0.90 (0.01)**

MRF 1, ethyl phenyl ether (112 mg) and octane (118 mg).
MRF 2, ethyl phenyl ether (98.2 mg) and octane (103 mg).

Table 6.146 Experimental molar response factor for benzene in octane.

Injection number	MRF 1	MRF 2
1	0.79	0.80
2	0.80	0.80
3	0.80	0.81
4	0.81	0.81
mean (standard dev.)	**0.80 (0.01)**	**0.81 (0.01)**

MRF 1, benzene (96.9 mg) and octane (95.4 mg).
MRF 2, benzene (103 mg) and octane (111 mg).

Table 6.147 Experimental molar response factor for 3-methoxyfluorobenzene in octane.

Injection number	MRF 1	MRF 2
1	0.86	0.85
2	0.88	0.86
3	0.88	0.86
4	0.88	0.85
mean (standard dev.)	**0.87 (0.01)**	**0.86 (0.01)**

MRF 1, 3-methoxyfluorobenzene (100 mg) and octane (142 mg).
MRF 2, 3-methoxyfluorobenzene (98.3 mg) and octane (100.1 mg).

Table 6.148 Experimental molar response factor for ethyl 3-methoxyphenyl ether in undecane.

Injection number	MRF 1	MRF 2
1	0.92	0.94
2	0.97	0.93
3	0.97	0.95
4	0.95	0.94
mean (standard dev.)	**0.95 (0.02)**	**0.94 (0.01)**

MRF 1, ethyl 3-methoxyphenyl ether (149 mg) and octane (142 mg).
MRF 2, ethyl 3-methoxyphenyl ether (114 mg) and octane (127 mg).

Table 6.149 Experimental molar response factor for methoxybenzene in octane.

Injection number	MRF 1	MRF 2
1	0.84	0.86
2	0.83	0.86
3	0.83	0.87
4	0.82	0.86
mean (standard dev.)	**0.83 (0.01)**	**0.86 (0.01)**

MRF 1, methoxybenzene (104 mg) and octane (110 mg).
MRF 2, methoxybenzene (98.7 mg) and octane (103 mg).

Table 6.150 Experimental molar response factor for nitrobenzene in undecane.

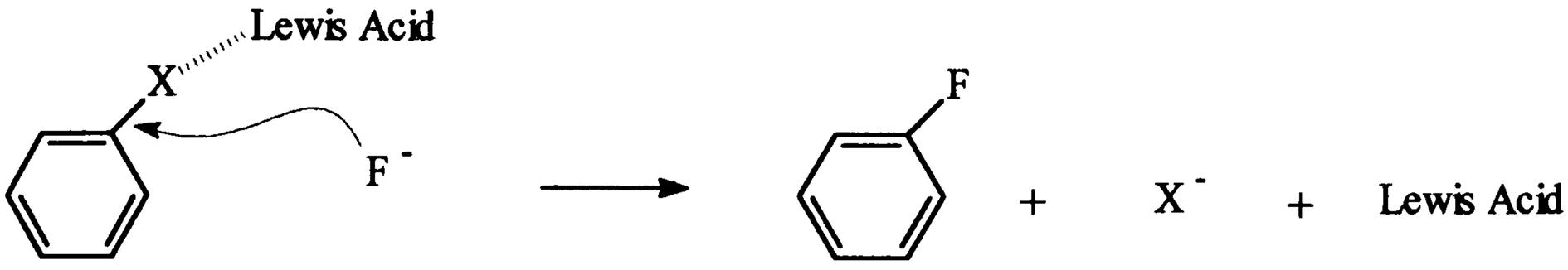
Injection number	MRF 1	MRF 2
1	0.46	0.46
2	0.48	0.47
3	0.49	0.48
4	0.48	0.47
mean (standard dev.)	**0.48 (0.01)**	**0.47 (0.01)**

MRF 1, nitrobenzene (41.2 mg) and undecane (32.5 mg).
MRF 2, nitrobenzene (46.7 mg) and undecane (35.8 mg).

Appendix C. Industrial placement at Zeneca (Grangemouth).

6.1 Aim.

The aim of the project was to investigate the feasibility of preparing fluoroaromatics from halobenzenes by using a Lewis acid catalyst in conjunction with a fluoride nucleophile. The aim of the Lewis catalyst was to polarise the aryl-halogen bond so as to encourage nucleophilic attack.



X = Cl or Br

6.2 Background.

At present, the main industrial method for producing polyfluoroaromatics relies on using a diazonium ion intermediate in situ.

ICI

$PhNH_2 + NaNO_2 + 2HF \rightarrow PhF + NaF + 2H_2O + N_2$

(via $NaNO_2 + HF \rightarrow NaF + HNO_2$

$HNO_2 + HF \rightarrow NOF + H_2O$)

Dupont.

$2PhNH_2 + N_2O_3 + 2HF \rightarrow 2PhF + 3H_2O + N_2$

(via $N_2O_3 + 2HF \rightarrow 2NOF + H_2O$)

The important fact to notice in both the ICI and Dupont procedures is that water is produced. This provides an unwanted complication as it leads to the formation of phenol which undergoes coupling with unreacted diazonium ions present to give diazo products. Lowering the amount of water produced provides a more efficient reaction (contrast the

Dupont method with 1.5 moles water per diazonium ion with the ICI method 2 moles of water per diazonium ion). The ICI method is less favoured due to NaF being formed.

" Minimum total cost for maximum economic return" is the buzz phrase for industry. Market forces govern which route is chosen for the desired product. This is in direct contrast to classical laboratory methods where preparation is via the most convenient manner, e.g. the cheapest method may not be the best in terms of human person hours. Another concern may be impurities. These may be unacceptable to industry but may not be a worry to the research chemist, who may only be concerned with characterisation of the product.

Past research methods.

Heating diazonium fluoroborates is by far the best way of introducing fluorine into an aromatic ring. The diazonium fluoroborate is prepared by diazotisation. This involves reacting the aniline with nitrous acid, in the presence of aqueous HBF_4 to form a precipitate (diazonium tetrafluoroborate salt). The salt then undergoes decomposition to the fluoroaromatic when heated in the dry state.

An alternative method for aromatic fluoride preparation is by halogen exchange between aromatic chlorides and potassium fluoride. Difficulties arise in the choice of solvent. Potassium fluoride is insoluble in most organic solvents; the choice is limited to only a few solvents such as dimethylformamide (DMF) and dimethyl sulfoxide (DMSO). However, high temperatures are required for the KF to be reasonably soluble. This leads to unwanted by-products containing sulphur. A way round this problem would be to use a higher boiling solvent; a candidate might be tetramethylene sulfone (b.p >250°C). Other inorganic metal fluorides such as CsF and CaF_2 can be used in conjunction with KF as fluorinating agents. CaF_2 used as a support reagent results in rate acceleration. In the reaction of KF with benzyl bromide in sulpholane, at 80°C less than 10% conversion to benzyl fluoride is obtained. The same reaction in the presence of CoF_2 gives 30% conversion after the same period of time. Raising the temperature to 120°C, 74% fluorination is achieved with CoF_2 after 2 hr compared to 36% fluorination using KF alone.

Regarding the reactivity of the fluorinating agent, the activity of the fluoride increases with the size of the metal cation in the order KF<RbF<CsF. The high cost of the last two limits their use as sole fluorinating agents.

Crown ethers provide an affective medium for fluorination to occur. They act as catalysts by increasing the activity of the alkali metal fluoride. The increase in reaction rate can be explained by

a) increased solubility of the alkali metal fluoride hence the increased concentration of fluoride ion and

b) increased nucleophilicity of fluoride ion as a consequence of complexing of the alkali metal cations by crown ethers.

6.3 Experimental.

All the chemicals supplied were from Aldrich. The potassium fluoride used in these experiments was spray dried. The GC machine used was a Hewlett Packard series II, model 7673. The capillary column used measured 25 meters and contained cp sil 13CB stationary phase (serial number 435306). The peak areas were determined by use of a Hewlett Packard integrator. Unidentified peaks were characterised by GC/MS. Samples were submitted to Mrs Jean Wood lab.3 (machine ID 93). All of the halogen exchange reactions were run in glass apparatus.

The tables of results are included at the end of this appendix.

6.3.1 Fluorination of hexachlorobenzene. [Table 1]

A mixture of hexachlorobenzene (5 g, 1 mole equivalent), potassium fluoride (7 g, 6 mole equivalents) and tetramethylene sulfone (sulfolane, ~100g) was stirred and heated at temperatures of up to 200°C for 14 hours. The reaction was monitored by GC. Small extracts were taken at certain time intervals, worked up (quenched with water, neutralised with base and extracted with dichloromethane) and analysed. From GC/MS, trichlorotrifluorobenzene, dichlorotetrafluorobenzene, and tetrafluorodichlorobenzene were identified. Identification of particular isomers was not possible.

6.3.2 Fluorination of hexabromobenzene. [Table 2]

Hexabromobenzene (5 g), potassium fluoride (4.4 g) and sulfolane (100 g) were heated at 200°C for 14 hours. The solution turned from white to brown at this temperature. Six products were identified by GC/MS, they were;

$C_6H_2BrF_3$, $C_6H_3BrF_2$, $C_6H_2Br_2F_2$, $C_6HBr_2F_3$, $C_6HBr_3F_2$, $C_6H_2Br_3F$.

6.3.3 Fluorination of Hexachlorobenzene with the aid of Lewis acids.

(i) *$AlCl_3$*

Hexachlorobenzene (5g), potassium fluoride (7.2 g), $AlCl_3$ (4.8 g), and sulfolane (100 g) were mixed together and heated to 200°C for 23 hours. Addition of $AlCl_3$ to KF caused a white gas (probably HCl) to be given off. No products were seen with this reaction. Hexachlorobenzene was present at the end.

(ii) *$SnCl_4$*

$SnCl_4$ in dichloromethane (14 ml of a 1M solution) was added under nitrogen to the reaction mixture of hexachlorobenzene (5 g), potassium fluoride (8.2 g) and sulfolane (100 g). The reaction mixture was initially heated at 150°C, analysed by GC and then raised to 200°C slowly. The reaction temperature was maintained at this temperature for 10 hours.

(iii) *$ZnCl_2$*

Hexachlorobenzene (5g), potassium fluoride (8.2g), zinc chloride (2.4g) and sulfolane (100g) were mixed together and heated at 200°C for 17 hours. No products were seen with this reaction.

(iv) *CoF_2*

Cobalt difluoride (6.2g) was added to hexachlorobenzene (5g) in sulfolane (100g). The reaction mixture was heated at 100°C for 2 hours. No reaction was seen to occur by GC. The temperature of the reaction mixture was raised to 150°C (no reaction was observed). Further heating at 200°C for 14 hours led to no products.

6.3.4 Fluorination with KF/CoF_2

A mixture of potassium fluoride (8g) and cobalt difluoride (1.8g) was added to hexachlorobenzene (5.4g) in sulfolane (100g). The reaction mixture was stirred at 150°C for 14 hours. From GC/MS, trichlorotrifluorobenzene, dichlorotetrafluorobenzene, and tetrafluorodichlorobenzene were identified.

6.3.5 Fluorination of Hexabromobenzene with the aid of Lewis acids.

(i) *$AlBr_3$*

$AlBr_3$ was added under nitrogen to hexabromobenzene (5 g), potassium fluoride (10.8 g), and sulfolane (100 g). The reaction was heated at 150°C. No reaction was seen, so the reaction mixture was raised to 200°C and maintained at this temperature for 17 hours. Compounds identified by GC/MS were
$C_6H_3BrF_2$, $C_6H_2Br_2F_2$, $C_6HBr_2F_3$ and $C_6HBr_3F_2$.

(ii) *$AlCl_3$*

Hexabromobenzene (5.1g), potassium fluoride (4.5 g), $AlCl_3$ (4.8 g), and sulfolane (74 g) were mixed together and heated to 200°C for 14 hrs. Addition of $AlCl_3$ to KF caused a white gas to be given off. The products identified from GC/MS were $C_6Br_2Cl_4$, C_6BrCl_5 and $C_6Br_3Cl_3$. For each compound assigned at least two peaks were present on the GC trace which suggested more than one isomer existed.

(iii) *CoF_2*

Cobalt difluoride (5.3g) was added to hexabromobenzene (5g) in sulfolane (100g). The reaction mixture was heated at 100°C for 2 hours. No reaction was seen to occur by GC. The temperature of the reaction mixture was raised to 150°C (no reaction). Further heating at 200°C for 14 hours led to no products.

(iv) *KF/CoF_2*

Cobalt difluoride (0.9 g) and potassium fluoride (3.5g) were added to hexabromobenzene (5.2g) dissolved in sulfolane (100 g). The reaction mixture was heated at 100°C for 14 hours. No reaction was seen to occur so the temperature was

raised to 150°C. This was maintained for 14 hours. No reaction was seen, only starting materials were present.

6.3.6 Reactions of chlorobenzene. [Table 3]

(i) *KF*

Potassium fluoride (15.8 g) was added to chlorobenzene (5g) in sulfolane (100g). This was heated at 150°C for 14 hours. No reaction occurred; only starting material was present.

(ii) *KF/CoF_2*

As above except CoF_2 (4.3g) was added. No reaction was seen.

6.3.7 Reactions of 1,3-dichlorobenzene

(i) *KF*

Potassium fluoride (12 g) was added to 1,3-dichlorobenzene (5g) in sulfolane (120g). The reaction was initially heated at 150°C for 14 hours (no reaction). This was gradually raised to 200°C over a period of 18 hours. No reaction occurred, only starting materials were present at the end.

(ii) *KF/CoF_2*

As above except cobalt difluoride (3.3g) was added as well as potassium fluoride. The temperature was raised in the manner described above. No reaction was seen.

6.3.8 Reactions of 1,4-dichlorobenzene

(i) *KF*

Potassium fluoride (6.06g) was added to 1,4-dichlorobenzene (5g) in sulfolane. The reaction mixture was heated at 150°C for 4 hours. This was raised to 200°C over a period of 14 hours. No reaction was seen.

(ii) *KF/CoF_2*

As above except CoF_2 (3.3g) was added. The temperature was raised from 150°C to 200°C over a period of 14 hours. No reaction was seen.

6.3.9 Reactions of 1,2,4-trichlorobenzene.

(i) *KF*

Potassium fluoride (4.9g) was added to 1,2,4-trichlorobenzene (5g) in sulfolane (100g). This was heated at 150°C for 3 days. No reaction occurred so the temperature was raised to 200°C. This was maintained for 24 hours. Upon analysis, only starting material could be seen.

(ii) *KF/CoF_2*

The method is as described for KF above, except CoF_2 (2.7 g) was added to the reaction mixture as well. No products were seen after heating at 200°C for 24 hours.

6.3.10 Reactions of *m*-dibromobenzene. [Table 4]

(i) *KF*

m-Dibromobenzene (5g) was added to sulfolane (160g). The reaction mixture was stirred and potassium fluoride (8.6g) was added. The reaction mixture was initially heated at 150°C for 2 hours, the temperature was then raised to 200°C. No reaction was seen to occur.

(ii) *KF/CoF_2*

The method is as described above for KF except cobalt difluoride (1.8g) was added to the reaction mixture. The reaction mixture was heated at 150°C for 4 hours and then raised to 200°C for a further 14 hours. No reaction was seen.

Table 1. Reactions of hexachlorobenzene.

Conditions (mole equivalents)	*Products*
KF (6) 200°C (14 hours)	$C_6Cl_2F_4$, $C_6Cl_3F_3$,, $C_6Cl_4F_2$
$KF/AlCl_3$ (6:1) 200°C/23 hours	NO REACTION
$KF/SnCl_4$ (6:1) 200°C/10 hours	$C_6Cl_3F_3$, $C_6Cl_4F_2$
$KF/ZnCl_2$ (6:1) 200°C/17 hours	$C_6Cl_2F_4$, $C_6Cl_3F_3$, $C_6Cl_4F_2$
CoF_2 (6) 200°C/14 hours	NO REACTION
KF/CoF_2 (6:1) 150°C / 14 hours	$C_6Cl_2F_4$, $C_6Cl_3F_3$,, $C_6Cl_4F_2$
KF/CoF_2 (6:2) 150°C / 14 hours	$C_6Cl_2F_4$, $C_6Cl_3F_3$,, $C_6Cl_4F_2$

Table 2 Reactions of hexabromobenzene.

Conditions (mole equivalents)	*Products*
KF (6) 200°C (14 hours)	$C_6HBr_3F_2$, $C_6H_2BrF_3$, $C_6H_3BrF_2$, $C_6H_2Br_2F_2$, $C_6HBr_2F_3$
$KF/AlCl_3$ (6:1) 200°C/14 hours	$C_6Br_3Cl_3$, C_6BrCl_5, $C_6HBr_3Cl_2$, $C_6Br_2Cl_4$
$KF/AlBr_3$ (6:1) 200°C/17 hours	$C_6H_3BrF_2$, $C_6H_2Br_2F_2$, $C_6H_2Br_2F_2$, $C_6H_2Br_3F$
CoF_2 (6) 200°C/14 hours	NO REACTION
KF/CoF_2 (6:1) 150°C / 14 hours	NO REACTION

Table 3 Reactions of chlorobenzene derivatives.

substrate	*Conditions*	*Products*
chlorobenzene	KF (6) 150°C/ 14 Hrs	*NO REACTION*
	KF/CoF_2 (6:1) 150°C / 14 hours	*NO REACTION*
1,2-dichlorobenzene	KF (6) 200°C/ 14 Hrs	*NO REACTION*
	KF/CoF_2 (3:1) 200°C/ 14 Hrs	*NO REACTION*
1,3-dichlorobenzene	KF (6) 200°C/ 18 Hrs	*NO REACTION*
	KF/CoF_2 (3:1) 200°C/ 14 Hrs	*NO REACTION*
1,4-dichlorobenzene	KF (6) 200°C/ 14 Hrs	*NO REACTION*
	KF/CoF_2 (3:1) 200°C/ 14 Hrs	*NO REACTION*
1,2,4-trichlorobenzene	KF (6) 200°C/ 24 Hrs	*NO REACTION*
	KF/CoF_2 (3:1) 200°C/ 24 Hrs	*NO REACTION*

Table 4 Reactions of m-dibromobenzene.

Conditions *(mole equivalents)*	*Products*
KF (6) 150°C / 14 hours	NO REACTION
KF/CoF_2 (6:2) 200°C / 14 hours	NO REACTION

Table 5. Reactions of hexachlorobenzene.

Conditions *(mole equivalents)*	*% Yield of* $C_6Cl_3F_3$
KF (6) 200°C (14 hours)	22
KF/CoF_2 (6:1) 150°C / 14 hours	20

6.4 Summary.

Hexachlorobenzene was fluorinated with KF in sulfolane to produce di, tri, and tetra fluoro substituted chlorobenzenes. The addition of a Lewis acid to this reaction reduced the yields of fluorinated products seen. Adding a catalytic amount of CoF_2 to the reaction produced similar yields of the fluorinated compounds. Further work needs to be done to see if it is possible to differentiate between the two in terms of reaction conditions.

No reactions were seen for the fluorination of mono, di, and tri chlorobenzene nor for hexabromobenzene. For fluorination to occur at these moderate temperatures, the aromatic ring needs to be sufficiently activated. It would appear that the ring requires six chloro substituents to be attached before halogen exchange can occur.

Future work may be concerned with investigating halogen exchange reactions at much higher temperatures (gas phase) to see if extreme conditions facilitate fluorination with mixtures of CoF_2/KF as heterogeneous reagents.