



Durham E-Theses

Aspects of nitrosation & diazotization

Thompson, John Terence

How to cite:

Thompson, John Terence (1978) *Aspects of nitrosation & diazotization*, Durham theses, Durham University. Available at Durham E-Theses Online: <http://etheses.dur.ac.uk/8307/>

Use policy

The full-text may be used and/or reproduced, and given to third parties in any format or medium, without prior permission or charge, for personal research or study, educational, or not-for-profit purposes provided that:

- a full bibliographic reference is made to the original source
- a [link](#) is made to the metadata record in Durham E-Theses
- the full-text is not changed in any way

The full-text must not be sold in any format or medium without the formal permission of the copyright holders.

Please consult the [full Durham E-Theses policy](#) for further details.

ASPECTS OF NITROSATION & DIAZOTIZATION

BY

JOHN TERENCE THOMPSON, B.Sc.

(Graduate Society)

A thesis submitted for the degree of Doctor of
Philosophy in the University of Durham

December 1978

The copyright of this thesis rests with the author.
No quotation from it should be published without
his prior written consent and information derived
from it should be acknowledged.



Acknowledgements

The author wishes to express his thanks to Dr. D.L.H. Williams and Dr. M.R. Crampton for their continual advice and encouragement during the period in which this research was carried out.

Helpful discussions are also acknowledged with D. Close, G. Hallett, S.S. Johal and R. Ackroyd.

Thanks are also due to Mr. J.A. Parkinson for the loan of equipment and to Mr. R.N. Brown for the maintenance of the spectrophotometers.

The receipt of an S.R.C. studentship is also gratefully acknowledged.

- To my Wife and Parents -

"My work consists of two parts: the one presented here plus all that I have not written. And it is precisely this second part that is the important one."

Ludwig Wittgenstein

MEMORANDUM

The work described in this thesis was carried out in the University of Durham between October 1975 and June 1978 and has not been submitted for any other degree. It is the original work of the author except where acknowledged by reference.

C O N T E N T S

SECTION ONECHAPTER ONE: Acid Catalysed Reactions of Aromatic Nitrosamines

| | | |
|-----|---|----|
| 1.1 | Classification of reactions | 1 |
| 1.2 | The Intermolecular Mechanism | 2 |
| 1.3 | The Intramolecular Mechanism | 3 |
| 1.4 | Inter- versus Intra- ; the kinetic evidence | 4 |
| 1.5 | The Mechanism of Denitrosation | 8 |
| 1.6 | The Mechanism of Rearrangement | 17 |
| 1.7 | Alternative kinetic studies | 30 |

CHAPTER TWO: Halide Catalysed Diazotization

| | | |
|-----|--|----|
| 2.1 | Introduction | 34 |
| 2.2 | Diazotization in the absence of Halide | 35 |
| 2.3 | Halide Catalysed Diazotization | 40 |

SECTION TWOCHAPTER THREE: Denitrosation of N-nitrosodiphenylamine

| | | |
|-----|---|----|
| 3.1 | Effect of Added Nitrite Traps | 45 |
| 3.2 | Catalysis by various nucleophiles | 48 |
| 3.3 | Acidity Dependence | 64 |
| 3.4 | Formation of the Blue Coloration | 71 |
| 3.5 | Effect of Added Diphenylamine | 76 |
| 3.6 | Comparison with N-ethyl-N-nitrosourethane | 81 |

CHAPTER FOUR: Diazotization with N-nitrosodiphenylamine

| | | |
|-----|---|----|
| 4.1 | Introduction | 84 |
| 4.2 | Diazotization of Aniline | 85 |
| 4.3 | Substituent effects on the diazotization reaction | 92 |
| 4.4 | Reaction with Adenine & 5-methylcytosine | 95 |

| | | |
|-----|---|-----|
| 4.5 | Nitrosation of N,N-dimethylaniline | 98 |
| 4.6 | Consequences for Fischer-Hepp Rearrangement | 106 |

SECTION THREE

CHAPTER FIVE: Diazotization with Nitrosyl Bromide

| | | |
|-----|---|-----|
| 5.1 | Introduction | 110 |
| 5.2 | The Steady-State Treatment | 111 |
| 5.3 | Limiting Case $k_3 \gg k_2 [\text{Br}^-]$ | 113 |
| 5.4 | Limiting Case $k_2 [\text{Br}^-] \gg k_3$ | 121 |
| 5.5 | Non-Limiting Conditions | 127 |
| 5.6 | The Slow Process | 131 |

CHAPTER SIX: Diazotization with Nitrosyl Chloride

| | | |
|-----|--|-----|
| 6.1 | Introduction | 138 |
| 6.2 | Evaluation of values for k_1 and k_2/k_3 | 140 |
| 6.3 | Significance of the k_2/k_3 ratios | 144 |
| 6.4 | Correction of the k_1 values | 147 |
| 6.5 | Comparison of k_1 values for NOCl & NOBr reactions | 151 |

CHAPTER SEVEN: Experimental Technique:

| | | |
|-----|--|-----|
| 7.1 | Preparation & Purification of Materials | 155 |
| 7.2 | Denitrosation of $\text{Ph}_2\text{N.NO}$: experimental details | 157 |
| 7.3 | Denitrosation of N-ethyl-N-nitrosourethane | 165 |
| 7.4 | Diazotization by NOCl & NOBr : experimental details | 166 |
| 7.5 | Treatment of Errors | 176 |

ABSTRACT

In the presence of a relatively high concentration of sodium azide N-nitrosodiphenylamine undergoes irreversible denitrosation in aqueous acidic media to give diphenylamine. The reaction is catalysed by both H^+ (with $k_o \propto h_o$) and various nucleophiles, and for which, at low nucleophile concentrations, a solvent-isotope effect of $k_D/k_H = 2.0$ is observed. These facts are consistent with rate-determining attack by the nucleophile upon the protonated form of the nitrosamine. At high bromide concentrations k_o becomes independent of $[Br^-]$ and the solvent-isotope effect changes to $k_D/k_H = 0.8$. This suggests that the initial protonation of the nitrosamine then becomes rate-determining. Direct catalysis by aniline and its ring-substituted derivatives is also observed and has been interpreted in terms of π -complex formation between $Ph_2\ddot{N}H.NO$ and $Ar\ddot{N}H_3$. The applicability of such a mechanism to the Fischer-Hepp rearrangement and related reactions is also discussed. In general $k_o \propto 1/[Ph_2NH]$ and a study of this effect has revealed a reactivity sequence for some 'nitrite-traps' toward reaction with free nitrosating species such as NOBr.

The diazotization of several substituted anilines has been carried out in aqueous acidic media under conditions such that the active nitrosating agents are NOCl and NOBr. The variation of the observed rate-constant (k_o) with $[Halide]$ suggests that the process is reversible, particularly at high $[Halide]$ and for those anilines for which $pK_{BH^+} < 4.0$, and that this accounts for the earlier observation of an apparently large substituent selectivity for reaction at high $[HCl]$. This large selectivity was originally taken as evidence against diffusion-control but an analysis of k_o in terms of a reversible steady-state scheme has yielded values for the true bimolecular rate constants for encounter between NOX and $ArNH_2$ which do indeed approach the diffusion-controlled limit. For those amines

carrying electron-withdrawing groups a second relaxation can be observed and it is suggested that this corresponds to the tautomerisation of the intermediate primary nitrosamine.

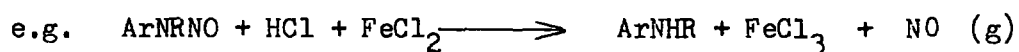
S E C T I O N O N E

CHAPTER ONE

Acid Catalysed Reactions of aromatic nitrosamines

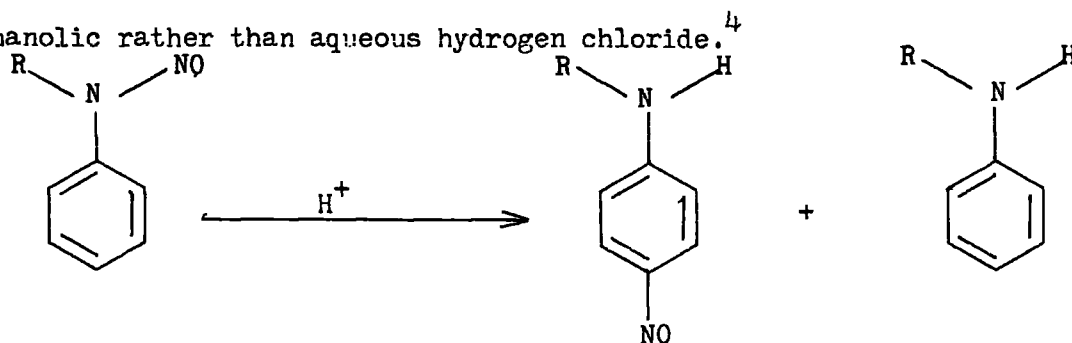
1.1 Classification of Reactions:

It is well known that secondary aromatic amines readily undergo nitrosation with, for example, sodium nitrite and hydrochloric acid, to yield thermally stable, isolable, secondary nitrosamines. For example, N-nitrosodiphenylamine forms yellow plates m.pt 66.5°C. The reverse process, i.e. denitrosation, is accomplished by heating the nitrosamine in hydrochloric acid containing an excess of urea¹ or ferrous ion.²



Thus the normally reversible process is made irreversible by removal of the active nitrosating agent, in this case as nitric oxide, from the equilibrium mixture.

In the absence of such 'nitrite traps' denitrosation is accompanied by the formation of the corresponding para-C-nitrosamine, the so-called Fischer-Hepp rearrangement.³ The usual products of acid hydrolysis of aromatic nitrosamines are therefore the amine and the rearrangement product in varying proportions according to the conditions used. In particular the yield of rearrangement product is maximised by use of ethanolic rather than aqueous hydrogen chloride.⁴



Mechanistically one can ask whether rearrangement is due to C-nitrosation by the nitrosating agent liberated during denitrosation (intermolecular mechanism) or due to some process which is independent of denitrosation (intramolecular mechanism). In either case one has to explain the exclusive formation of para-C-nitrosamine during rearrangement

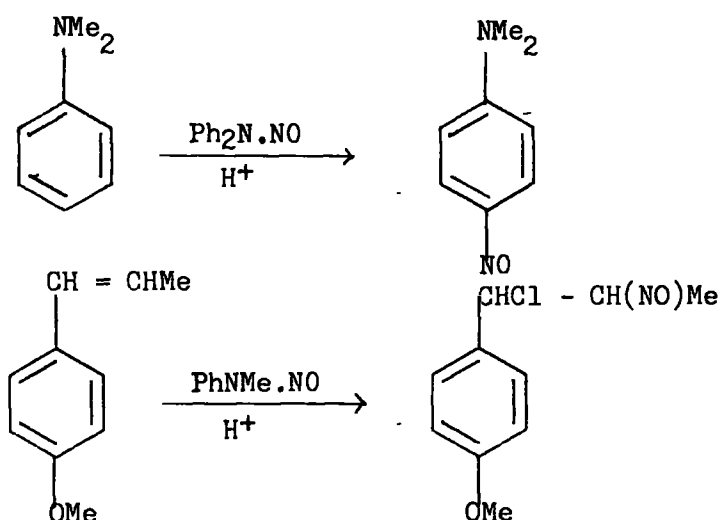


(no ortho-isomer has ever been positively identified). Historically the intermolecular mechanism was the first to be proposed.

1.2 The Intermolecular Mechanism for Rearrangement

This was first proposed by Houben⁵ to account for the following observations:-

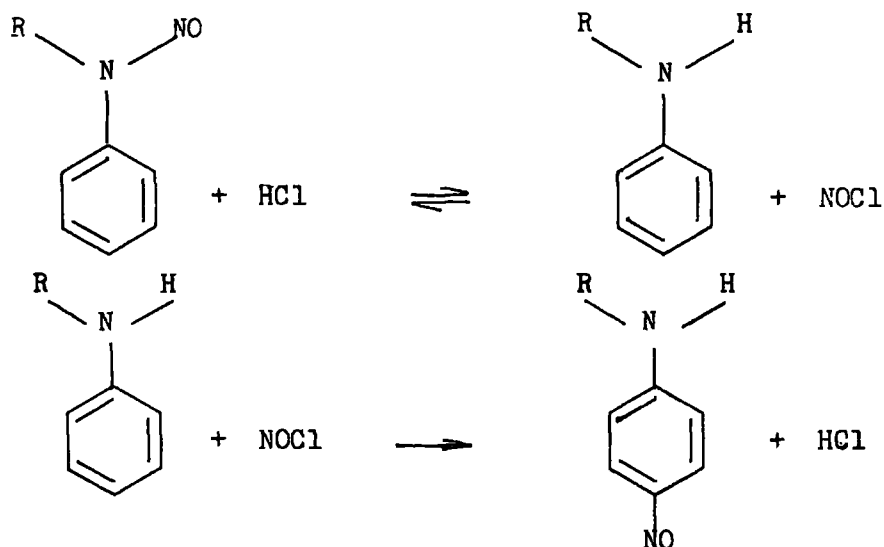
- (a) Added nitrite increased the yield of rearrangement product.⁵
- (b) Transnitrosations can occur. For example, $\text{Ph}_2\text{N}\cdot\text{NO}$ in the presence of N,N - dimethylaniline gave some para-nitroso-N,N - dimethylaniline, and $\text{PhNMe}\cdot\text{NO}$ in the presence of anethole gave the nitrosochloride adduct, in addition to their normal products of rearrangement.⁵



- (c) In the presence of a large excess of urea, meta-nitro-N-methyl-N-nitrosoaniline underwent denitrosation exclusively.
- (d) Low yields of rearrangement product were obtained in sulphuric and nitric acids,⁶ thus implying the importance of chloride in the rearrangement.
- (e) Hydrogen bromide gave mainly the product of denitrosation, plus bromo by-products.⁶

These results infer the importance of free nitrosyl chloride in attacking the para-position of the ring. That it exists is 'proven' by the trans-nitrosation reactions. Adding NaNO_2 to HCl creates more NOCl . A large excess of urea removes all the NOCl as gaseous nitrogen. In H_2SO_4 and HNO_3 no NOCl can exist and with HBr the NOBr formed is insufficiently reactive to attack the ring since it is less polarised than NOCl .

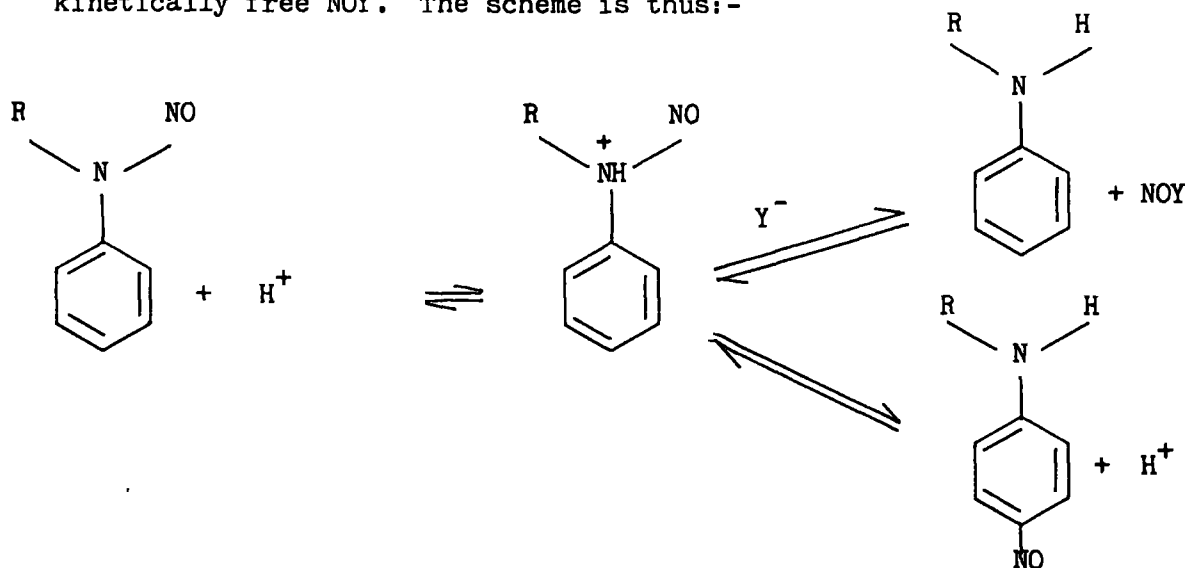
The scheme is thus:-



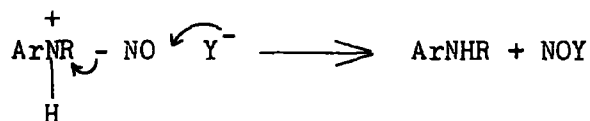
which has been accepted uncritically until very recently.

1.3 The Intramolecular Mechanism for Rearrangement:

The above observations do not demand that the reaction must be intermolecular. The trapping of kinetically free NOY with species such as *N,N*-dimethylaniline cannot be taken as evidence of intermolecularity since an intramolecular mechanism whereby denitrosation and rearrangement occur as simultaneous reactions of a common intermediate will also give kinetically free NOY. The scheme is thus:-



Furthermore, it is conceivable that transnitrosation to species such as N,N-dimethylaniline and anethole could take place without the intermediacy of free NOY and involve direct NO^+ transfer from the protonated nitrosamine. This is a theme which will be discussed in detail in Chapter Four. The other objections can also be rationalised by this mechanism. For instance, the addition of NaNO_2 could increase the yield of rearrangement product by increasing the rate of N-nitrosation of the product PhNHR so that denitrosation is suppressed and loss of NOY by reaction with the solvent becomes negligible. The increased stationary concentration of the protonated nitrosamine is then reflected in an increased rate of intramolecular rearrangement. The alleged preference for HCl in the rearrangement can be ascribed to other factors. For example, with HBr denitrosation may compete more effectively because of the greater nucleophilicity of Br^- as compared to Cl^- in the step:-



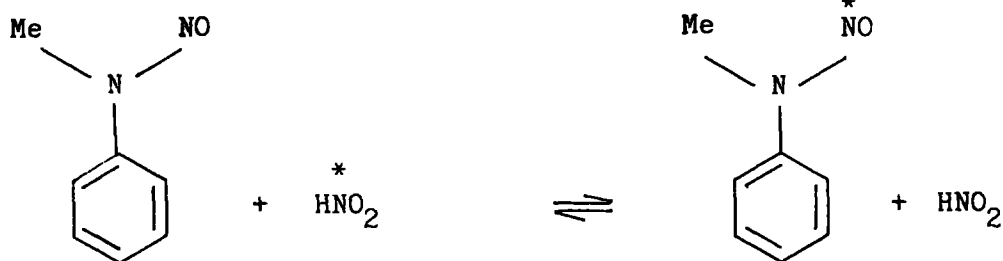
In sulphuric acid or nitric acid it may be that the solvation requirements of the transition state leading to rearrangement are not satisfied as well as in ethanolic HCl.

It is thus apparent that one cannot decide between the two mechanisms by means of product analyses alone. A detailed kinetic analysis is obviously necessary.

1.4 Inter- versus Intra- : the kinetic evidence

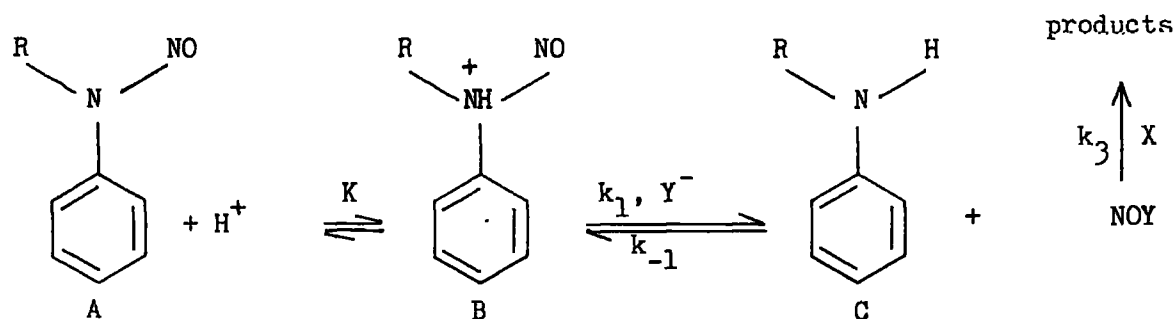
The observation that rearrangement of N-methyl-N-nitroso aniline takes place even in the presence of a large excess of urea^{7,8} casts some

doubt as to the validity of the intermolecular mechanism. Examination of the pickup of ^{15}N label by the C-nitroso product from added sodium ^{15}N nitrite proved to be unable to distinguish between the two mechanisms because of very rapid exchange between the label and the nitrosamine.⁹



However, the schemes outlined below for the two mechanisms are sufficiently different to allow direct kinetic tests of mechanism to be made on the basis of a steady-state treatment. This has been reviewed elsewhere¹⁰ so only brief mention of relevant details will be made here.

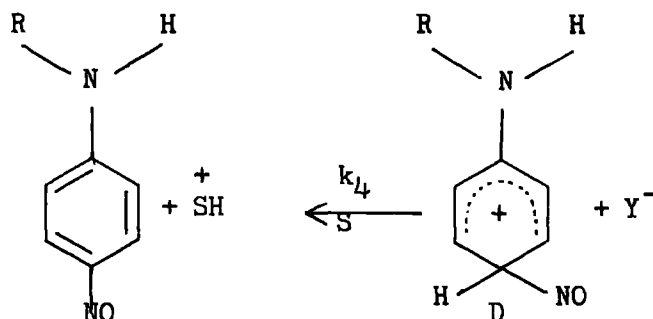
Scheme (a) : Intermolecular

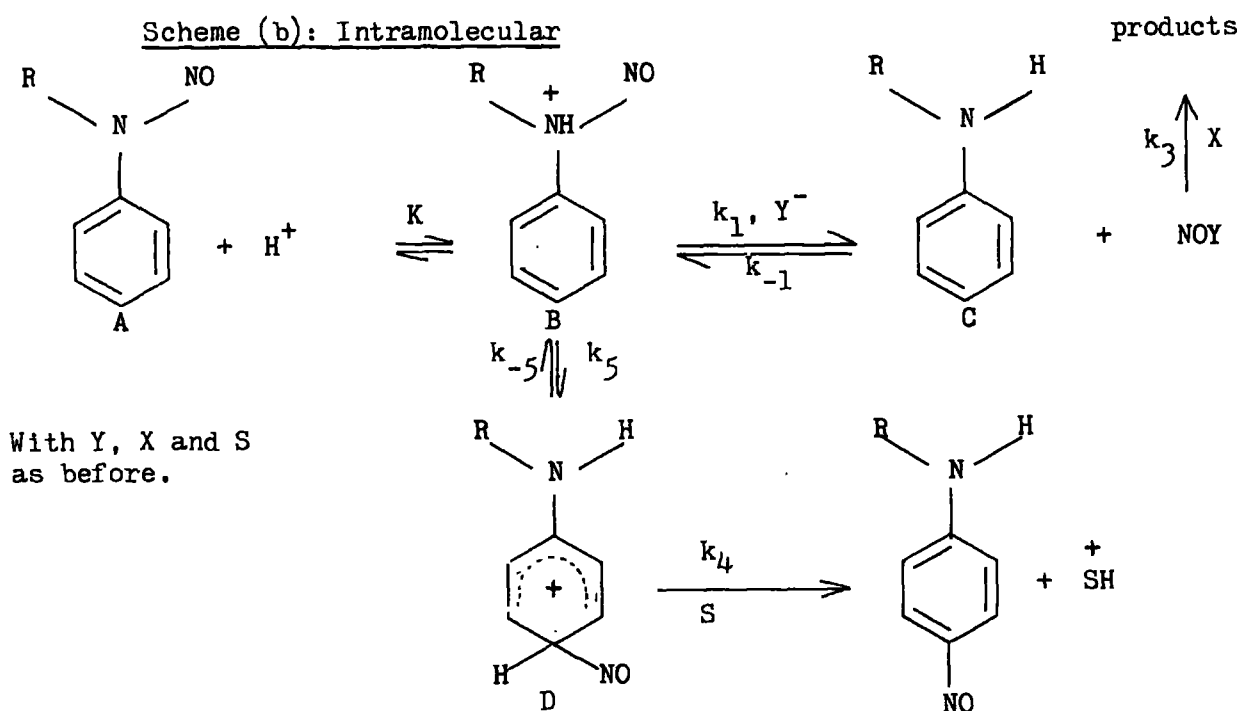


Y = some nucleophile
(e.g. H_2O , Cl^- , Br^-)

X = 'nitrite trap'
(e.g. urea, hydrazine)

S = solvent





The intermediates D and NOY are assumed to be highly reactive and to exist only in steady-state concentrations. The protonation of A is assumed to be fast and reversible, as is usual in proton transfers between oxygen and nitrogen, and its extent is assumed to be small in view of the expected weak basicity of nitrosamines. Thus we can expect the protonation to follow Hammett's acidity function and write $[B] = Kh_o [A]$. (The validity of correlating the observed rate constants with H_o in the denitrosation reaction will be discussed later). Algebraic details are given elsewhere,¹¹ the results being:-

$$\text{Inter: } k_o = \frac{k_1 [Y] Kh_o (k_3 [X] + k_2^1 [C])}{k_3 [X] + (k_{-1} + k_2^1) [C]}$$

$$\text{Intra: } k_o = \frac{k_1 [Y] Kh_o k_3 [X]}{k_3 [X] + k_{-1} [C]} + \frac{k_4 k_5 Kh_o}{k_4 + k_{-5}}$$

where k_o is the observed first-order rate constant for the disappearance of A and $k_2^1 = k_2 - (k_{-2} k_2 [Y] / (k_{-2} [Y] + k_4))$.

The predictions made by these equations have been tested by Williams and co-workers in a series of experiments; the observational results in all cases supporting the intramolecular mechanism.^{10,11} Differences in behaviour were predicted as follows:-

(a) Reaction at high [X]

At a sufficiently high concentration of 'nitrite trap' X (e.g. sulphamic acid) $k_3 [X] \gg k_{-1} [C]$ or $k_2^1 [C]$. Hence, the rate equations become:-

Inter:- $k_o = k_1 [Y] Kh_o$

Intra: $k_o = k_1 [Y] Kh_o + k_4 k_5 Kh_o / k_4 + k_{-5}$

Thus the intermolecular mechanism predicts that the % of rearrangement should fall to zero as [X] is increased whereas the intramolecular mechanism predicts that it should remain constant at any one acidity and nucleophile concentration and be independent of [X]. The latter is observed.

(b) Reaction at high [C]

At a sufficiently high concentration of added secondary amine then $k_{-1} [C] \gg k_3 [X]$ so that virtually no NOY is lost by reaction with the nitrite trap. The intramolecular mechanism predicts that k_o should become independent of [Y], [C] and [X] since the rate equation reduces to:-

$$k_o = (k_4 k_5 / k_4 + k_{-5}) Kh_o$$

If we write the full intermolecular rate equation as:

$$k_o = k_1 [Y] K h_o \left[1 - \frac{k_{-1} [C]}{k_3 [X]} + (k_{-1} + k_2^1) [C] \right]$$

we see that k_o should never become independent of Y . Also, k_o should approach zero since the term $\frac{k_{-1} [C]}{(k_{-1} + k_2^1) [C]} \simeq 1$. This is because the rate of N-nitrosation $k_{-1} [C]$ can be expected to be much faster than the rate of C-nitrosation $k_2 [C]$ and further because $k_2^1 < k_2$.

Thus all of the direct kinetic evidence points towards the intramolecular mechanism as being correct. However, it must be emphasised that the above kinetic tests were applied to N-methyl-N-nitrosoaniline in aqueous acidic media. For other nitrosamines and other solvents the results could well be different. In particular further work in Durham has demonstrated that solvent effects may be important and that the reaction could be partially intermolecular in alcoholic media.¹²

1.5 The Mechanism of Denitrosation:

We have seen that denitrosation is favoured if the free NOY can be removed as it is formed by 'nitrite traps' such as urea, sulphamic acid, aniline, hydrazine, hydroxylamine and hydrazoic acid. If an efficient nucleophile is also present then denitrosation becomes virtually quantitative. Urea has been shown to be the least reactive of the conventional traps and with N-methyl-N-nitrosoaniline is only effective in concentrations above 0.1 M.¹³

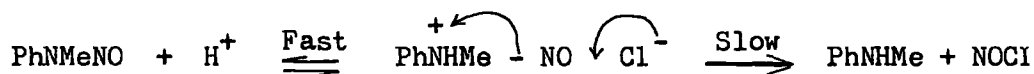
It is thus feasible to study the denitrosation process without competition from rearrangement and without complications due to reversibility so long as sufficient trap is present in order to suppress the reverse process

of N-nitrosation and to ensure that $k_3 [X] \gg k_{-1} [C]$. At this limiting concentration of trap k_0 becomes independent of $[X]$ and the intramolecular rate equation effectively reduces to:-

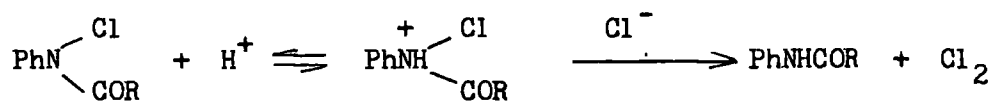
$$k_0 = k_1 [Y] K h_0$$

since the rearrangement term disappears. It thus becomes indistinguishable from the limiting form of the intermolecular expression at high $[X]$.

The equation suggests that catalysis by acid and by nucleophiles should be operative. This has been confirmed for N-methyl-N-nitrosoaniline in hydrochloric acid¹⁴ when k_0 was found to be linearly dependent upon $h_0 [Cl^-]$ up to 5M acid. The solvent isotope effect k_{D_2O}/k_{H_2O} of ~ 3 is consistent with a fast protonation of the nitrosamine followed by rate-determining nucleophilic attack at the nitroso-nitrogen.



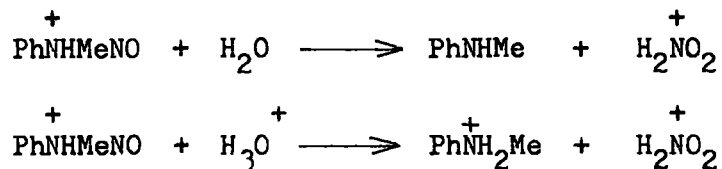
An analogous scheme is held to be operative as the first stage of the Orton rearrangement of N-chloroanilides.¹⁵



In sulphuric acid it is possible to maintain constant acidity whilst varying the nucleophile concentration by the addition of suitable salts. Furthermore, plots of k_0 versus $[Y]$ should be linear with slope $k_1 K h_0$. In this way Biggs and Williams¹⁴ obtained the $k_1 K$ values for several nucleophiles (Cl^- , Br^- , SCN^- and I^-) and successfully correlated $\log k_1 K$ with 'n' the nucleophilic constant of Swain and Scott.¹⁶ The slope of this

correlation gave a value of 2.1 for the susceptibility constant showing denitrosation to be strongly dependent upon the reactivity of the nucleophile.

In the absence of added nucleophiles denitrosation in sulphuric acid is accompanied by rearrangement. At low acidities water is believed to be the active nucleophile whereas at higher acidities attack by H_3O^+ is believed to occur.¹⁴ (HSO_4^- and SO_4^{2-} are believed not to be involved).



The reverse of the latter reaction had been proposed by Ridd¹⁷ by analogy with the diazotization of aniline, which, under comparable conditions, is believed to react as PhNH_3^+ .¹⁸

We have seen that at low acidities the limiting condition $k_3 [X] \gg k_{-1} [C]$ can be satisfied as the concentration of nitrite trap X is increased. The order of reactivity of the various traps towards nitrosation by H_2NO_2^+ or NOCl has been shown to be¹⁹: hydrazoic acid \sim hydrazine $>$ sulphamic acid $>$ hydroxylamine $>$ urea, for reaction with N-methyl-N-nitrosoaniline. Thus, hydrazoic acid is needed in lowest concentration to satisfy the limiting condition. Experiments have now been carried out using the limiting concentrations of the various traps whilst varying the acidity of the medium.²⁰ The results show that the limit is satisfied below 5.5M HCl, $\log k_0$ being a linear function of $-\text{H}_0$, whereas above this acid concentration the linear relationship breaks down for all the traps studied. This was interpreted as follows:-

(a) For the least reactive traps urea, hydroxylamine and sulphamic acid, extensive protonation in the highly acidic media reduces the effective

concentration of X so that $k_3 [X]$ no longer greatly exceeds $k_{-1} [C]$ and the simple linear relationship between k_0 and $-H_0$ can no longer hold. Rather, the full rate equation applies in this region. This is not unreasonable since the protonated trap species would be expected to be less reactive towards electrophilic nitrosation than the free bases. Furthermore, the value of k_0 reaches a maximum and then decreases as the acidity is increased, the position of the maximum varying from trap to trap. This is obviously due to differing trap basicities.

(b) With hydrazine and hydrazoic acid in these acidic solutions it is thought that the active species toward electrophilic nitrosation are NH_2NH_3^+ and HN_3 respectively, and that further protonation to NH_3NH_3^+ and H_2N_3^+ does not occur to any significant extent. Rather, the deviation from linearity of k_0 versus $-H_0$ (the curve does not reach a maximum) is ascribed to extensive protonation of the nitrosamine.

The equation:

$$k_0 = k_1 [Y] K h_0$$

should then be replaced by:

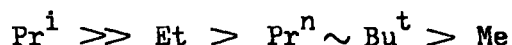
$$k_0 = k_1 [Y] K h_0 / (1 + K h_0)$$

which simplifies to $k_0 = k_1 [Y]$ when the protonation is virtually complete. Thus k_0 should become zero order with respect to acidity as $-H_0$ is increased.

At low acidities the normal solvent isotope effect of $k_{\text{D}_2\text{O}} / k_{\text{H}_2\text{O}} > 1.0$ is observed which is consistent with a fast, reversible initial proton transfer. However, at higher acidities this is reversed where it is thought that protonation of the trap is the dominant factor and that such protonation is more extensive in $\text{DCl}/\text{D}_2\text{O}$ than in $\text{HCl}/\text{H}_2\text{O}$ of

the same concentration. The rate maximum therefore occurs at a lower acid concentration in $\text{DCl}/\text{D}_2\text{O}$.²⁰ Slow proton transfer is thought not to occur.

The effect of various substituents upon the rate of denitrosation has recently been studied.²¹ For the halide ion catalysed reaction the rate-sequence for N-alkyl-N-nitrosoanilines was found to be:-



where the anomalous reactivity of the N-t-butyl nitrosamine is thought to reflect steric hindrance to the approach of the nucleophile. Relative rates $k_o(\text{Bu}^t) : k_o(\text{Me})$ of 2.45 (Cl^-), 2.39 (H_2O), 1.45 (Br^-) and 0.94 (I^-) lend support to this argument. In sulphuric acid without any added halide the same pattern of reactivity is found where the nucleophile is believed to be the water molecule. Alternatively, the above rate-sequence could reflect the differing basicities of the various N-alkyl-N-nitrosoanilines or perhaps the two factors operate simultaneously.

For meta- and para- ring substituents no steric complications exist and the relatively small range of reactivity is interpreted as being due to two opposing effects, namely the effect of ring substitution on k_1 and K , i.e. on the attack at the nitroso-nitrogen by the nucleophile and on the protonation of the nitrosamine, respectively.

For the halide catalysed reaction the rate-sequence for para-substituents is $\text{Cl} > \text{H} > \text{Me} > \text{OMe}$ reflecting that the major effect is that upon the susceptibility of the nitrosamine to nucleophilic attack. In sulphuric acid containing no added halide this sequence is reversed implying that attack at the nitroso-nitrogen is by a positive species. It is suggested that H_3O^+ is responsible, particularly at high acidities.

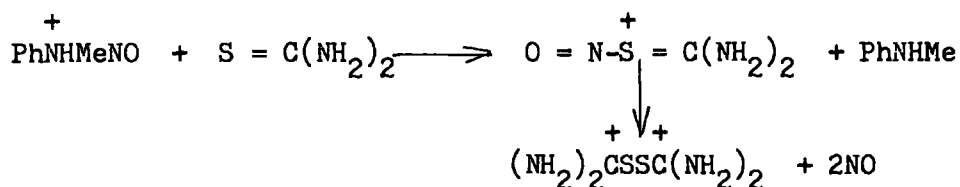
A simple correlation of the Hammett type was not attempted because although the k_o versus $-H_o$ plots for para- Cl, H, Me and OMe were approximately parallel, those for p-NO₂ and m-NO₂ were not. Thus the relative reactivities are a function of the acidity of the medium, and make such a correlation meaningless. The nitro compounds could possibly follow a different acidity function.

One aspect of the denitrosation process which is of current interest is its catalysis by various sulphur containing species such as thiourea and thiocyanate ion. In a preliminary communication Williams reported that thiourea exhibited nucleophilic reactivity towards the protonated form of N-methyl-N-nitrosoaniline somewhat between that of bromide and iodide.²² The reaction was reported in more detail in a later publication²³ where the formation of an unstable >S-NO^+ intermediate was proposed. The essential details are outlined below.

In the absence of trap the reaction between the nitrosamine and thiourea resulted in the formation of a transient yellow colour. This had been observed also by Stedman and co-workers during the nitrosation of thiourea with nitrous acid.²⁴ In the original work of Werner²⁵ more concentrated solutions had been used and the colour appeared red rather than yellow. It is interesting to remark on the very early observation by Döbereiner²⁶ that $\text{NO}^+\text{HSO}_4^-$ in concentrated sulphuric acid gave a red precipitate of sulphur on passing hydrogen sulphide through the solution and that ferrous sulphide was turned bright red by the same reagent. We may speculate as to whether this too is an example of S-nitrosation.

In the case of reaction between thiourea and N-methyl-N-nitrosoaniline fading of the yellow colour resulted in the formation of the C,C¹-dithiodiformamidinium dication in high yield. The scheme proposed

is essentially the same as that for reaction between thiourea and nitrous acid²⁴ except that the formation of thiocyanate via N-nitrosation of the thiourea was not recorded.



The nitrosamine is eventually regenerated by reaction of the N-methyl-aniline with nitrous acid formed by aerial oxidation of the nitric oxide in solution. In de-oxygenated solutions no such regeneration occurred. When most of the thiourea had reacted as above, the regenerated nitrosamine gave its usual acid-hydrolysis products, namely N-methyl-aniline and some Fischer-Hepp rearrangement product.

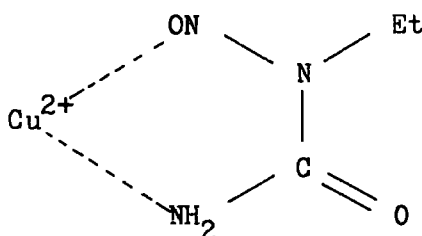
The importance of the above scheme lies in the fact that nitrosamines, which are well known as carcinogens²⁷, may well be able to induce such disulphide formation in the living cell from thiolic species such as cysteine, glutathione and co-enzyme A. In particular, during mitosis various thiolic proteins coagulate via the formation of disulphide bridges thereby forming the spindle along which the chromosomes separate.²⁸ In such a delicately balanced system as the living cell premature spindle formation through reaction between the protein thiol groups and nitrosamines could conceivably initiate chromosome separation and ultimately cell-division. If this were to happen rapidly and frequently cancerous growth could well ensue.

Current work on the catalysis of denitrosation by various N-alkyl substituted thioureas and the sulphur containing amino acids cysteine and methionine has indicated that the reactions are kinetically complex.²⁹ However, S-nitrosation is believed to occur in all cases. Cysteine is

only weakly nucleophilic being about as reactive as chloride. The effect of methyl substitution in thiourea upon the rate of denitrosation is small for N-substitution. One might expect increasing deactivation by protonation in the series mono, di-, tri- and tetra-N-methyl thiourea but the pK_{BH^+} values are all so small so as to make protonation a minor factor in the reaction. Thus all the thioureas exhibit similar reactivity towards the protonated nitrosamines. Only with S-methyl substitution is there a dramatic rate reduction. This tends to support the idea of nitrosation at the sulphur site.

In connection with the nitrosation of sulphur nucleophiles by N-methyl-N-nitrosoaniline it might be added that the interaction of N-alkyl-N-nitrosourethanes with thiolic species such as cysteine has been reported and a bewildering array of products identified.³⁰ However, no mechanistic details were proposed. These compounds are extremely potent as carcinogens and indeed, the first nitroso compound shown to be able to produce chromosomal aberrations was N-methyl-N-nitrosourethane³¹, $MeN(NO).COOEt$. Obviously it would prove useful to obtain details of their mode of action and to compare the results with those obtained for N-methyl-N-nitrosoaniline. However, it has been shown that the initial proton transfer to N-ethyl-N-nitrosourethane in aqueous sulphuric acid is probably rate-determining (see Section 3.6) and therefore that subsequent stages in the reaction are not kinetically observable. Furthermore, at low acidities (1.5M H_2SO_4) the denitrosation is accompanied by approximately 30% deamination. The deamination reaction has been invoked as a possible source of carbenium ions to account for the in vivo alkylation of the N-7 site of DNA bound guanine.³² These results are in accord with those obtained by Challis for the acid-catalysed denitrosation and deamination of N-n-butyl-N-nitrosoacetamide³³ and N-nitroso-2-pyrrolidone,³⁴ and with those of Williams for the acid-catalysed denitrosation of N-methyl-N-nitrosotoluene-4-

sulphonamide.³⁷ Generally, it thus appears that N-nitroso compounds in which the amino nitrogen carries a further electron attracting substituent such as $-SO_2R$, $-CONH_2$, $-COR$ or $-COOR$ undergo slow initial proton transfer as a result of their very weak basicity. The reported catalysis of the degradation of N-ethyl-N-nitrosourea by various metal ions in weakly acidic aqueous solution thus seems rather surprising.³⁵ There appears to be no correlation between the reported reactivities of these ions ($Cu^{2+} \gg Ni^{2+} > Co^{2+} \sim Mn^{2+} \sim Fe^{2+}$) and the pK_{BH^+} values of the aquo complexes. It therefore seems likely that the effect is due to some novel factor such as rate-determining decomposition of complexes of the type:-



Note that the above order of reactivity parallels exactly the Irving-Williams series for the stability constants of complexes of divalent first-row transition metal ions.⁶¹ No such catalysis was reported for N-methyl-N-nitrosourethane,³⁵ N-methyl-N-nitrosoaniline,³⁶ or N-methyl-N-nitrosotoluene-4-sulphonamide.³⁶ These presumably cannot form chelate complexes.

Finally, let it be emphasised that direct transfer of NO^+ from the protonated nitrosamines to the various trap species is thought not to occur. Support for this view comes from the observation of halide catalysis in the nitrosation of, for example, azide by both nitrosamines³⁸ and nitrous acid.³⁹ Williams has shown that halide-catalysis is generally operative for denitrosation of N-methyl-N-nitrosoaniline in the presence of excess trap, and that the zero-order dependence in trap when $k_3 [X] \gg k_{-1} [C]$ also rules out direct NO^+ transfer. The discrepancy lies in the case of anilines for which Challis & Osborne had proposed a direct NO^+ transfer in their

reaction with $\text{Ph}_2\text{NH}^+\text{NO}$. Thus it was argued that direct transfer did indeed take place since the reactions were not catalysed by halide ions. On the other hand Williams¹⁴ had argued that direct transfer from the protonated nitrosamine (in this case N-methyl-N-nitrosoaniline) of the -NO group to aniline was unlikely to be observable in view of the extensive protonation of the aniline in the acidic reaction medium. Thus it was believed that reaction was likely to occur with the unprotonated form of aniline (not an unreasonable assumption), which would be present in concentrations too small to effect observable rate enhancements.

However, this approach neglects the possibility of reaction between the protonated nitrosamine and the protonated form of aniline. Thus although this reaction involves two positively charged species it might not be too unreasonable to expect its occurrence, especially if proton loss is largely complete in the transition state. We may recall that direct reaction between the nitrous acidium ion (H_2NO_2^+) and PhNH_2Me^+ is believed to occur under certain conditions.¹⁷ It is one of the objectives of this thesis to show clearly that such a reaction does occur between $\text{Ph}_2\text{NH}^+\text{NO}$ and PhNH_3^+ . (Ch.4).

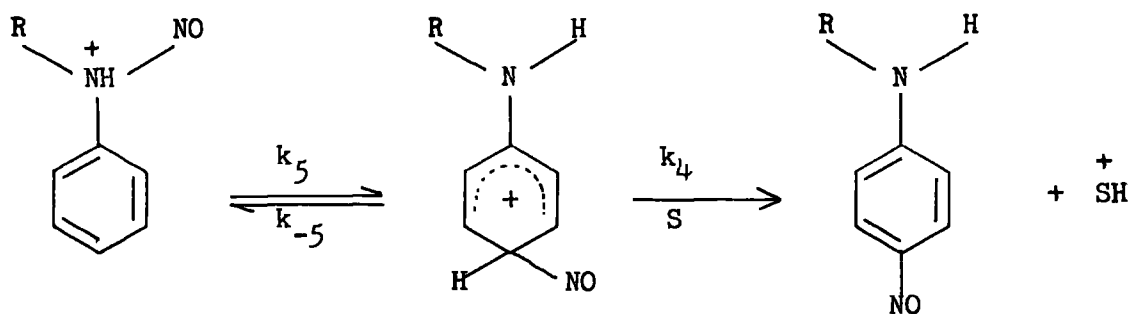
1.6 The Mechanism of Rearrangement:

As we have seen the actual rearrangement of aromatic N-nitrosoamines to their para-C-nitroso isomers is now generally believed to be an intramolecular process, at least in aqueous acidic media. Denitrosation can be suppressed by the omission of any nitrite trap and the addition of an excess of the product of denitrosation (C). Under these conditions, with $k_{-1} [C] \gg k_3 [X]$, the intramolecular rate equation reduces to:

$$k_0 = \frac{k_4 k_5 K_h}{k_4 + k_{-5}}$$

so that k_0 becomes independent of Y, C and X. In the case of N-methyl-N-nitrosoaniline increasing the concentration of N-methylaniline resulted in a decrease in the value of k_0 to a limiting value of $2.8 \times 10^{-4} \text{ sec}^{-1}$ in 5.90M HCl which was taken to be the rate-constant for rearrangement at this acidity. Simultaneously the yield of rearrangement product was observed to increase from 28% with no added N-methylaniline to $>80\%$ at the limit.⁴⁰ It was also observed that meta- electron withdrawing groups reduced the rate and yield of the rearrangement step whilst meta-electron releasing groups acted in the opposite sense. The rearrangement is therefore one of electrophilic C- nitrosation. The effect of these substituents upon the rate of denitrosation was felt to be negligible in view of their remote position from the nitroso-group. In the extreme cases it was found that for the meta-OMe compound only rearrangement occurred even in the absence of added secondary amine whilst for the meta-NO₂ compound only denitrosation occurred⁴⁰. Thus the observation by Macmillan & Reade¹ that no rearrangement of the meta-NO₂ compound occurred in the presence of urea must be qualified in that no rearrangement occurs even in the absence of urea.

The rearrangement of 2,4,6-trideutero-N-methyl-N-nitrosoaniline was found to be slower than that of the non-deuterated compound by a factor of 1.7 thus implying that proton loss from the final σ - complex is partially rate-determining.⁹ Increasing the concentration of added N-methylaniline to suppress denitrosation increased k_H/k_D to 2.4. Such primary kinetic isotope effects have been found to be typical of electrophilic aromatic nitrosations in general and have been interpreted as being due to rapid regeneration of reactants.⁴¹ In the case of the Fischer-Hepp rearrangement this implies that $k_{-5} > k_4$ in the scheme:-

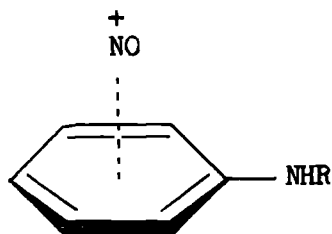


Rearrangement of various N-alkyl-N-nitrosoanilines in sulphuric acid has now been successfully carried out by use of an added excess of the corresponding secondary amine.²¹ Yields of rearrangement product were found to be virtually quantitative. This dismisses the earlier evidence in favour of free nitrosyl chloride as the only active nitrosating agent in the Fischer-Hepp rearrangement,⁶ (see Section 1.2). Furthermore, N-t-butyl-N-nitrosoaniline was found to rearrange under these conditions although at a lower rate than that expected on the grounds of the normal electronic effect of the t-butyl group. Steric hindrance to protonation of the nitrosamine was suggested as a likely cause. This compound was previously believed not to undergo rearrangement at all.⁴²

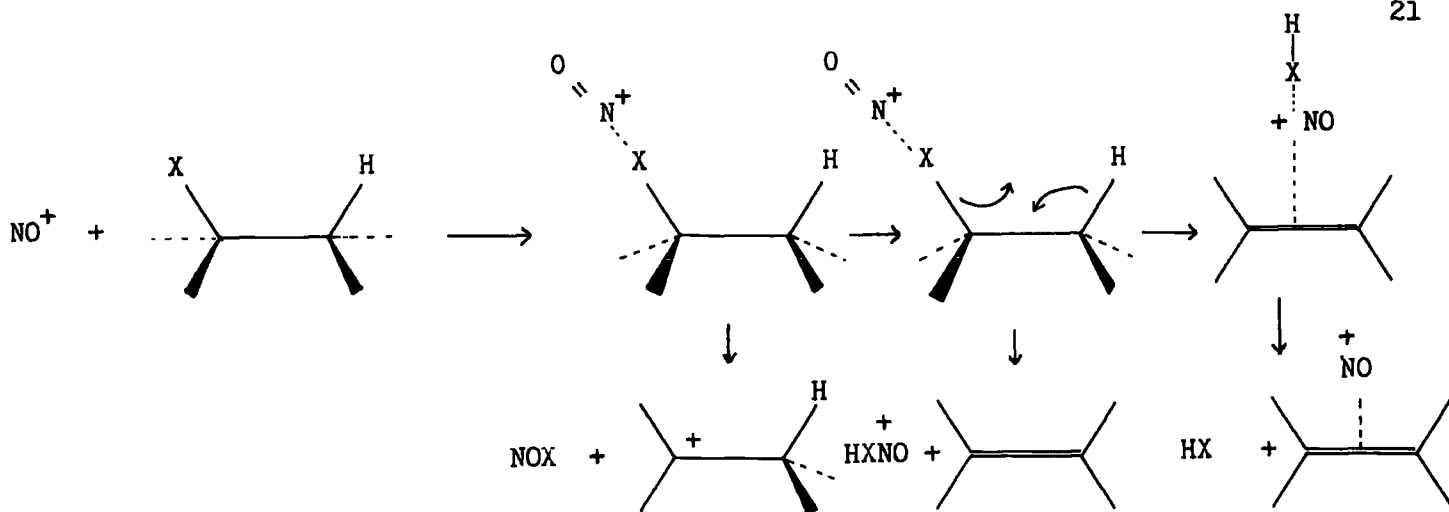
The effect of acidity upon the rate of rearrangement has also been studied.^{9,20} For PhNMeNO in the range 2 - 8M HCl, $\log k_0$ versus $-H_0$ is linear with slope of 1.2 implying that rearrangement occurs via a singly protonated intermediate as expected. This also rules out catalysis by chloride ion since a second-order dependence on HCl would then be expected. The rate-profile then reaches a maximum at 10M HCl when it is believed that the nitrosamine is fully protonated. At higher acidities $\log k_0$ decreases linearly with $-H_0$ where the rapidly increasing activity of the proton is thought to inhibit proton loss from the para-nitroso σ -complex (k_4).

Despite success in demonstrating the validity of the intramolecular mechanism for the Fischer-Hepp rearrangement the kinetic data shed little light upon the physical details of the actual migration of the -NO group. It is thought that the distance involved in migration from the amino nitrogen to the para- position of the ring is too large to allow reaction to take place without the involvement of a further intermediate and this

is usually represented as a π - complex of the type:⁴⁰



Such species have never been unambiguously identified in electrophilic aromatic substitution reactions in general although analogous complexes have been proposed to account for the observed ring substituent effects in the diazotization of aniline by H_2NO_2^+ .⁴³ However, Dimitrov & Fratev⁴⁴ have observed the formation of deep red colours when aromatics such as benzene and toluene are mixed with a solution of sodium nitrite in sulphuric acid. Observation of their visible spectra and their destruction by donor solvents such as EtOH and H_2O was interpreted in terms of initial π - complex formation followed by a $\pi \longrightarrow \sigma$ transition. Somewhat later Allan and co-workers⁴⁵ observed the formation of red-brown colours during the mixing of $\text{NO}^+\text{HSO}_4^-$ with aromatics such as benzene, diphenyl, naphthalene, thiophene and phenol. On heating, products such as ArN_2^+ and ArNO_2 were identified and the involvement of π - complexes proposed on the basis of n.m.r and UV/visible data. Furthermore, the NO^+ cation has an extensive gas-phase chemistry and its reactions with organic species under such conditions are of interest in that the products formed often bear close similarity to several types of 'reactive intermediate' frequently proposed in solution chemistry. Thus NO^+ reacts with alkanes by a hydride-transfer mechanism to produce a variety of novel species as has been demonstrated by a recent ion-cyclotron resonance study.⁴⁶



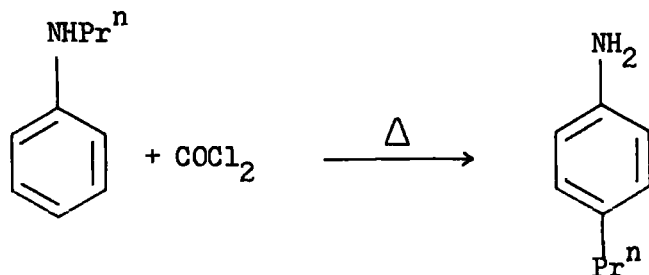
It was therefore suggested that the Lewis acidity of NO^+ is quite a significant feature in its chemistry.

However, under the low acidities normally used in the Fischer-Hepp rearrangement where the water activity is still significantly large, one might expect rapid destruction of such complexes to the amine and kinetically free H_2NO_2^+ . The involvement of π -complexes is thus based on very tentative arguments but it is conceivable that the transition state lies very close to the relatively stable σ -complex and that the formation of the latter takes place very rapidly via NO^+ migration across the π -cloud. This assumes that the energy barrier to migration across the ring π -system is so low as to allow complete transfer of the NO^+ across the ring before any collisions with solvent molecules can take place. The model is thus analogous to that for the very rapid transfer of electrons across bridging groups in transition metal complexes.⁴⁷ The rate of rearrangement would therefore be largely governed by the rate of proton loss from the σ -complex which, as has already been mentioned, is at least partially rate-determining.⁹

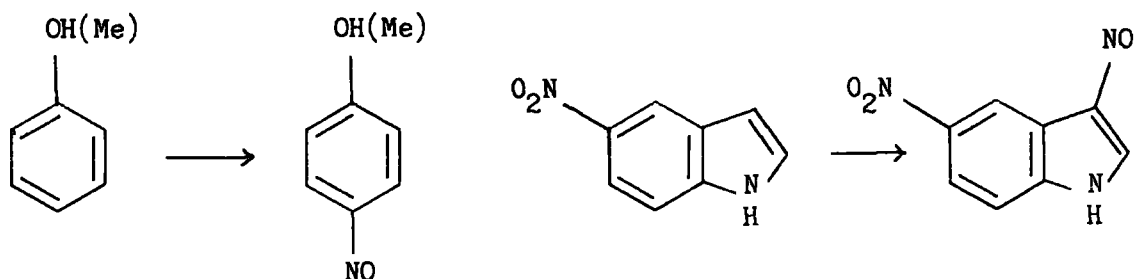
We recall that any successful mechanism for Fischer-Hepp rearrangement must account for the apparently exclusive formation of para- as opposed to ortho-C-nitroso isomer. Firstly, it may prove useful to again mention that Williams⁴⁰ obtained a maximum yield of $\sim 80\%$ for the rearrangement of N-methyl-N-nitrosoaniline. The remaining 20% can

possibly be accounted for in terms of denitrosation plus the formation of an unidentified yellow substance²¹ which may be derived from the ortho-isomer. However, experience with the behaviour of N-nitrosodiphenylamine in sulphuric acid (see Chapter 3) suggests that the formation of Wurster's Blue via a radical-cation mechanism can become dominant over both rearrangement and denitrosation and it is likely that the above yellow colour is due to the corresponding reaction with PhNMeNO.

That the Fischer-Hepp rearrangement gives exclusively the para-isomer is well documented.⁴⁸ However, the reaction is not unique in this respect. For example, the Reilly-Hickinbottom rearrangement of N-n-propylaniline gives largely the para-n-propyl isomer.⁴⁹

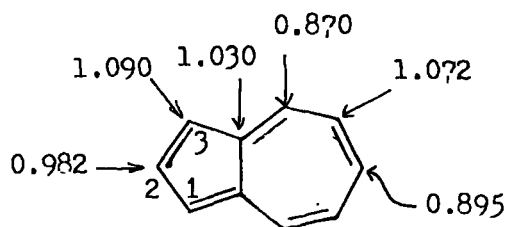


Also, Challis and co-workers⁴¹ had noted that in the nitrosation of electron rich aromatics by H_2NO_2^+ , NOCl etc., the predominant products were the para-C-nitroso isomers, e.g.:-



It is interesting to note that the result for azulene (nitrosation at position 3) can be rationalised in terms of the π - charge densities

calculated by Dewar.⁵⁰



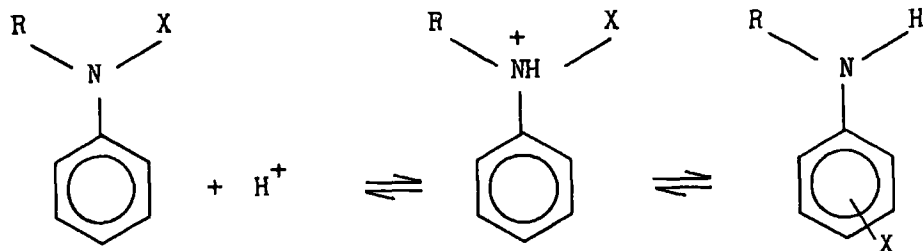
Perhaps similar SCF MO calculations will indicate a high π - charge density at the para-position of N-methyl-N-nitrosoaniline, as compared with the ortho-position.

An alternative approach is given by modern generalized perturbation theory⁵¹ which regards electrophilic aromatic substitution as a reaction between a donor molecule (the aromatic substrate) and an acceptor molecule (the electrophile). Basically, the GP equation for the energy change due to partial bond formation between the interacting atoms contains two terms, one representing the electrostatic interaction and the other the covalent interaction. If the energy difference between the HOMO of the donor and the LUMO of the acceptor is large then it is found that both terms favor interaction between the two centres carrying the highest opposite charges. This situation is referred to as charge-controlled reaction. However, when the donor HOMO and acceptor LUMO are nearly degenerate the covalent term becomes extremely large and as an approximation the electrostatic term can be neglected. The reaction then occurs between the two centres possessing highest electron density in the interacting (frontier) orbitals. This situation is referred to as orbital-controlled reaction. Estimation of the HOMO - LUMO energy gap can be made in a qualitative manner by use of the concept of hard & soft acids and bases. As a rule hard acid-hard base and soft acid-soft

base interactions will be approximately degenerate and the reactions will be orbital-controlled. Conversely hard acid - soft base and hard base - soft acid interactions will involve large energy differences between HOMO and LUMO and the reactions will be charge-controlled.

Thus with an aromatic π -system as donor (soft base) we expect reaction with a hard electrophile to be charge-controlled (e.g. NO_2^+), and reaction with a soft electrophile to be orbital-controlled (e.g. Br^+). With regard to possible sites of electrophilic attack in substituted benzenes both PND0 and CND0 theories predict that for toluene C-2 carries the highest negative charge and C-4 the highest electron density in the HOMO. Thus C-2 is preferred by hard electrophiles whilst C-4 is preferred by soft electrophiles. It is further argued that charge-controlled electrophiles will not be able to distinguish between the various sites in alternant hydrocarbons, i.e. will be unselective, whereas orbital-controlled electrophiles will be highly selective. Hence, nitration of toluene should lead to a mixture of ortho- / para- isomers whereas bromination should give almost exclusive para-isomer.⁵¹

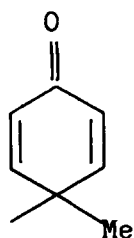
If we regard the Fischer-Hepp rearrangement as π -donation to NO^+ from the aromatic amine it would appear that the same factors will operate here as in toluene. Thus although NO^+ is classified as borderline in the hard/soft classification of Lewis acids⁵¹ it appears to react in an orbital-controlled manner, being highly selective in giving exclusive para-C-nitroso isomer. We must therefore now attempt to use this theory to try and explain the orientation of substitution in several related rearrangements. This is of course only speculative. Formally we can regard reaction as being due to electrophilic attack by X^+ on the aromatic ring.



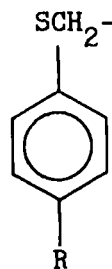
The following Table has been compiled from data presented in reviews by Banthorpe,⁶² Shine⁶³ and Williams.⁶⁴ The hard-soft classification is from the article by Klopman.⁵¹

| REARRANGEMENT | R | X | Ortho-para ratio | Comments |
|--|-------|---------------------|--|--|
| Fischer-Hepp | Alkyl | -NO | Exclusive para. | NO ⁺ borderline. Any ortho isomer may decompose. |
| Orton | Alkyl | -Hal | Mainly para. Very little (~5%) ortho | Br ⁺ soft, Cl ⁺ is presumably hard but Br ₂ & Cl ₂ soft. |
| Benzidine | H | -NHAr | Mainly para. | Symmetrical case ∴ expect degenerate donor & acceptor. |
| Quinamine | H | see below (a) | Exclusive para. | Analogous to Benzidine rearrangement. |
| Hoffmann-Martius & Reilly-Hickinbottom | H | Alkyl | Predominantly para. | Carbenium ions borderline. |
| N-alkyl-N-aryl sulphonamide | Alkyl | -SO ₂ Ar | Exclusively ortho | Probably genuine intramolecular 'cartwheel'. |
| Nitramine | Alkyl | -NO ₂ | Mainly ortho (70-90%) | NO ₂ ⁺ hard. Probably intra-'cartwheel' mechanism. |
| Diazoaminoaromatic | H | -N=NAr | Exclusive para unless blocked then ortho. | Like diazo-coupling ArN ₂ ⁺ not classified |
| Chattaway | Acyl | Acyl | Mainly para. | RCO ⁺ hard unusual. Steric effect? |
| N-arylaminoethyl-aryl sulphide | Alkyl | see below (b) | Exclusive para. No ortho even if para blocked. | Steric effect could be dominant. |

(a)



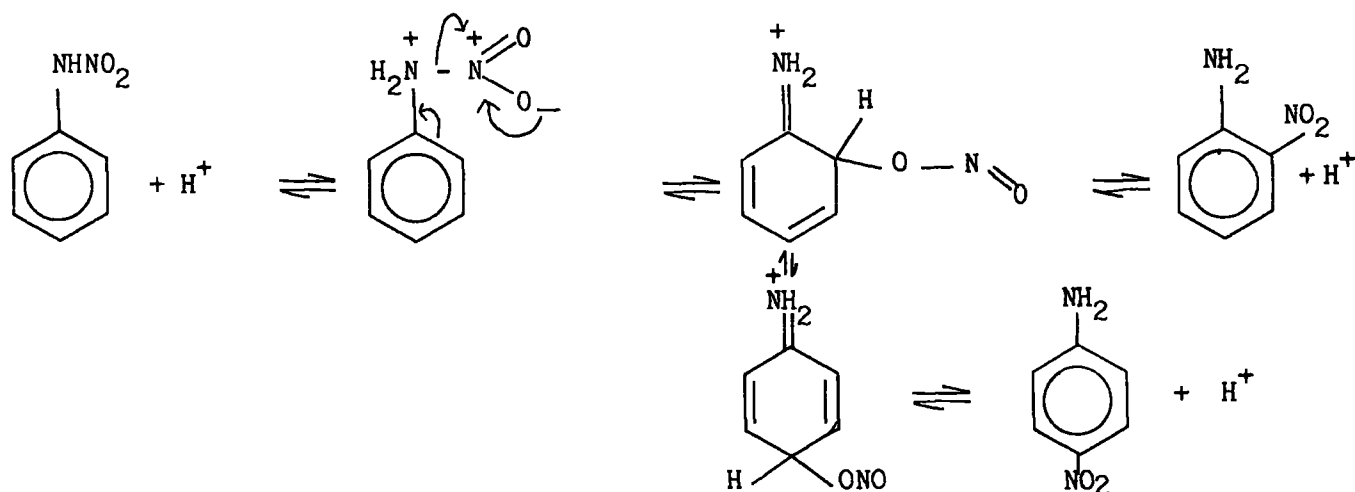
(b)



As can be seen para-substitution appears to be the rule rather than the exception, in line with the low electrophilicity of species such as NO^+ , Hal_2 , ArNH_2^+ , ArN_2^+ etc.. However, one or two further points need to be mentioned. In the Orton rearrangement where electrophilic attack by Hal_2 is believed to occur the yield of ortho-isomer is usually quite low ($\sim 5\%$). With more reactive electrophilic species such as $\text{H}_2\text{O}^+-\text{Hal}$ or $\text{Hal}^+ \text{Al}(\text{Hal})_4^-$ one would expect an increase in the proportion of ortho-substitution. The ortho-para ratio will thus be strongly dependent upon the conditions used. The Chattaway rearrangement is believed to involve Friedel-Crafts type electrophilic substitution by RCO^+ species,⁶⁵ as is the related Fries rearrangement of phenyl esters. However, the former gives only para-substitution whereas the latter gives ortho- and para- (usually). Thermodynamic rather than kinetic control may therefore be important here since the ortho-para ratio in the Fries rearrangement is known to be temperature dependent.⁶⁶ It is worth emphasising however, that the Chattaway rearrangement has only received scant attention and that early product analyses could well be suspect. There is clearly room here for well-designed research.

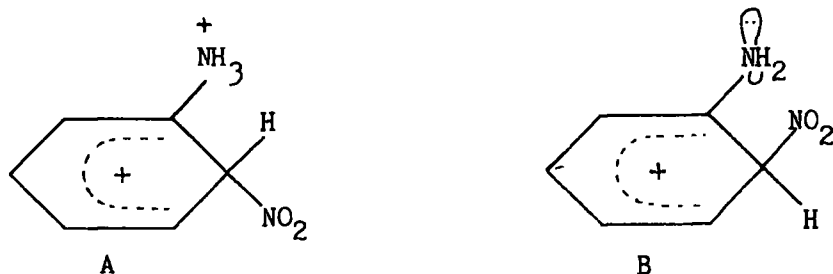
However, the success or failure of the theory depends to a large extent upon the observed ortho-para ratios in the nitramine rearrangement. High yields of ortho-isomer are usually obtained as would be

expected for reaction with the hard electrophile NO_2^+ . For instance, rearrangement of N-nitroaniline in 84% sulphuric acid gives 93% ortho- and 7% para-substitution.⁶⁷ It has been argued, however, that the reaction does not involve N-N fission to give NO_2^+ but rather that fission occurs in the opposite sense, and a 'cartwheel' type mechanism has been suggested to account for the intramolecular nature of the reaction:⁶⁸



The observation that nitration of aniline under similar conditions, (where NO_2^+ is believed to be involved) gave 6% ortho, 34% meta, and 59% para-substitution,⁶⁷ was taken as evidence against the involvement of NO_2^+ in the rearrangement since otherwise identical product distributions would be expected. However, in highly acidic media aniline would be expected to react as PhNH_3^+ (hence meta substitution) whereas in the rearrangement the departing nitro group still keeps the amino basicity low so that reaction can be thought of as involving PhNH_2 and not its conjugate acid. With a weakly basic aniline one might therefore expect direct nitration, and rearrangement of the N-nitro derivative, to give identical product distributions. This has been shown to be so by Ridd⁶⁹ since nitration of 2,3-dinitroaniline and rearrangement of N,2,3-trinitroaniline each gave 34% 2,3,4- and 66% 2,3,6-trinitroaniline. One must therefore

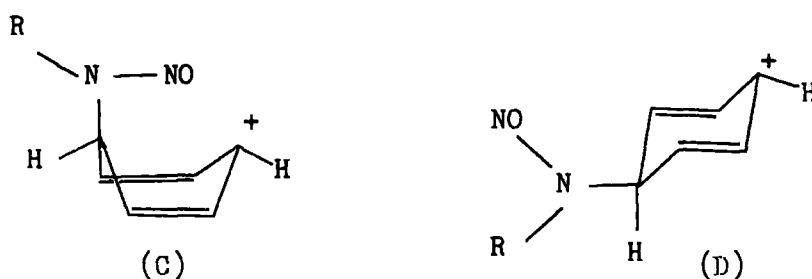
conclude that the rearrangement involves either prior N-nitration followed by 'cartwheel' migration OR the electrophilic involvement of NO_2^+ . However, there is no need to invoke the cartwheel mechanism in order to account for the intramolecularity of the reaction since such a process is clearly not possible in the Fischer-Hepp rearrangement which is also intramolecular. (In other words intramolecular rearrangement still occurs when the cartwheel process is not possible.) The formation of by-products derived from nitrous acid could arise via concurrent fission in the sense $\text{PhNH}-\overset{\delta+}{\text{N}}-\overset{\delta-}{\text{NO}_2}$. Thus the NO_2^+ π -complex mechanism may not be so dead as was once thought. However, it is still necessary to account for the observed isotope effect in the nitramine rearrangement since these are largely absent in direct nitrations. It is likely, however, that proton loss would be faster from an intermediate such as A than from B, because of the greater positive charge on the former. Furthermore, rapid reversion



to N-nitroamine is possible in B but unlikely in A because of the protonation of the amino nitrogen. Rapid regeneration of reactant (s) has been suggested to account for the isotope effects observed in electrophilic aromatic nitrosation.⁴¹

It is hoped that this brief survey of aromatic rearrangements will have shown that the orientation effects in these reactions can be explained by current molecular orbital theory in a general way, and that the use of novel mechanisms such as the cartwheel process may be unnecessary. The exclusive formation of para-C-nitroso isomer in the

Fischer-Hepp rearrangement is particularly well accounted for where it is difficult to envisage novel reaction pathways. Indeed the only other attempt to account for this feature comes from Allan⁵² who has proposed direct transfer of the nitroso group to the para position in a bent, ring protonated intermediate (C).



The observed ring isotope effect⁹ would be satisfied if proton loss occurred simultaneously with -NO migration. However, transfer of NO^+ to positive carbon would not be expected to be particularly favorable and the other apical hydrogen atom must transfer to the amino nitrogen in order to restore benzenoid character in the product. Furthermore, one would expect an intermediate of this type (C) to also exist in the crown form (D) where ortho-migration might be favorable. Indeed, the crown form will be energetically more favorable since it is sterically less strained.

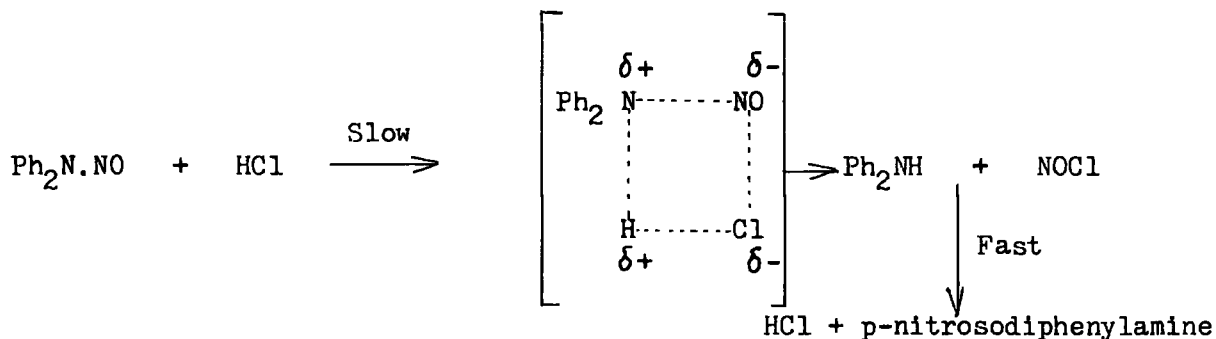
The evidence for protonation at ring carbon in benzenoid compounds is virtually non-existent. A study of the H_3O^+ catalysed detritiation of a number of aromatic substrates has given a crude pK_{BH^+} value of -15.3 for ring protonation in anisole⁵³ and one might expect the corresponding pK_{BH^+} values for ring protonation in anilines to be of the same order of magnitude. Indeed Olah found only N-protonation for aniline and ten of its derivatives in superacid media.⁷⁰ N,N-dimethylaniline is, however, believed to undergo ring protonation

in aqueous acidic media, but only in equilibrium with the N-protonated form.⁷¹

Since low rates are usual in proton transfer to unsaturated carbon the Allan proposal conflicts with the observed fast pre-equilibrium protonation of N-methyl-N-nitrosoaniline¹⁴ for which $k_{D_2O}/k_{H_2O} \simeq 3$. Quite frankly the Allan scheme seems untenable.

1.7 Alternative kinetic studies

The hydrogen chloride catalysed rearrangement of N-nitrosodiphenylamine in methanol has been studied by Baliga.⁵⁴ The reaction was found to be first-order in both nitrosamine and hydrogen chloride. However, catalysis by chloride ion was not observed, the small rate increase on addition of LiCl being attributed to a salt effect. The proposed mechanism involved the slow formation of diphenylamine and nitrosyl chloride via a four-centre transition state.



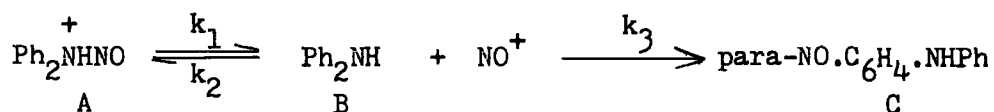
This scheme has been criticised by Williams¹⁰ as follows:-

- (a) Reaction via kinetically free NOCl has been ruled out by the observation of rearrangement in the presence of excess added 'nitrite trap'.
- (b) The observed solvent isotope effect is only consistent with a fast initial protonation.
- (c) The observed ring isotope effect indicates that the final proton loss is rate-determining.

- (d) It cannot account for the observed acid catalysis at constant chloride concentration.
- (e) Rearrangement in sulphuric acid can be made quantitative in the absence of chloride ion.

However, Williams' data were accumulated for reaction in aqueous acidic media whereas those for Baliga in methanol and methanol-toluene mixtures. Until the solvent effects upon the reaction are clearly understood it will remain uncertain as to whether these criticisms generally apply.

More recently, Russian workers^{55,56} have also studied the rearrangement of N-nitrosodiphenylamine in methanolic hydrogen chloride. (4M). They assume in the first-place that the reaction is intermolecular.



and assume NO^+ to be a reactive intermediate whence:-

$$k_1 [A] = k_2 [B] [\text{NO}^+] + k_3 [B] [\text{NO}^+]$$

$$\therefore [\text{NO}^+] = k_1 [A] / (k_2 + k_3) [B]$$

$$\text{and } d[C]/dt = k_3 [B] [\text{NO}^+] = k_1 k_3 [A] / (k_2 + k_3) = k_{\text{obs}} [A]$$

k_{obs} was found to be 0.055 min^{-1}

In order to determine values for k_1 , k_2 and k_3 the equilibrium constants for the denitrosation of several di-para-substituted - N - nitrosodiphenylamines were determined and from a Hammett plot of $\log K_d$ versus σ a K_d value of 2.1×10^{-3} was interpolated for N-nitrosodiphenylamine itself. This was then followed by measurement of

rate-constants for the C-nitrosation of N-substituted diphenylamines Ph_2NHR ($\text{R} = \text{Me, Et, Ph, COMe}$), the correlation of $\log K$ with σ_{R} giving an interpolated value of $32 \text{ l mole}^{-1} \text{ min}^{-1}$ for k_3 in the case of diphenylamine. In this way it was thus hoped that each stage in the actual rearrangement could be studied separately. From $k_{\text{obs}} = k_1 k_3 / (k_2 + k_3)$ and the above values of k_3 and $K_{\text{d}} (= k_1/k_2)$ the constants k_1 and k_2 were calculated to be 0.3 min^{-1} and $147 \text{ l mole}^{-1} \text{ min}^{-1}$, respectively, and it was thus concluded that denitrosation is rate-determining.

These values of k_1 , k_2 and k_3 were then used to solve the differential equations:-

$$\frac{d[A]}{dt} = -k_1[A] + k_2[B]^2$$

$$\frac{d[B]}{dt} = k_1[A] - k_2[B]^2 - k_3[B]^2$$

$$\frac{d[C]}{dt} = k_3[B]^2$$

and the resulting curve claimed to closely resemble the experimental kinetic curve for the actual rearrangement. Thus the reaction was claimed to be probably intermolecular.

However, several criticisms can be levelled at this approach. Firstly, since the intramolecular model was not subjected to the same kind of treatment no meaningful comparison can be made. Secondly, the use of Hammett type correlations for the interpolation of data is considered to be unreliable unless a large substituent basis set is used.⁵⁷ In the present case only four points were used to define the straight line in each correlation. Furthermore, the influence of the substituents upon the acid-base properties of the substrates cannot

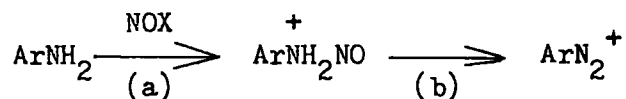
be ignored. It has already been shown that the relative reactivities of various ring substituted N-methyl-N-nitrosoanilines towards denitrosation, and therefore any mechanistic conclusions based upon them, are a function of the acidity of the medium.²¹ Finally, the proposed mechanism involves denitrosation to give free NO^+ as the nitrosating agent. This would seem unlikely since in aqueous media nitrosation by kinetically free NO^+ ions is only thought to occur at high acidities, for example in $\sim 60\% \text{HClO}_4$ or H_2SO_4 where $-\text{H}_0 \sim 4.5 - 5.0$ and the water activity is too low for effective solvation to H_2NO_2^+ to occur.⁵⁸ With 4M hydrochloric acid this is not the case since $-\text{H}_0$ is approximately 1.4 for both water and ethanol as solvent.⁵⁹ In such media one would at least expect solvation of the NO^+ to occur. However, there is also the additional factor of nitrosyl chloride formation. In 4M aqueous hydrochloric acid containing added nitrite NOCl can be detected spectrophotometrically ($\lambda_{\text{max}} = 460 \text{ nm}$) and it has been calculated⁶⁰ that any free nitrous acid is almost completely converted into NOCl under such conditions. There would seem to be no reason why this should not also be true of 4M methanolic hydrochloric acid, and as a result, since denitrosation has been proposed as the rate-determining stage in the rearrangement, one might expect chloride catalysis to be observed. This conflicts with the observations of both Williams¹⁰ and Baliga.⁵⁴

CHAPTER TWO

Halide Catalysed Diazotization

2.1 Introduction

The diazotization of aromatic amines can be conveniently summarised by the scheme:-



The decomposition of the primary nitrosamine is in fact a multi-stage process involving several tautomeric proton shifts and the final loss of a water molecule. Such processes are generally very rapid and this therefore results in rate-determining initial nitrosation, (step a). Indeed, at ordinary temperatures the intermediate nitrosamine is not observable spectrophotometrically. However, such species have been identified at -70°C by means of their U.V. spectra in ethereal solutions of the amine containing nitrosyl chloride.⁷⁵

The observed kinetics in aromatic diazotization are therefore largely dominated by the various mechanisms of nitrosation. That this is a general phenomenon is shown in the work of Kalatzis & Ridd¹⁷ where similar rate equations were obtained for the diazotization of aniline and the nitrosation of *N*-methylaniline.

However, in aqueous acidic media the situation is complicated by the fact that several inorganic nitrosating agents can exist in equilibrium with molecular nitrous acid depending upon the conditions. In decreasing order of reactivity these are:-

| | |
|---------------------------|---------------------|
| NO^+ | nitrosonium ion |
| H_2NO_2^+ | nitrous acidium ion |
| NOX | nitrosyl halide |
| N_2O_3 | nitrous anhydride |

and it is thought that nitrous acid itself (HNO_2) is insufficiently reactive to nitrosate amines directly. With solutions of nitrite in

perchloric or sulphuric acid the only active species possible are NO^+ , H_2NO_2^+ and N_2O_3 , and which is kinetically significant depends upon the acidity. In the presence of halide ion, however, the formation of the corresponding nitrosyl halide becomes important. This is also the case for solutions of nitrite in the corresponding hydrohalic acid, for example, in 4M HCl the formation of NOCl from dissolved sodium nitrite is virtually quantitative.⁶⁰

Further kinetic complications can arise from the fact that under certain conditions the formation of the active nitrosating agent from molecular nitrous acid can become rate-determining. Then the active species is consumed as rapidly as it is formed by reaction with the amine and the overall rate equation corresponds to the stoichiometry of its formation.

It is thus apparent that the elucidation of the mechanisms of diazotization has been long and arduous and resulted in much confusion in the past. The field has been reviewed in more detail elsewhere,^{72,74,76} and the next section is provided merely to put the halide catalysed reaction into perspective.

2.2 Diazotization in the Absence of Halide

In mechanistic studies the reaction has most commonly been carried out in perchloric and sulphuric acid, although aqueous nitric acid has also been used. The active nitrosating agents are, in each case, thought to be N_2O_3 , H_2NO_2^+ and NO^+ .

(a) Nitrous Anhydride Mechanism

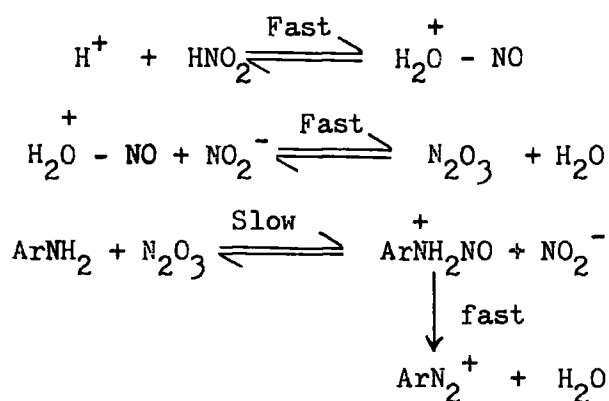
For amines of comparable basicity to aniline this mechanism is important at low acidities in perchloric and sulphuric acid (< 0.5M).

With aniline in sulphuric acid ($\sim 0.2M$) Schmid⁷⁷ observed third-order kinetics, viz:-

$$\text{Rate} = k [\text{ArNH}_2] [\text{HNO}_2]^2$$

and expressions of equivalent form had already been discovered for the deamination of methylamine⁷⁸ and diethylamine.⁷⁹

In 1940 Hammett⁸⁰ suggested that the second-order dependence upon nitrous acid was due to nitrosation by nitrous anhydride (N_2O_3) formed in a fast pre-equilibrium step.

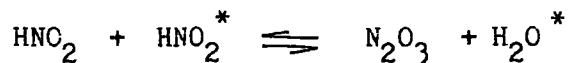


and this was later confirmed by Hughes, Ingold & Ridd^{81,82} who, in addition to duplicating the third-order kinetics of Schmid, succeeded in obtaining second-order kinetics of the form:-

$$\text{Rate} = k [\text{HNO}_2]^2$$

at lower acidities (0.002M). Under these conditions the proportion of free base is much higher and being more reactive than the protonated form towards electrophilic attack it effectively removes the N_2O_3 as rapidly as it is formed. The second-order kinetics then correspond with rate-determining formation of nitrous anhydride.

Further support for this mechanism was provided by a study of the ^{18}O - exchange between nitrous acid and water which, at low acidities and high nitrite concentration, is second-order in nitrous acid, viz:-



and proceeds at a similar rate to the diazotization under similar conditions.⁸³ It is implied that both processes share the same rate-determining step, i.e. N_2O_3 formation.

Nitrous anhydride is regarded as a weak electrophile in comparison with H_2NO_2^+ and the nitrosyl halides since it does not react with deactivated amines such as p-nitroaniline.⁸⁴ The existence of a reasonable correlation of the Hammett type⁸⁴ in the diazotization of aromatic amines by N_2O_3 precludes any possibility of diffusion-control. The true rate coefficient for the encounter between N_2O_3 and ArNH_2 molecules has been estimated to be $\sim 10^7 \text{ l mole}^{-1} \text{ sec}^{-1}$ which is indeed below the diffusion-controlled limit.⁷²

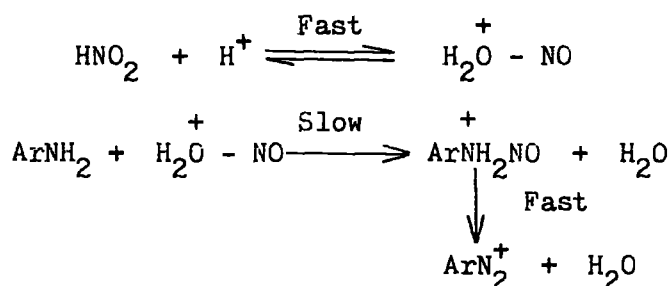
(b) Acid-Catalysed Diazotization:

Since nitrous anhydride is such a weak electrophile it is incapable of reaction with the protonated form of the amine and as a result one would expect the observed rate constant to decrease with increasing acidity because of the decrease in free base concentration. This is observed with those amines for which the N_2O_3 mechanism is applicable but as the acidity is further increased ($> 0.5\text{M HClO}_4$) the rate profile passes through a minimum and after which $k \propto [\text{H}^+]$. This is ascribed to a change in mechanism; the rate equation now

having the form:-

$$\text{Rate} = k [\text{ArNH}_2] [\text{HNO}_2] [\text{H}^+]$$

which has been interpreted as rate-determining attack by the nitrous acidium ion.⁸⁵ This reaction is most easily studied with the weakly basic amines for which complications arising from competition with the N_2O_3 mechanism do not apply. Furthermore formation of the nitrous acidium ion cannot be made rate-determining since proton transfers to and from oxygen are generally very rapid.



The fact that the nitrous acidium ion is capable of diazotizing the nitroanilines suggests that it is a more reactive electrophile than N_2O_3 , and the virtual independence of observed rate constants from amine basicity⁸⁴ further suggests diffusion-control, although the true bimolecular rate-constants for the encounter between H_2NO_2^+ and ArNH_2 have not been calculated since the equilibrium constant for the initial protonation is unknown. It has been argued that since the encounter between ArNH_2 and NOCl is diffusion-controlled and since H_2NO_2^+ would be expected to be a more reactive electrophile than NOCl , then the encounter between ArNH_2 and H_2NO_2^+ should also be diffusion-controlled. However, recent measurements have cast some doubt as to the validity of diffusion-control for the encounter between ArNH_2 and NOCl in contrast to earlier work. This will be discussed more fully later since it is the intention of this work to resolve this discrepancy.

Further increase in the acidity of the medium leads to two developments. Firstly, for the weakly basic amines such as p-nitroaniline increasing the concentration of perchloric acid whilst maintaining constant ionic strength by the addition of sodium perchlorate results in a rate expression of the form:-

$$\text{Rate} = k [\text{ArNH}_2] [\text{HNO}_2] h_0$$

where the observed rate-constant is virtually independent of acidity since increasing h_0 results in a decrease of free base concentration. The mechanism is believed to be the same as that above, the substitution of h_0 for $[\text{H}^+]$ being necessary in the more concentrated acid solutions. However, secondly, for the more basic amines such as aniline the catalytic effect of HClO_4 is more marked and is believed to be largely due to the incursion of a new mechanism with kinetics of the form:-

$$\text{Rate} = k [\text{ArNH}_3^+] [\text{HNO}_2] h_0$$

which corresponds to rate-determining attack by H_2NO_2^+ upon the protonated form of the amine.^{18,43} It is thought that this mechanism only becomes kinetically significant when the proportion of the more reactive free base becomes negligibly small hence its applicability to the more basic amines. A mechanism involving the formation of an intermediate π -complex has been proposed on the basis of a study of ring substituent effects⁴³ and is discussed in section 4.3 in relation to the analogous diazotization by N-nitrosodiphenylamine.

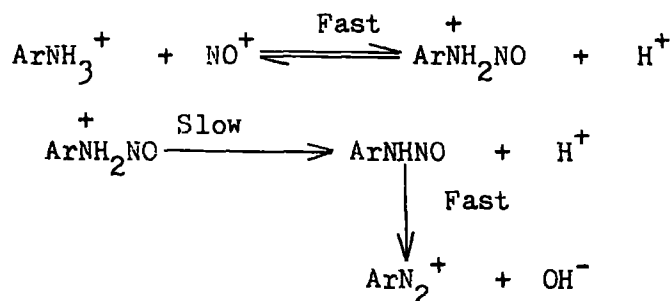
(c) Diazotization at High Acidities

As the acidity is increased still further the rate-profile passes

through a maximum at $\sim 6M HClO_4$ and thereafter the observed rate constant decreases rapidly with increasing acidity. The reaction then follows the equation:-⁵⁸

$$\text{Rate} = k [\text{ArNH}_3^+] [\text{HNO}_2] h_o^{-2}$$

At such acidities nitrous acid is virtually quantitatively present as free nitrosonium ion as is evident from the presence of a Raman line at $2213 - 2319 \text{ cm}^{-1}$ in $60\% HClO_4$ containing added nitrite.⁸⁶ Hence the following mechanism was proposed:-⁵⁸



which accounts for the large isotope effect ($k_H/k_D = 10$) by virtue of the slow proton loss. It has been suggested that two factors operate to make the second step rate-determining. Firstly, proton transfer from ArNH_2NO^+ to a highly acidic medium would not be expected to occur easily and secondly reversion of ArNH_2NO^+ to reactants via displacement of NO^+ by a proton would be expected to become rapid at high acidities.

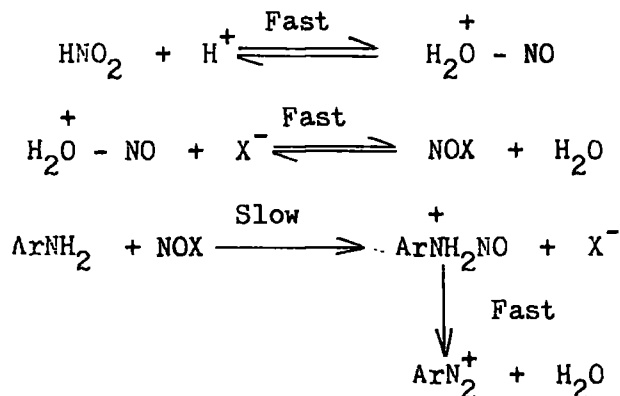
2.3 Halide Catalysed Diazotization

It has long been known that diazotization is catalysed by hydrochloric acid.⁸⁷ Schmid showed that the rate equation for the diazotization of aniline in hydrohalic acids had the form:-^{88,89}

$$\text{Rate} = k [\text{ArNH}_2] [\text{H}^+] [\text{HNO}_2] [\text{X}^-]$$

where X = Cl, Br or I. The same equation applies for diazotization in

perchloric or sulphuric acid containing added halide and Hammett⁸⁰ proposed that this was consistent with rapid formation of the corresponding nitrosyl halide which then nitrosates the amine in the rate-determining step.



This was confirmed when Hughes & Ridd⁸⁰ showed that for bromide and iodide the formation of the nitrosyl halide could be made rate-determining by using a sufficient excess of amine in order to remove the NOX as fast as it was formed. The rate equation then had the form:-

$$\text{Rate} = k [\text{HNO}_2] [\text{H}^+] [\text{X}^-]$$

which corresponds to formation of NOX from the nitrous acidium ion and not N_2O_3 since otherwise a second-order dependence upon nitrous acid would result. Although NOCI is expected to be more reactive than either NOBr or NOI on the basis of simple electronegativity principles, the formation of NOCI has not been made rate-determining in aromatic nitrosation reactions. This is because the equilibrium constants for the formation of NOX from nitrous acid lie in the order $\text{I} > \text{Br} > \text{Cl}$ so that the concentration of NOCI is never large enough to make the nitrosation step faster than the rate of its own formation. These equilibrium constants lie in the same sequence as the nucleophilic reactivities of

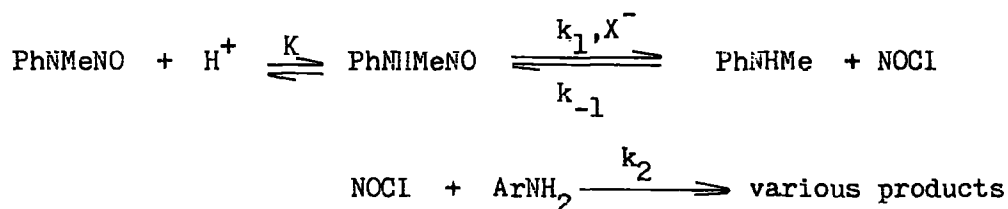
the corresponding X^- species which is in accord with nucleophilic attack by these anions upon the nitrous acidium ion in the NOX formation process. Thus NOX formation is most easily made rate-determining for iodide, and this also explains the apparent greater catalytic effect of bromide as compared to chloride on the observed rate constant for diazotization.

Studies in methanolic hydrochloric acid have shown that the mechanism remains unchanged from the one above, although the reaction is considerably slower,⁹¹ and this has been ascribed to reduction of the NOCI concentration by methanolysis.⁹²



The availability of the equilibrium constants for the formation of NOX from nitrous acid and X^- enabled Schmid & co-workers to calculate the true bimolecular rate coefficients for the reaction of unprotonated amines with both nitrosyl chloride,^{93,94,95} and nitrosyl bromide.^{93,96} However, a number of assumptions were made in evaluating these rate-constants and the kinetic method employed usually involved the analysis of one or two quickly taken points. Nevertheless, the results all lie within the range $1 - 3 \times 10^9 \text{ l mole}^{-1} \text{ sec}^{-1}$ at 25°C . Originally Schmid attempted to correlate these results with the basicities of the amines but the variation is very small and it was later suggested that the rate-constants do in fact approach closely to that expected for a diffusion-controlled process.⁷² This compares with the values of $\sim 10^7 \text{ l mole}^{-1} \text{ sec}^{-1}$ for the corresponding N_2O_3 reactions,⁷² and suggests that the nitrosyl halides are more efficient electrophiles than N_2O_3 .

However, it has been recently suggested that the nitrosyl halide reaction does not involve diffusion-control for the encounter between NOX and ArNH₂.⁹⁷ This contention is based upon an indirect determination of the relative rate-constants for the diazotization of a series of para-substituted anilines in 4.75M hydrochloric acid and in 3.45M sulphuric acid containing thiocyanate where the active nitrosating agents are thought to be NOCl and NOSCN, respectively. The method used is the same as that outlined in section 3.5 of this thesis, that is, the variation of the rate-constant for the denitrosation of N-methyl-N-nitrosoaniline with changing N-methyl-aniline concentration is measured in the presence of the aniline.



where,

$$k_o = \frac{k_1 K h_o [X^-] k_2 [\text{ArNH}_2]}{k_{-1} [\text{PhNHMe}] + k_2 [\text{ArNH}_2]}$$

so that:-

$$k_o^{-1} = \frac{k_{-1} [\text{PhNHMe}]}{k_1 K h_o [X^-] k_2 [\text{ArNH}_2]} + \frac{1}{k_1 K h_o [X^-]}$$

so that $k_{-1}/k_2 [\text{ArNH}_2]$ ratios can be calculated from the values of the slope and intercept for the linear plot of k_o^{-1} versus $[\text{PhNHMe}]$. By equating $[\text{ArNH}_2]$ with the concentration of unprotonated amine relative

k_2 ratios can be calculated since:-

$$\frac{(k_{-1}/k_2)_H}{(k_{-1}/k_2)_R} = \frac{(k_2)_R}{(k_2)_H}$$

These ratios then fall into a discernible pattern for both NOCl and NOSCN with the values for p-toluidine and p-anisidine being $\sim 10^3$ times larger than those for p-nitroaniline and p-aminobenzoic acid. Furthermore, the existence of good Hammett plots of $\log (k_2)_R - \log (k_2)_H$ versus σ_p with slopes of -3.1 and -3.6 respectively for NOCl and NOSCN was taken as evidence against diffusion-control.

It is the intention of this work to attempt to resolve this difference in the results of Schmid & Williams by a detailed examination of the kinetics of diazotization by NOCl and NOBr with the aid of a modern fast reaction technique (see Chapters 5 and 6).

S E C T I O N T W O

CHAPTER THREE

Denitrosation of N-nitrosodiphenylamine

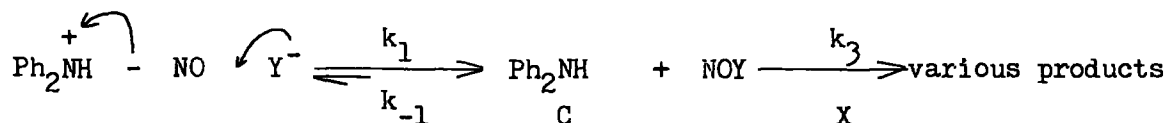
3.1 Effect of Added Nitrite traps (X)

In order to study the catalysis of the denitrosation of aromatic N-nitrosamines by various nucleophiles it is advantageous to work at high trap concentrations so that $k_3 [X] \gg k_{-1} [C]$ and the intramolecular rate expression reduces to:-

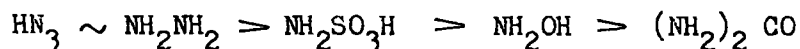
$$k_o = k_1 K h_o [Y] \quad + \quad \frac{k_4 k_5 K h_o}{(k_4 + k_{-5})}$$

(Denitrosation) (Rearrangement)

Physically this means that the step $\text{NOY} + X \longrightarrow \text{products}$ becomes sufficiently fast to remove any free nitrosating agent from the equilibrium system as molecular nitrogen so that the reverse step of N-nitrosation (k_{-1}) is suppressed and denitrosation (k_1) becomes effectively irreversible. No rearrangement then occurs, especially if an efficient nucleophile (Y) is also present in order to catalyse the denitrosation, viz:-



It is now well known that the various nitrite traps (X) exhibit differing reactivity towards a given nitrosating agent (NOY) and for the denitrosation of N-methyl-N-nitrosoaniline the sequence was found to be:-



However, preliminary experiments with N-nitrosodiphenylamine have indicated that the limit at high $[X]$ cannot easily be reached with any

of these species except hydrazoic acid. Moreover a relatively large concentration of hydrazoic acid is required before the limit can be reached. This contrasts with the case of N-methyl-N-nitrosoaniline where the limit can be satisfied for all the trap species. The most likely explanation for this is that the different basicities of the two products of denitrosation, diphenylamine and N-methylaniline, leads to more extensive protonation of the latter in solutions of comparable acidity. Since it is generally regarded that the free bases are more reactive towards nitrosation than the corresponding conjugate acids,⁷² and since there is proportionately more free base present in the case of diphenylamine, the bulk rate of the reverse step of N-nitrosation can be expected to be faster than in the case of N-methylaniline. Hence, in order to satisfy the condition $k_3 [X] \gg k_{-1} [C]$ for the denitrosation of N-nitrosodiphenylamine, a relatively large concentration of reactive trap will be needed.

The results obtained for denitrosation of N-nitrosodiphenylamine (initially $3.1 \times 10^{-4} M$) in sulphuric acid (0.625M) containing potassium bromide ($3.15 \times 10^{-2} M$) are drawn up in Table 1.

TABLE I

| $10^3 k_o \text{ sec}^{-1}$ | $10^2 [\text{Azide}] M$ |
|-----------------------------|-------------------------|
| 11.2 | 1.58 |
| 16.2 | 3.17 |
| 19.8 | 4.74 |
| 21.6 | 6.33 |
| 22.4 | 7.91 |
| 23.3 | 9.50 |
| 22.6 | 11.08 |
| 23.9 | 12.66 |
| 23.7 | 14.24 |
| 23.9 | 15.83 |

$10^3 k_0$ (sec⁻¹)

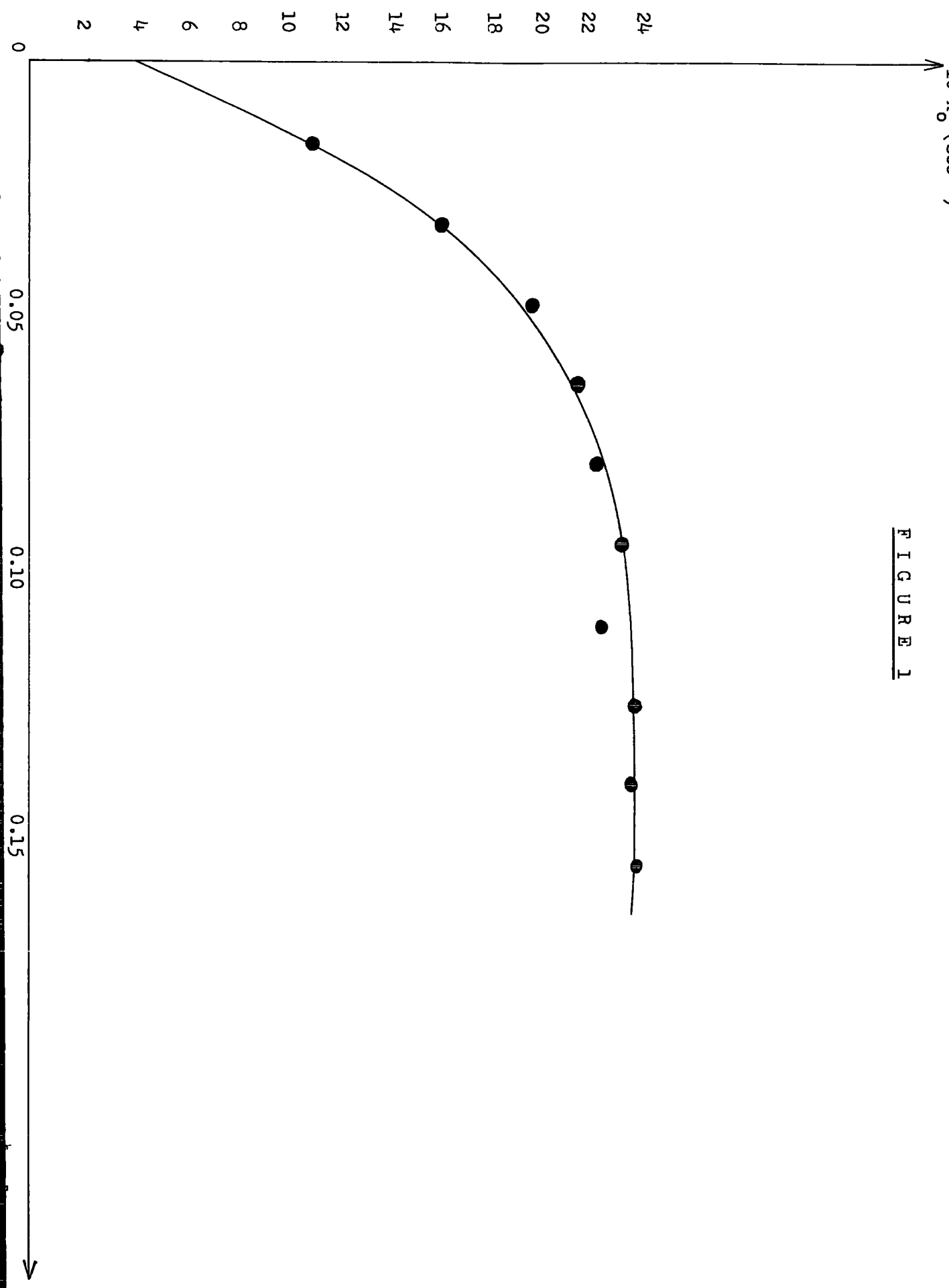


FIGURE 1

The curve is shown in Figure 1, where it can clearly be seen that k_o becomes independent of azide concentration at around 0.16M. No rearrangement product was detected spectrophotometrically in these solutions.

Measurement of the relative reactivities of several trap species toward reaction with NOY during the denitrosation of N-nitrosodiphenylamine is discussed in Section 3.5.

3.2 Catalysis by various nucleophiles: (Y)

With rearrangement and the reversibility of denitrosation suppressed at the limit of high $[X]$ the quantitative assessment of the relative reactivity of various nucleophiles in the denitrosation process can be easily achieved since the rate expression reduces to the form $k_o = k_1 K h_o [Y]$. Hence, for a given nucleophile, a plot of k_o versus $[Y]$ should be linear with slope $k_1 K h_o$. The intercept corresponds then, not with rearrangement, but with denitrosation by the solvent (i.e. $Y = H_2O$) and at any one acidity should be common to all added nucleophiles.

Catalysis was demonstrated by carrying out the reaction at one acidity in sulphuric acid containing varying amounts of NaCl, KBr, KCNS, KI and thiourea. Sufficient sodium azide was used to satisfy the limiting condition $k_3 [X] \gg k_{-1} [C]$. Good straight lines were obtained in each case. The results are summarized in Tables 2 to 6.

TABLE 2

$$[\text{H}_2\text{SO}_4] = 0.528\text{M}, [\text{Ph}_2\text{N.NO}] = 3.06 \times 10^{-4}\text{M}, [\text{NaN}_3] = 0.159\text{M}$$

corr.coef.
= 0.998

| $10^4 k_0 \text{ sec}^{-1}$ | $10^2 [\text{Chloride}] \text{ M}$ |
|-----------------------------|------------------------------------|
| 44.9 | 9.7 |
| 72.3 | 19.4 |
| 97.6 | 29.1 |
| 118.6 | 38.8 |
| 140.9 | 48.5 |

TABLE 3

$$[\text{H}_2\text{SO}_4] = 0.518\text{M}, [\text{Ph}_2\text{N.NO}] = 3.12 \times 10^{-4}\text{M}, [\text{NaN}_3] = 0.158\text{M}$$

corr.coef.
= 0.997

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{Bromide}] \text{ M}$ |
|-----------------------------|-----------------------------------|
| 83.4 | 8.01 |
| 146.5 | 16.02 |
| 180.3 | 24.04 |
| 233.5 | 32.05 |
| 290.2 | 40.06 |

TABLE 4

$$[\text{H}_2\text{SO}_4] = 0.521\text{M}, [\text{Ph}_2\text{N.NO}] = 1.62 \times 10^{-4}\text{M}, [\text{NaN}_3] = 0.158\text{M}$$

| | $10^4 k_o \text{ sec}^{-1}$ | $10^4 [\text{SCN}^-] \text{ M}$ |
|-----------------------|-----------------------------|---------------------------------|
| | 47.2 | 7.78 |
| corr.coef. = 0.997 | 80.1 | 15.56 |
| | 118.8 | 23.26 |
| | 143.5 | 31.05 |
| | 187.7 | 38.83 |

The thiocyanate concentrations have been corrected to allow for protonation.

$$[\text{SCN}^-] = [\text{SCN}^-]_{\text{TOTAL}} / (1 + K [\text{H}^+])$$

With $K = 1/K_{\text{BH}^+} = 10^{\cdot pK_{\text{BH}^+}} = 0.199^{98}$ and $[\text{H}^+] = 0.884$, i.e. by using the H_3O^+ left over after assuming complete protonation of the azide.

TABLE 5

$$[\text{H}_2\text{SO}_4] = 0.523\text{M}, [\text{Ph}_2\text{N.NO}] = 1.62 \times 10^{-4}\text{M}, [\text{NaN}_3] = 0.158\text{M}$$

| | $10^4 k_o \text{ sec}^{-1}$ | $10^4 [\text{Thiourea}] \text{ M}$ |
|-----------------------|-----------------------------|------------------------------------|
| | 39.1 | 8.34 |
| corr.coef. = 0.995 | 74.8 | 16.68 |
| | 100.9 | 24.93 |
| | 139.1 | 33.27 |
| | 157.7 | 41.61 |

The thiourea concentrations have been corrected for protonation as in the case of thiocyanate with $K = 0.110^{99}$ and $[\text{H}^+] = 0.888$.

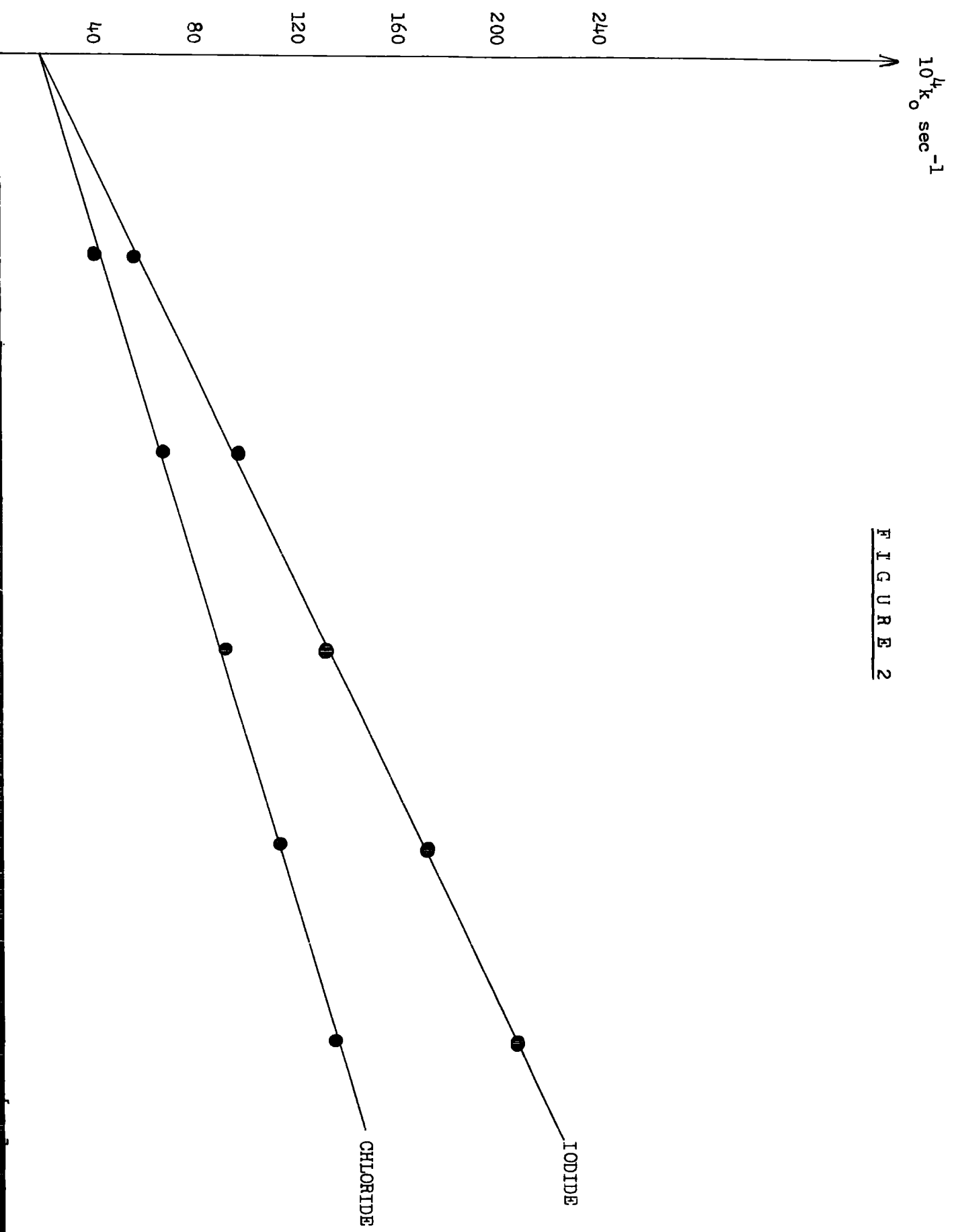


FIGURE 2

TABLE 6

$$[\text{H}_2\text{SO}_4] = 0.531\text{M}, [\text{Ph}_2\text{N.NO}] = 1.62 \times 10^{-4}\text{M}, [\text{NaN}_3] = 0.158\text{M}$$

| | $10^4 k_o \text{ sec}^{-1}$ | $10^4 [\text{Iodide}] \text{ M}$ |
|------------|-----------------------------|----------------------------------|
| | 60.1 | 0.97 |
| corr.coef. | 102.7 | 1.94 |
| = 0.999 | 136.8 | 2.92 |
| | 176.9 | 3.89 |
| | 213.3 | 4.86 |

Figure 2 illustrates, on different scales, the lines for chloride and iodide. From those for all the nucleophiles studied a common intercept of $(2.2 \pm 0.5) \times 10^{-3} \text{ sec}^{-1}$ can be calculated. The error is quite high being $\sim 20\%$ but then small errors in the slopes will lead to a relatively large scatter about the mean intercept.

The slope of each line represents the value of $k_1 K h_o$ for the corresponding nucleophile. Calculation of the $k_1 K$ values requires a knowledge of h_o . As an approximation it has been assumed that the azide is completely protonated (being about as basic as aniline with $pK_{\text{BH}^+} = 4.74$.⁹⁸) so that the residual H^+ concentration has been used to estimate h_o from the calibration of H_o with sulphuric acid concentration given by Robertson and Dunford.¹⁰⁰ The values of $k_1 K$ calculated in this way are given in Table 7.

One might reasonably expect these $k_1 K$ values to reflect the nucleophilic reactivity of the above nucleophiles towards reaction with the protonated form of N-nitrosodiphenylamine. However, the subject of nucleophilic reactivity is very complex, and in the absence of detailed

knowledge of the potential energy surfaces for heterolytic reactions in solution, relies heavily upon the correlation of the observed rate-constants with various other parameters associated with the reaction in question.

TABLE 7

| NUCLEOPHILE | $10^2 k_1 k_{h_0}$ | $[H^+]$ free | h_0 | $10^2 k_1 K$ |
|-------------|--------------------|--------------|-------|--------------|
| Chloride | 2.46 | 1.056 | 0.785 | 3.13 |
| Bromide | 62.5 | 1.037 | 0.762 | 82.02 |
| Thiocyanate | 443.9 | 1.042 | 0.771 | 575.75 |
| Thiourea | 362.7 | 1.047 | 0.778 | 466.19 |
| Iodide | 391.1 | 1.062 | 0.794 | 492.57 |

Thus Ingold¹⁰¹ had originally proposed that nucleophilicity could be reasonably well correlated with basicity, a view now known to be erroneous, except for closely related nucleophiles where the reactivity can be correlated with the corresponding pK_{BH^+} values as in the familiar Bronsted relationship.¹⁰² Following the pattern of logic established by the introduction of the Hammett equation,¹⁰³ Swain & Scott¹⁶ defined a nucleophilic parameter 'n' as a measure of nucleophilic reactivity for substitution at a saturated carbon atom in terms of the equation:-

$$\log k/k_0 = sn$$

for which the standard substrate is methyl bromide ($s = 1.0$) and the standard nucleophile, water ($n = 0$). A series of 'n' values was then built up by fitting $\log k/k_0$ to this standard line where k is the second-order rate-constant for reaction with the nucleophile and k_0 the corresponding rate-constant for the water reaction. It must be noted that 'n' is therefore a logarithmic quantity, for example $n_{Cl} = \log k_{Cl}/k_{H_2O}$, and the usual criticisms of log - log correlations must be borne in mind

when correlating 'n' values with $\log k/k_0$ values obtained for reaction with a different substrate. It is immediately obvious that the minimum requirement for successful correlation is the same nucleophilic reactivity sequence in both reactions, and this is not always the case. It is therefore surprising to find that the $\log k_1K$ values obtained for the denitrosation of N-methyl-N-nitrosoaniline by various nucleophiles correlate very well with the 'n' values of Swain & Scott, even though reaction now occurs at positive nitrogen rather than neutral carbon.¹⁴ This is quite possibly due to the two types of reaction centre being isoelectronic. Furthermore, the denitrosation process can be seen to be analogous to the standard reaction by regarding the product amine as the leaving group. However, before proceeding with the Swain-Scott correlation it is as well to realise that this type of analysis is open to severe criticism.

Firstly, linear free energy relationships nearly always attempt to express 'reactivities' in terms of $\log k$ or $\log K$ as seen in the case of the 'n' parameter. However, these quantities are strongly temperature dependent and it is thus conceivable that the relative reactivity within a reaction series could also change with temperature. Furthermore, LFER were originally thought to be applicable only to those reaction series for which ΔS^\ddagger is constant, i.e. invariant with respect to changing substrate structure. This is now known to be untrue, a sufficient criterion being the existence of a linear relationship between ΔH^\ddagger and ΔS^\ddagger as the substrate structure is changed. This is the so-called isokinetic relationship. However, establishing the existence of such a relationship within a reaction series is rendered difficult by the fact that ΔH^\ddagger and ΔS^\ddagger by definition, must be linearly related to each other, and excellent correlation becomes unavoidable. Exner has pointed

out in a penetrating review¹⁰⁴ the absolute necessity of correct statistical analysis before concluding that a reaction series satisfies the isokinetic relationship. Indeed, by using data from earlier studies, Exner has shown that for several purportedly well-behaved reaction series no isokinetic relationship can be detected at all. It would thus appear that the number of reaction series to which LFER can be legitimately applied is not so great as was once thought.

Secondly there is the problem of deciding what exactly constitutes an excellent correlation. This is usually determined by the value of the correlation coefficient (r) which for perfect correlation has the value ± 1.0 . In a recent student textbook Shorter gives the following general advice,¹⁰⁵ $r = 0.99 - 1.00$ (excellent), $r = 0.95 - 0.99$ (satisfactory), $r = 0.90 - 0.95$ (fair) and $r < 0.90$ (poor). However, Heilbronner¹⁰⁶ has pointed out that the correlation of two sets of N random numbers which are ranked in the same order, will yield a correlation coefficient in excess of 0.9. For example, with $N = 10$, a Monte-Carlo method gives an expectation value for r of 0.94. For $N = 40$ this is increased to ~ 0.98 . The conclusion is therefore that "r values must be much larger than is usually assumed before a theoretical model can be said to be better than random." Of course this state of affairs becomes even more apparent for log-log graphs.

Finally, problems arise from (a) deciding what exactly constitutes a representative reaction series, (b) having a large selection of possible parameters with which to attempt correlation and (c) the possibility of overlooking real non-linear relationships. The method is therefore open to a more subjective approach than the usual scientific procedure of using deductive logic to derive experimentally testable

predictions from rival theoretical models.

With these points in mind the Swain-Scott correlation for the denitrosation of N-nitrosodiphenylamine is presented in Table 8 and Figure 3 solely for comparison with that given for N-methyl-N-nitrosoaniline in reference 14.

TABLE 8

| NUCLEOPHILE | $2 + \log k_1 K$ | 'n' |
|-------------|------------------|------|
| Chloride | 0.391 | 4.37 |
| Bromide | 1.796 | 5.79 |
| Thiocyanate | 2.647 | 6.70 |
| Thiourea | 2.559 | 7.27 |
| Iodide | 2.592 | 7.42 |

The 'n' values are those due to Pearson.¹⁰⁷ Drawing the line through the first three points only, as in Figure 3, is possibly vindicated by the excellent value of 0.9999 thus obtained for the correlation coefficient. The deviance of iodide and thiourea can then be ascribed to a steric effect. The slope of the line gives a measure of the susceptibility of the denitrosation of N-nitrosodiphenylamine to changes in 'n' and has a value of 0.97. This compares with the value of 1.41 obtained for N-methyl-N-nitrosoaniline.¹⁴ (N.B. this reference quotes $s = 2.1$ by using the original 'n' values of Swain & Scott. The value of $s = 1.41$ is obtained from the same data but by using the 'n' values of Pearson).

However, it is quite possible that the apparent deviation of iodide and thiourea is due to the influence of the diffusion-controlled limit upon k_1 . For I^- , SCN^- , and $SC(NH_2)_2$ the mean value of $k_1 K$ is 0.51 ± 0.03 . If we assume that $k_1 \sim 7 \times 10^9$ l mole sec^{-1} (ref.153) then:-

$$K_{\text{BH}^+} = 1/K = 1.37 \times 10^{10}$$

so that $\text{p}K_{\text{BH}^+} \sim -10$

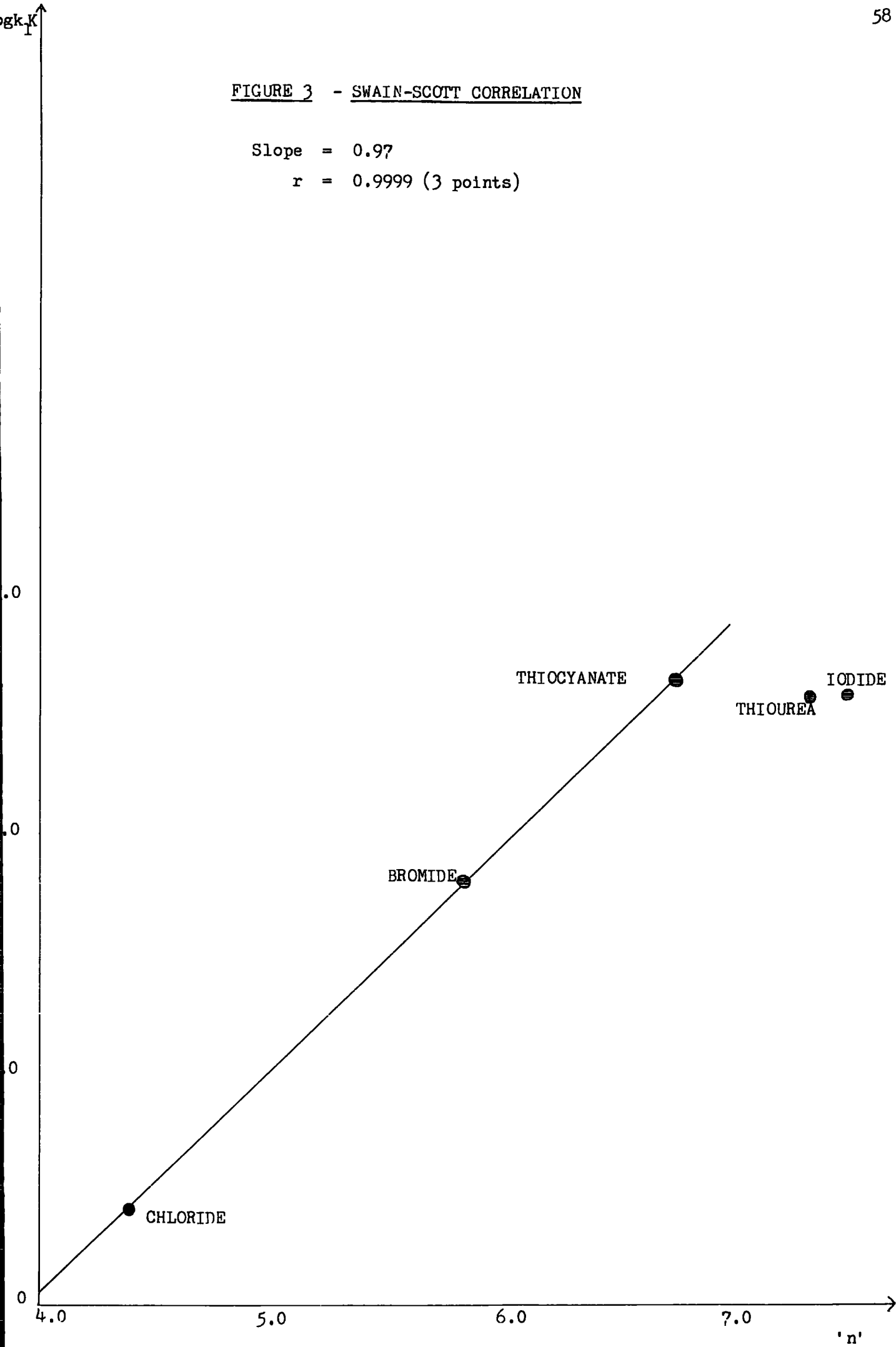
This agrees quite well with the results of the Bunnett correlation of section 3.3 where the $\text{p}K_{\text{BH}^+}$ of the protonated nitrosamine is shown to lie in the range -1.2 to -15.

Thus it would appear that, with respect to denitrosation, $\text{Ph}_2\text{NH}^+\text{NO}$ is less selective than PhNHMe.NO toward changes in 'n'. That this reflects the greater 'reactivity' of the former because of the different electronic effects of methyl and phenyl substituents is open to debate. The reactivity - selectivity principle, recently reviewed by Pross,¹⁰⁸ is open to the same kind of criticism as outlined above for LFER, so mechanistic interpretations in terms of differences in transition-state structure will be avoided.

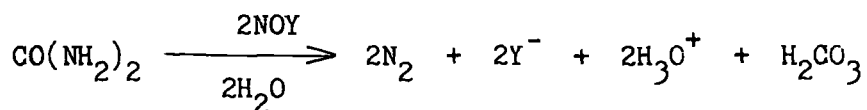
However, whatever the conclusions drawn from the Swain-Scott correlation, one thing is certain, and this is the fact that thiourea behaves as a nucleophile in reacting directly with the conjugate acids of both nitrosamines. Urea itself does not, preferring to react via prior dissociation of the nitrosamines into species such as H_2NO_2^+ and NOCl . Why this should be so is not quite clear. Both nitrosamines can be regarded as soft electrophiles since the positive charge in each conjugate acid is delocalised, and as a result might be expected to prefer to react directly with soft bases such as the sulphur site in thiourea. Incidentally, all of the nucleophiles used in this study are classified as soft bases, except chloride. Conversely, urea only contains relatively hard N and O sites and would therefore prefer to react with the relatively harder electrophiles such as H_2NO_2^+ and NOCl . As a result urea undergoes N-nitrosation and

FIGURE 3 - SWAIN-SCOTT CORRELATION

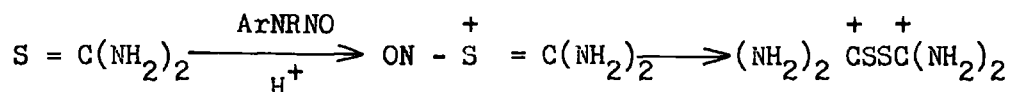
Slope = 0.97

 $r = 0.9999$ (3 points)

deamination:-

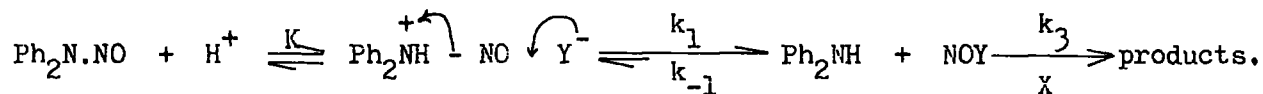


as is well known, whereas thiourea undergoes S-nitrosation to give the C,C¹ - dithiodiformamidinium dication during which the amino groups remain intact.²³



With nitrous acid thiourea is believed to undergo initial S-nitrosation as above coupled with rearrangement to the N-nitroso isomer and subsequent deamination.²⁴ This would suggest that NO⁺ and its 'carriers' tend to lie on the soft side of borderline in the hard-soft classification of Lewis acids. It could well be that protonated aromatic nitrosamines form the 'softest' set of nitrosonium ion carriers currently available.

Challis and Osborne³⁸ have reported that the denitrosation of N-nitrosodiphenylamine in 50% aqueous ethanol becomes independent of the nucleophile concentration when the latter is sufficiently high. This has been confirmed for the bromide catalysed reaction, the results being given in Table 9 and Figure 4. This observation could be due to either (i) the effect of approaching the diffusion-controlled limit on k₁ or (ii) the shift of the rate-determining step to an earlier stage of the reaction.



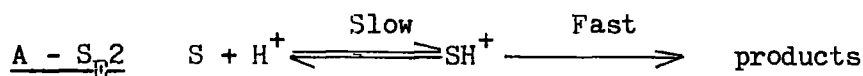
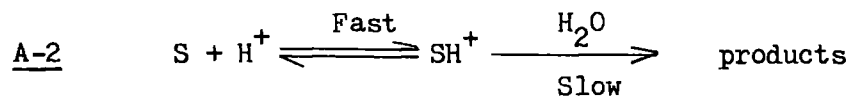
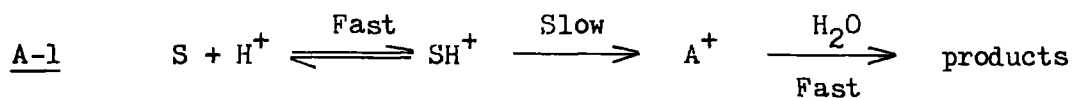
The latter therefore requires the initial protonation to become rate-determining. There are three possible types for this mechanism depending upon which steps are fast and which are slow. These are the

A-1, A-2, and A-S_E2 mechanisms for acid-catalysed reactions.

$$[\text{H}_2\text{SO}_4] = 0.21\text{M}, \quad [\text{Ph}_2\text{N.NO}] = 3.09 \times 10^{-3}\text{M}, \quad [\text{NaN}_3] = 0.165\text{M}$$

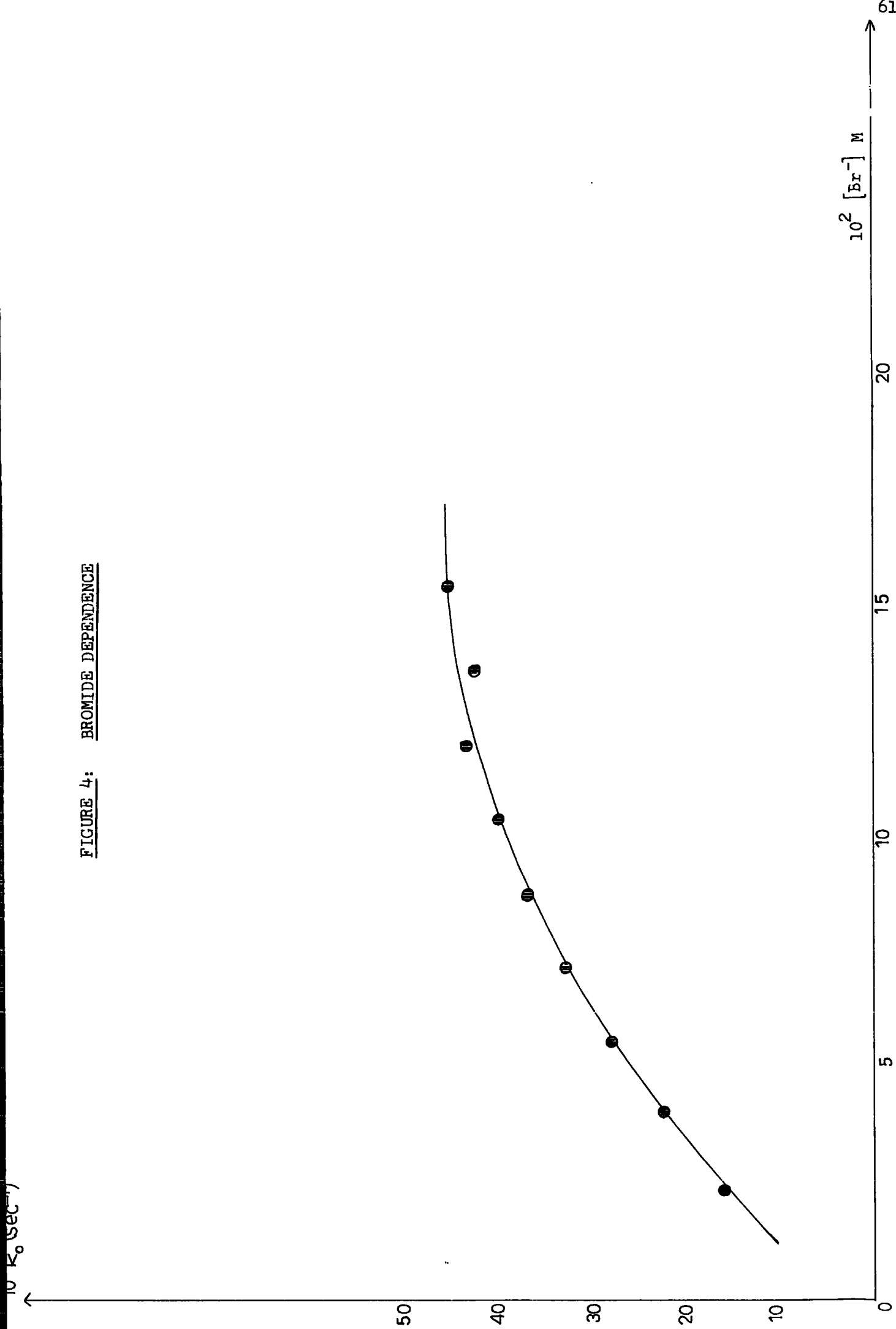
TABLE 9

| $10^4 k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|-----------------------------|--------------------------------|
| 16.2 | 2.4 |
| 22.7 | 4.1 |
| 28.2 | 5.6 |
| 33.3 | 7.2 |
| 37.5 | 8.8 |
| 40.6 | 10.4 |
| 44.1 | 12.0 |
| 43.2 | 13.6 |
| 46.0 | 15.4 |



The analog of the A-2 mechanism cannot be operative at high bromide concentration because of the zero-order dependence on bromide in this region. The choice lies between the A-1 and A - S_E2 mechanisms. For the latter, where proton transfer is rate-determining, statistical mechanical calculations predict that the solvent isotope effect $k_{\text{D}_2\text{O}} / k_{\text{H}_2\text{O}}$ will be less than unity compared with values of $\sim 2.5 - 3.3$

FIGURE 4: BROMIDE DEPENDENCE



for the A-1 mechanism.¹⁰⁹ The results are shown in Table 10 where exact concentrations have not been given because of variations in the acidity in the two cases.

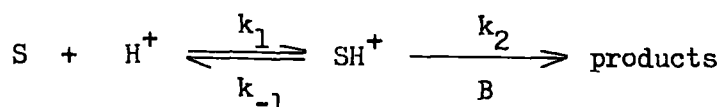
TABLE 10

| Bromide | k_{D_2O}/k_{H_2O} |
|---------|---------------------|
| LOW | 2.0 |
| HIGH | 0.8 |

It thus appears that the initial proton-transfer is indeed rate-determining at high bromide concentration. This isotope effect compares favorably with those obtained for N-nitrosamides (0.5)^{33,34} and N-methyl-N-nitrosotoluene-p-sulphonamide (0.7)³⁷ for which the initial proton transfer is believed to be rate-determining at all nucleophile concentrations. The isotope effect at low bromide concentration does not distinguish clearly between the A-1 and A-2 mechanisms but the observation of bromide catalysis in this region supports the A-2 mechanism.

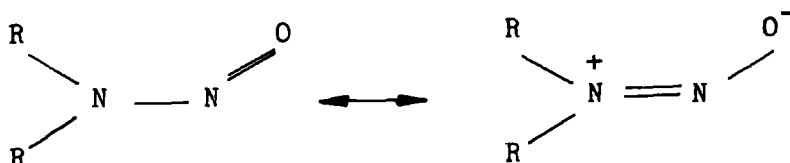
Westheimer's model for proton transfer reactions¹¹⁰ predicts a k_D/k_H ratio of ~ 0.2 for a symmetrical transition state. The observed value of 0.8 is too large for this but is in line with the predictions for unsymmetrical transition states of ~ 1.0 (reactant-like) and 0.7 - 1.4 (product-like). The model cannot distinguish between the latter two types.

The different behaviour of nitrosamines and nitrosamides can be rationalised as follows:

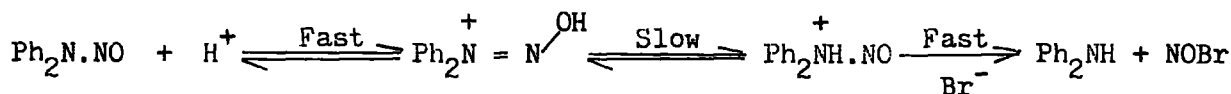


For nitrosamines k_1 is below the diffusion-controlled limit because of their weak basicity, and so, when $k_2 [B]$ approaches this limit at high $[B]$, k_1 can become rate-determining. The nitrosamides are even weaker bases so that k_1 is well below the diffusion-controlled limit and $k_2 [B] > k_1$ at all values of $[B]$.

In this thesis the protonation of the nitrosamine has been assumed to occur at the amino nitrogen. This may not be the case since evidence has been presented, from n.m.r. studies on aliphatic nitrosamines, in support of protonation at the oxygen atom¹¹¹ viz. $R_2N^+ = N-OH$ and this is consistent with the known dipolar character of neutral $R_2N.NO$ molecules.^{112,113}



However, Layne et alia have reported the existence of several protonated species in dilute acidic media.¹¹⁴ The exact nature of the protonated form of the nitrosamine which actually reacts with the nucleophile is therefore in some doubt. Challis & Osborne³⁸ prefer a scheme whereby at high halide concentration the protonation of the neutral nitrosamine is not rate-determining but rather that rearrangement of one protonated form to another becomes the slow step.



However, this is an example of the A-1 mechanism for which the solvent isotope effect k_D/k_H is expected to lie in the range 2.5 - 3.3¹⁰⁹ and which is ruled out by the observed k_D/k_H of 0.8. Challis & Osborne themselves measured k_D/k_H to be 1.2 for reaction at high $[Cl^-]$ in 50% aqueous ethanol but were reluctant to accept an unsymmetrical transition

state. The difference between the observed values of 1.2 and 0.8 may be due to the different solvent systems employed. However, whatever the detailed conclusions all are agreed that the rate-determining step shifts to an earlier part of the reaction as the halide concentration is raised. If the disappearance of halide catalysis were solely due to the influence of the diffusion-controlled limit upon the selectivity of the nitrosamine one would still expect fast initial proton transfer (overall) and this is not observed.

3.3 Acidity Dependence:

In the absence of added nucleophiles one might expect Fischer-Hepp rearrangement to compete more effectively with denitrosation since the rate of the latter is then much reduced. However, no rearrangement product could be detected spectrophotometrically in the aqueous sulphuric acid solutions that were used. The denitrosation was found to be acid-catalysed. It is interesting to note that Challis & Osborne³⁸ only observed significant acid catalysis at high azide concentration. This is no doubt due to the fact that at low acidity the active trap N_3^- is increasingly deactivated by protonation as the acidity is raised and this counterbalances to some extent the effect of the increasing protonation of the nitrosamine. At the limit $k_3 [X] \gg k_{-1} [C]$ the reaction is zero-order in azide and only the increasing protonation of the nitrosamine has any significant kinetic effect. At much higher acidities protonation of the trap again becomes kinetically significant.²⁰

The results for denitrosation in aqueous sulphuric acid are shown in Table 11 where initially $[Ph_2N.NO] = 1.6 \times 10^{-4} M$ and $[NaN_3] = 0.16M$. Again complete protonation of the azide has been assumed and the quoted values of $[H^+]$ are those calculated from $[H^+]_{tot} - [HN_3]$. General acid catalysis is believed not to occur since the denitrosation is catalysed by Cl^- , Br^- , I^- , SCN^- and $SC(NH_2)_2$ but not by the anions

HSO_4^- or NO_3^- . This is analogous to the diazotization of aniline and o-chloroaniline.¹¹⁵

TABLE 11

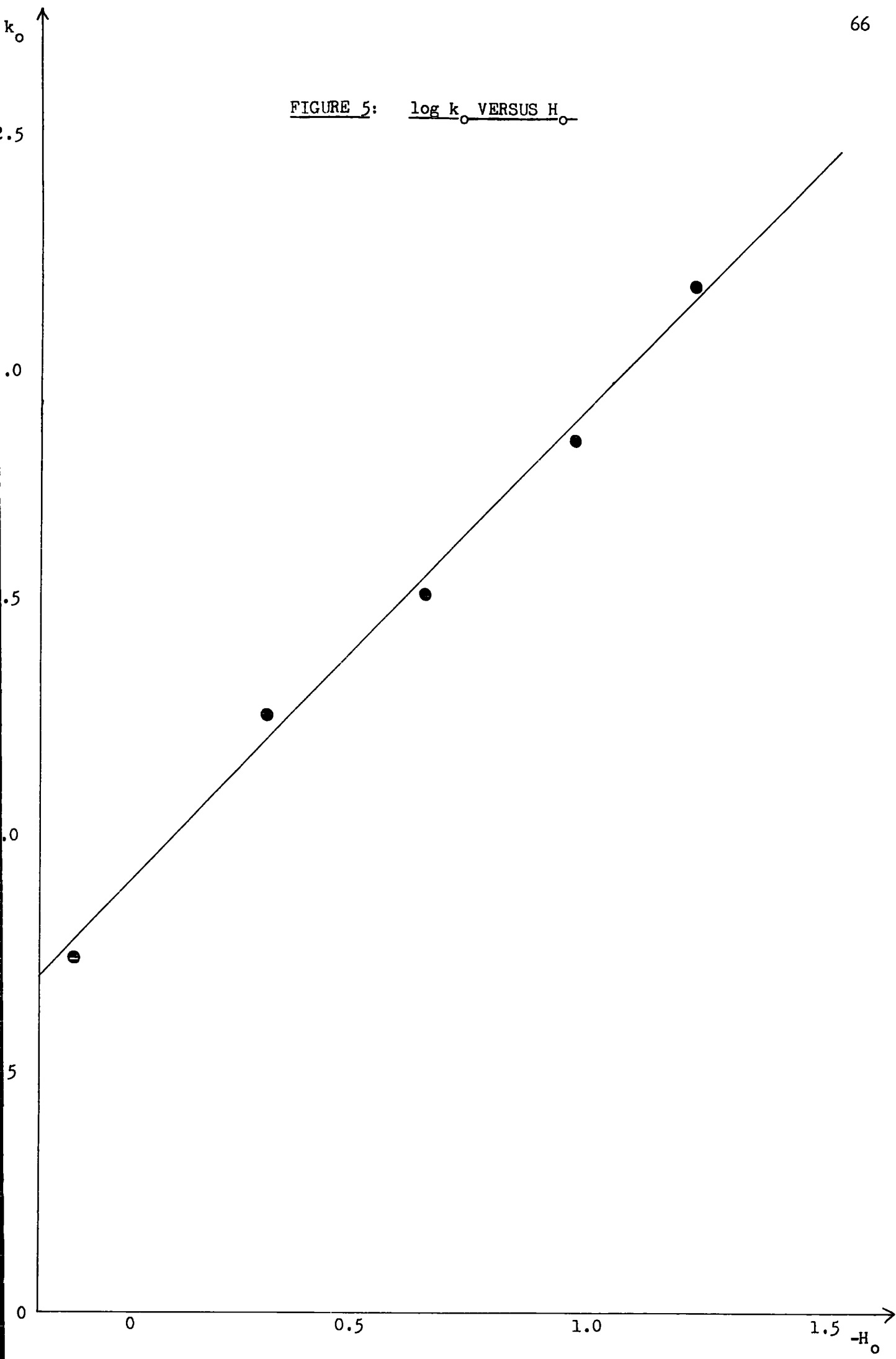
| $10^4 k_o \text{ sec}^{-1}$ | $[\text{H}^+] \text{ M}$ | $4 + \log k_o$ | $\log[\text{H}^+]$ | $-\text{H}_o$ |
|-----------------------------|--------------------------|----------------|--------------------|---------------|
| 5.7 | 1.04 | 0.756 | 0.017 | -0.13 |
| 18.8 | 2.14 | 1.274 | 0.330 | 0.28 |
| 34.2 | 3.30 | 1.534 | 0.518 | 0.62 |
| 73.6 | 4.62 | 1.867 | 0.665 | 0.94 |
| 155.4 | 5.82 | 2.191 | 0.765 | 1.20 |

The values of H_o have been obtained by interpolation from the data of Robertson & Dunford.¹⁰⁰ Since the substrate molecule is closely related to the aniline derivatives used to define the H_o acidity function one might reasonably expect its use to be valid here. Another acidity function H'_o has been defined for tertiary amines and at high acidities in sulphuric acid deviates markedly from H_o .¹¹⁶ One might expect this to be a better function to use than H_o but at low acidities the differences are small and as an approximation H_o has been used for simplicity.

The use of H_o allows the Zucker-Hammett hypothesis¹¹⁷ to be invoked, according to which a distinction can be made between reactions following the A-1 and A-2 mechanisms. The hypothesis claims that for A-1 reactions $\log k$ will be a linear function of H_o whereas for A-2 reactions $\log k$ and $\log [\text{H}^+]$ will be linearly related. (k = observed first-order rate constant).

In the present example it is found that the graph of $\log k$ versus $\log [\text{H}^+]$ is curved whereas that between $\log k$ and H_o is linear. The latter is shown in Figure 5 and for which $r = 0.997$. The slope is 1.04 which is consistent with the theoretical value of unity for reaction via a singly protonated intermediate. A similar result was obtained for the denitrosation of N-methyl-N-nitrosoaniline but with a slope of 1.2.⁹ The Zucker-Hammett criterion therefore comes down in favor of the A-1 mechanism.

However, the observed halide catalysis and solvent isotope effect at low halide concentration support the A-2 mechanism. Also, the derivation of the rate equations for both inter- and intramolecular mechanisms assumes that denitrosation can be brought about by reaction with the solvent in the rate-determining step. Thus the simultaneous demonstration of halide catalysis and the linearity of $\log k_o$ versus H_o is logically inconsistent.¹¹⁸ In order to clear up this inconsistency it has been assumed that, in this case, the Zucker-Hammett treatment is in error since it is now regarded as not being generally valid.¹¹⁹

FIGURE 5: $\log k_0$ VERSUS H_0 

On the basis of the failure of the Zucker-Hammett hypothesis in several instances Bunnett¹²⁰ suggested an alternative criterion of mechanism. He introduced empirical equations to take into account the solvation requirements of the transition state. These equations involve the water activity (a_w), a factor neglected in the Zucker-Hammett treatment,

$$\text{A-1} \quad \log k + H_o = w \log a_w + \text{constant}$$

$$\text{A-2} \quad \log k - \log [H^+] = w^* \log a_w + \text{constant}$$

and as a result are regarded as being more satisfactory. For substrates protonated on oxygen or nitrogen the slopes of such plots (w & w^*) are believed to be characteristic of the way in which water is involved in the rate-determining step of acid catalysed reactions. There are three broad classes of involvement as shown in Table 12.¹²⁰

TABLE 12

| INVOLVEMENT OF WATER | w | w* |
|---|------------|------|
| Not involved ($SH^+ \rightarrow$ products) | -2.5 - 0.0 | |
| Nucleophile ($SH^+ + H_2O \rightarrow H_2O.SH^+$) | 1.2 - 3.3 | < -2 |
| Base ($SH^+ + H_2O \rightarrow S + H_3O^+$) | > 3.3 | > -2 |

The experimental results for N-nitrosodiphenylamine do not fit the first Bunnett equation (A-1), correlation being ridiculous ($r = -0.47$). However, they do fit the second equation, the relevant data being given in Table 13 and the graph shown in Figure 6. The values of a_w have again been interpolated from the data of Robertson & Dunford.¹⁰⁰

FIGURE 6: BUNNETT CORRELATION

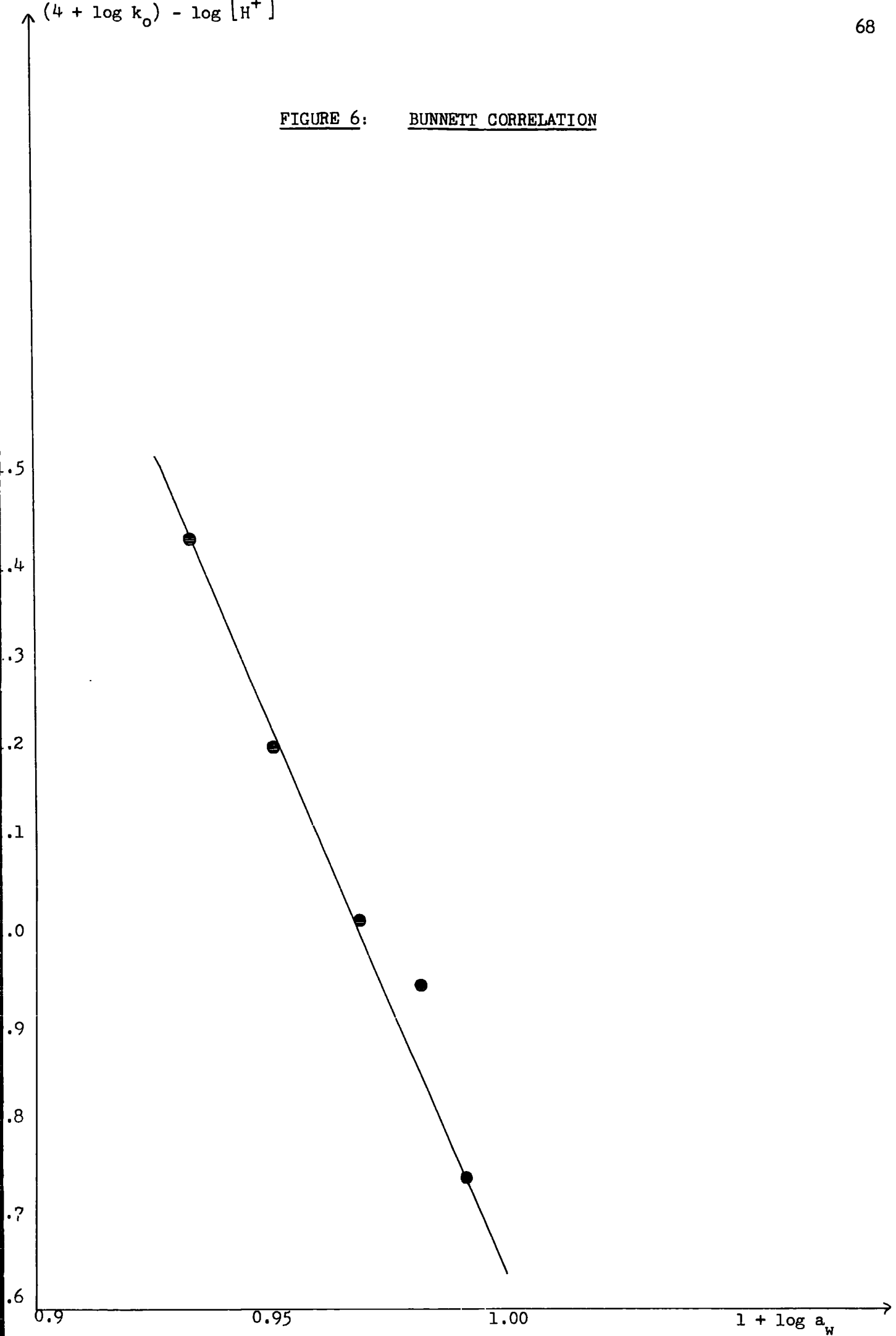


TABLE 13

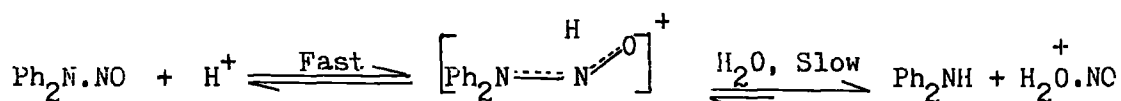
| $(4 + \log k_o) - \log [H^+]$ | $1 + \log a_w$ |
|-------------------------------|----------------|
| 0.739 | 0.992 |
| 0.994 | 0.982 |
| 1.016 | 0.969 |
| 1.202 | 0.952 |
| 1.426 | 0.933 |

Figure 6 clearly shows that the second point in this Table is significantly deviant to warrant its exclusion from the least squares calculation. Thus the slope (w^*) has a value of -11.6 with $r = -0.9998$. This successful correlation of the experimental results by means of Bunnett's second equation with $w^* \ll 2$ implies that water does in fact behave as a nucleophile in the rate-determining step, and that the mechanism is A-2, in line with the observation of halide catalysis. In fact this equation is only theoretically valid when (a) $[B] \gg [BH^+]$ and (b) $K_{BH^+} \gg h_o$. The first condition is assumed in the steady-state treatment of the intra- and intermolecular mechanisms. The second condition shows, in the equivalent form $H_o \gg pK_{BH^+}$, that pK_{BH^+} must be less than -1.2 for protonated N-nitrosodiphenylamine. ($H_o = -1.2$ is the highest acidity studied). The true pK_{BH^+} value will therefore probably lie somewhere between -1.2 and -15, the latter being a crude estimate of the pK_{BH^+} value of N-n-butyl-N-nitrosoacetamide.³³

The value of w^* can be taken as a crude measure of the difference in solvation number between the transition state and reactants. (B & H⁺).

Thus the transition state leading to denitrosation of N-nitrosodiphenylamine contains approximately $12H_2O$ less than the solvated free base and proton. This is not too surprising since the positive charge on the conjugate acid of the nitrosamine is largely delocalised so that the molecule will be much less polarising than the proton.

The overall scheme, as indicated by the Bunnett treatment, is then:-



Although Bunnett's criterion of mechanism appears to work very well here it is known to predict the wrong answers in some cases. For the hydrolysis of methyl- α -D-glucopyranoside an A-2 mechanism was suggested¹²⁰ but the ΔV^\ddagger value for this reaction strongly suggests an A-1 mechanism.¹²¹ Accurate determination of ΔV^\ddagger for the present reaction would therefore prove useful.

Finally, it may be of interest to note that the Zucker-Hammett treatment was rejected, not because it failed to give good correlation, but because it suggested a mechanism which conflicted with alternative evidence. This emphasises the fact that obtaining an excellent linear correlation can be fortuitous and this should be taken together with the critique of LFER in general, as outlined in section 3.2. Most importantly it shows that mechanistic conclusions should be based on evidence obtained from as wide a range of techniques as possible. The correlation of $\log k_0$ with $-H_0$ for N-methyl-N-nitrosoaniline⁹ should therefore be regarded as probably being fortuitous.

3.4 Formation of the Blue Coloration

In the absence of both added nucleophile and azide it was again hoped that Fischer-Hepp rearrangement would be observed. However, the addition of $2.6 \times 10^{-4} \text{ M}$ methanolic N-nitrosodiphenylamine to 3M sulphuric acid resulted in the very rapid formation of a deep blue colour. More precisely, the absorption at 290 nm due to the nitrosamine disappears and is replaced by a broad band centered at 570 nm. The absence of significant absorption in the region of 280 nm precludes the existence of diphenylamine in the blue solution. The blue colour is stable to air and persists for approximately one week when air is excluded.

It is well known that a solution of diphenylamine in concentrated sulphuric acid gives a deep blue colour in the presence of oxidizing agents such as nitrous acid,¹²² and this has led to the use of such solutions as indicators, for example in the oxidation of iron (II) with dichromate.¹²² However, this colour does not form readily in dilute ($\sim 1\text{M}$) sulphuric acid and is destroyed on dilution with water. This contrasts with the behaviour of the blue from N-nitrosodiphenylamine.

The rapidity of reaction and the intense colour suggests that a relatively stable free radical is responsible. Support for this view came from the observation that the colour was rapidly discharged on the addition of either ascorbic acid or diphenylpicrylhydrazyl, both of which are well known radical scavengers. The colour could not be extracted into non-hydroxylic solvents such as Et_2O , CHCl_3 and cyclohexane and was destroyed on neutralisation of the solution with sodium carbonate. These results further suggest that the radical is protonated in the aqueous acidic medium, that is, it exists as a radical cation.

These last two observations rule out the possibility that the blue substance is a nitroxide. Nitroxides are generally stable in both acidic and alkaline media and are most stable in dilute solution where dimerisation is negligible. Diphenylnitroxide is reported to have a characteristic UV absorption in the region 320 - 325 nm¹²⁴ which is not observed in the present case.

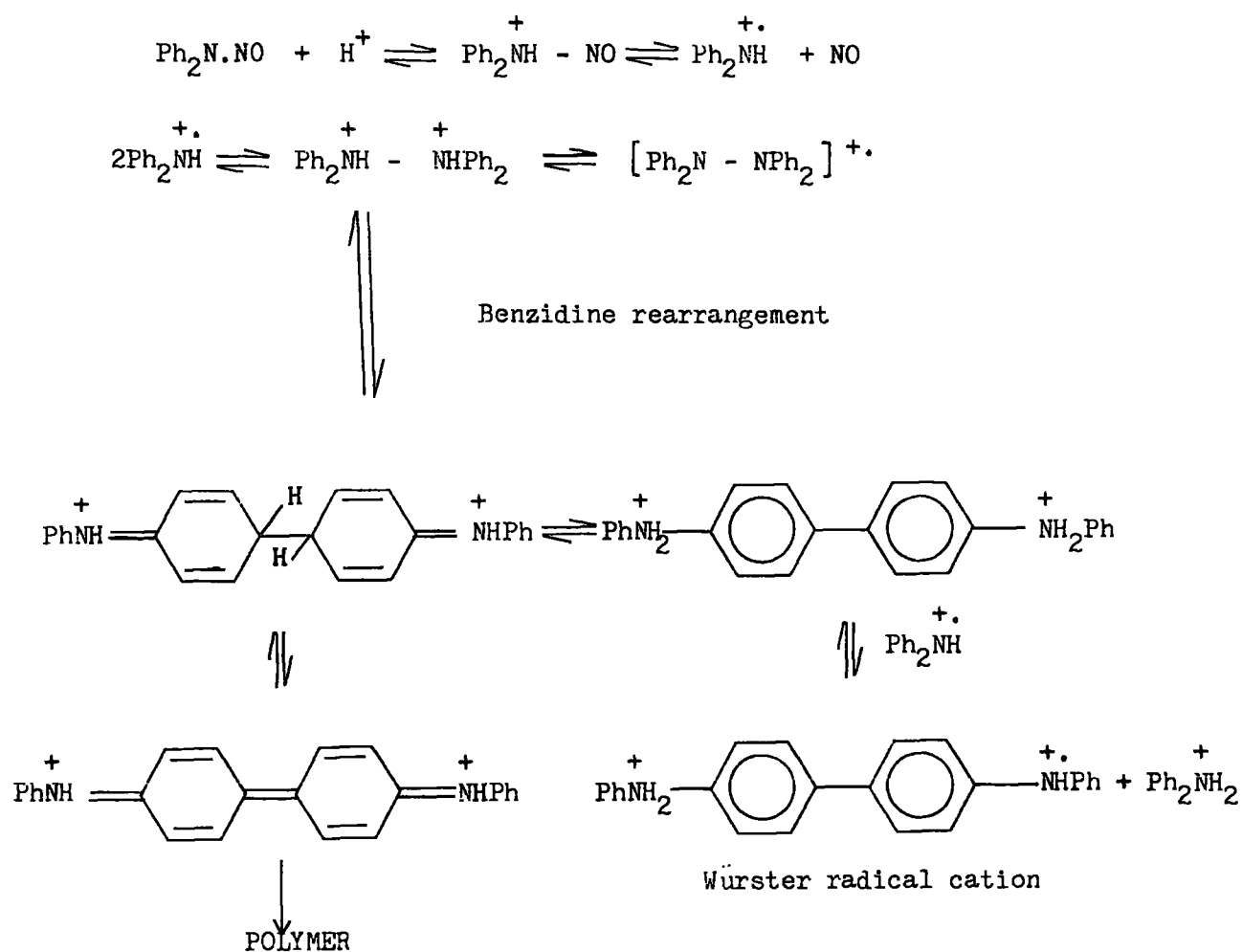
It has been claimed¹²² that the blue colour from diphenylamine and sodium nitrite in concentrated sulphuric acid is due to the formation of a Würster radical cation. This would seem the most plausible cause of the blue colour from N-nitrosodiphenylamine but for the fact that the latter is stable to air for quite long periods whereas the former disappears in approximately ten minutes to give a flocculent yellow precipitate. However, it is possible that various side reactions are enhanced in concentrated H₂SO₄ and that this accounts for the relative instability of the diphenylamine blue.

The Würster radical cations usually have characteristic, strong absorption in the 450 - 610 nm region, can usually be precipitated by large anions such as perchlorate, and generally dimerize below -12°C to give diamagnetic products differing in colour from the monomer.^{125,126,127} However, the N-nitrosodiphenylamine blue was found not to form a precipitate with NaClO₄, nor to decolourize on cooling in cardice-acetone. These results are probably due to too low a radical concentration, and the structure of ice preventing radical recombination, respectively.

It is conceivable that the blue solution might contain other radical species. The diphenylamine radical cation (Ph₂NH⁺) is formed during the irradiation of solutions of diphenylamine in toluene with

a reported maximum absorption at 670 nm.¹²⁸ In aqueous media one might expect this to be lowered into the 500 - 600 nm region by a solvent induced hypsochromic shift. Hydrazinium radical cations could also be present as a result of coupling of diarylamino species. These are well known, and are readily formed in acidic solutions of tetra-arylhydrazines,^{129,130} as has been confirmed by e.s.r. measurements.^{131,132,133}

The proposed scheme is thus:-





This is essentially the same scheme as that developed on the basis of the work of Wieland¹³⁴ and Kehrmann,¹³⁵ for the oxidation of diphenylamine.

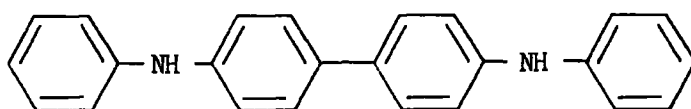
It is of interest to note that the blue colour is destroyed on the addition of the nucleophiles Cl^- , Br^- , SCN^- , $\text{SC}(\text{NH}_2)_2$ and I^- in increasing order of rapidity. Whether this is due to the incursion of denitrosation and the resulting shift in the position of equilibrium, or to reduction of the radical cation remains to be seen. However, decolourisation by azide appears to involve the latter process. This was ascertained as follows:-

The blue substance was generated from methanolic $\text{Ph}_2\text{N.NO}$ (20 cm^3 ; 0.005M) and sulphuric acid (20 cm^3 ; 40%) and then destroyed by the addition of small quantities of solid sodium azide. The resulting green solution was then neutralised with sodium carbonate and extracted with diethyl ether. The ether layer, after separation, was dried over anhydrous magnesium sulphate and a sample run against Ph_2NH and $\text{Ph}_2\text{N.NO}$ on fluorescent silica-gel TLC plates with chloroform as eluent. Exposure to UV followed by development in iodine vapour showed the product to be distinct from the two reference substances. Furthermore, it was apparently a single substance. The solvent was then removed from the ethereal solution by rotary evaporator and the small quantity of solid thus obtained finally freed from solvent on a vacuum line. The infra-red spectrum of the product (KBr disc) was found to be quite different from the reference spectra of Ph_2NH and $\text{Ph}_2\text{N.NO}$. Band assignment was made as follows.¹³⁶

TABLE 14

| BAND cm^{-1} | ASSIGNMENT |
|-------------------------------|--|
| 3,400 (m) | Secondary N-H stretch |
| 1,600 (s) 1,500 (s) | Aromatic C-C in plane deformation |
| 810 (s) |  2 adjacent aromatic C-H out of plane deformation. |
| 880 (w) 750 (s) 700 (s) |  5 adjacent aromatic C-H out of plane deformation. |
| 1,320 (s) | Aromatic C-N stretch |

Thus, although band assignment may be unreliable in view of the poor resolution of the spectrum, the substance appears to be a secondary aromatic amine, but not diphenylamine. The results are accommodated the structure of N,N' - diphenylbenzidine, viz:-



It is therefore probable that the blue colour is due to the Würster radical cation derived from it. In fact, this substance has been obtained from the diphenylamine blue by reduction with zinc dust.^{134,135} An e.s.r. study by Hallett¹³⁷ has confirmed the presence of free radicals in the blue from $\text{Ph}_2\text{N}\cdot\text{NO}$. However, poor resolution

prevented the positive identification of individual species.

Finally, it might be noted that the use of species such as Fe^{2+} and Cu^+ as nitrite traps² may, with certain nitrosamines, lead to the formation of radical cations rather than to the normal products of denitrosation.

3.5 Effect of Added Diphenylamine:

It has already been mentioned (section 1.4) that the full intramolecular rate expression is given by:-

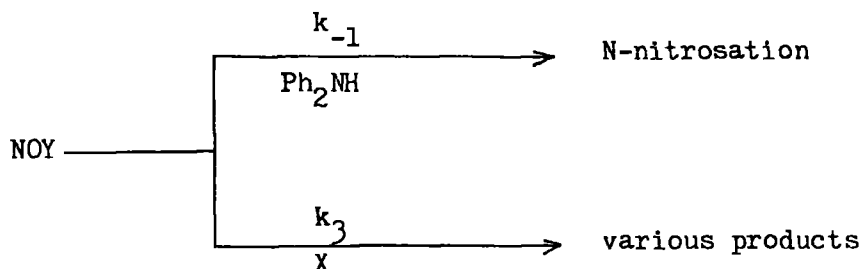
$$k_o = \frac{k_1 [Y] K h_o k_3 [X]}{k_3 [X] + k_{-1} [C]} + \frac{k_4 k_5 K h_o}{k_4 + k_{-5}}$$

However, in the case of N-nitrosodiphenylamine the rearrangement term is negligibly small at the low acidities studied, and is swamped by denitrosation when an efficient nucleophile is present. It is interesting to note that Lachman¹³⁸ also obtained quantitative denitrosation of $\text{Ph}_2\text{N.NO}$ with HCl in contrast to the original work of Fischer & Hepp.³ It is thus feasible to approximate the rate expression by:-

$$k_o = \frac{k_1 [Y] K h_o k_3 [X]}{k_3 [X] + k_{-1} [C]}$$

so that:- $1/k_o = k_{-1} [C] / k_1 [Y] K h_o k_3 [X] + 1 / k_1 [Y] K h_o$

Hence, at constant h_o , $[Y]$ and $[X]$, k_o^{-1} should be a linear function of $[C]$, and from the experimental values of slope and intercept it should be possible to calculate k_{-1}/k_3 ratios for a variety of nitrite traps. This has been done in the case of N-methyl-N-nitrosoaniline.^{19,23}



In the present system these ratios measure the relative reactivity of Ph_2NH and X towards reaction with nitrosyl thiocyanate.

The low solubility of diphenylamine in dilute acids necessitated the use of a methanol-water mixture (50:50 v/v) as solvent. The k_{-1}/k_3 ratios could then be determined for hydrazoic acid, sulphamic acid and hydroxylamine. Work with hydrazine was prevented by the low solubility of dihydrazinium sulphate in aqueous methanol and urea was not used because excessively large concentrations would have been required.

The experimental results are summarized in Tables 15, 16 and 17 and the graph of k_o^{-1} versus $[\text{Ph}_2\text{NH}]$ illustrated for hydrazoic acid in Figure 7.

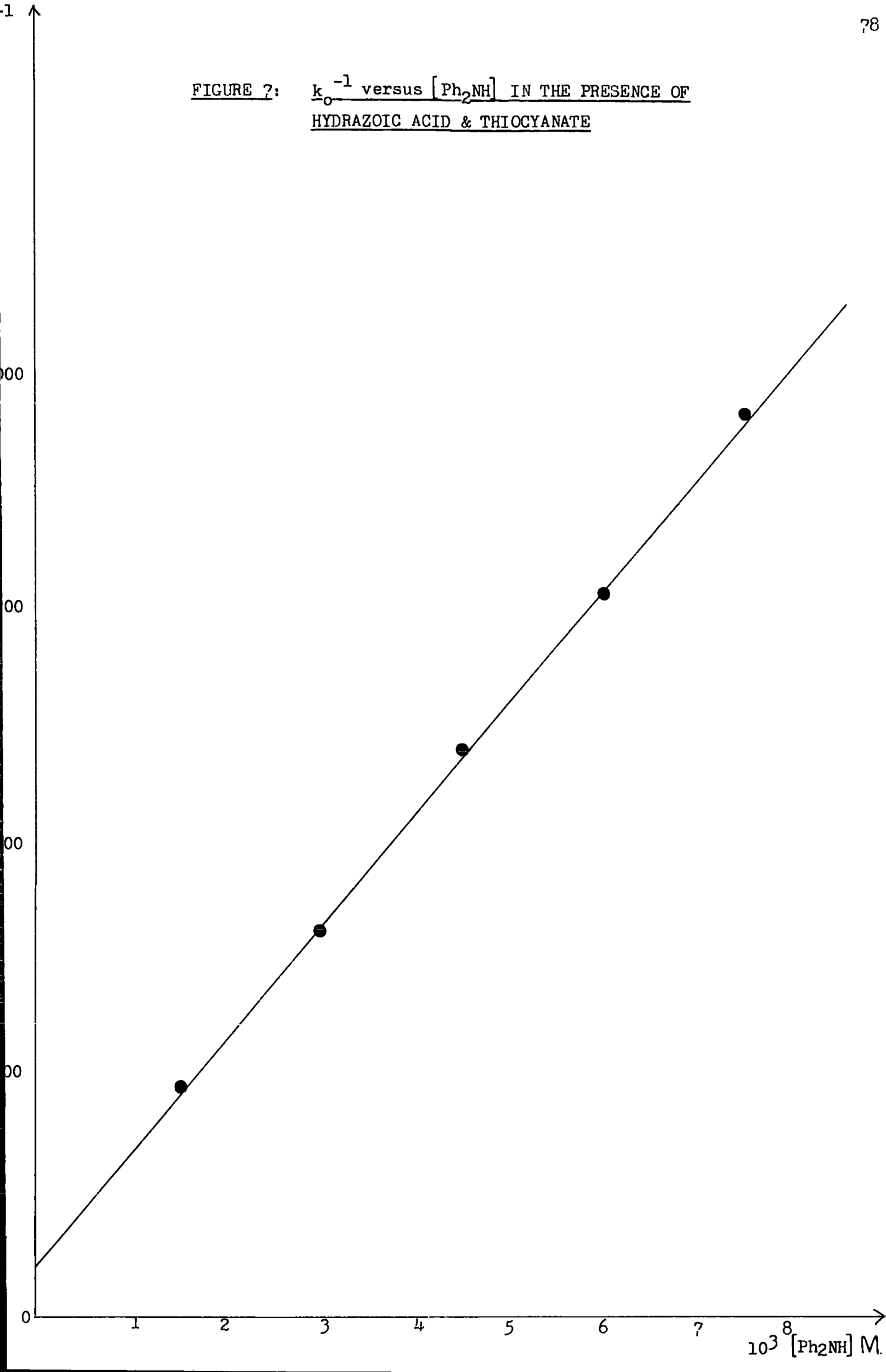
TABLE 15: (Hydrazoic Acid)

$$[\text{H}_2\text{SO}_4] = 0.56\text{M}, [\text{Ph}_2\text{N.NO}] = 2.62 \times 10^{-4}\text{M}, [\text{NaN}_3] = 6.37 \times 10^{-3}\text{M},$$

$$[\text{KCNS}] = 4.9 \times 10^{-3}\text{M}.$$

| $10^4 k_o \text{ sec}^{-1}$ | $k_o^{-1} \text{ sec}$ | $10^3 [\text{Ph}_2\text{NH}] \text{ M}$ |
|-----------------------------|------------------------|---|
| 20.5 | 488 | 1.51 |
| 12.2 | 820 | 3.02 |
| 8.3 | 1205 | 4.54 |
| 6.5 | 1538 | 6.05 |
| 5.2 | 1920 | 7.56 |

FIGURE 7: k_o^{-1} versus $[Ph_2NH]$ IN THE PRESENCE OF
HYDRAZOIC ACID & THIOCYANATE



$$\text{Slope} = k^{-1}/k_3 [X] k_1 K h_o [Y] = 2.3675 \times 10^5 \quad r = 0.999$$

$$\text{Intercept} = 1/k_1 K h_o [Y] = 1.203 \times 10^2$$

$$k^{-1}/k_3 = \text{Slope} \times 1/\text{Int.} \times [X] = 12.5$$

A concentration of HN_3 well below the limiting value of 0.16 was used so that reasonable rate alterations could be achieved with small changes in diphenylamine concentration.

TABLE 16 (Sulphamic Acid)

$$[\text{H}_2\text{SO}_4] = 0.56\text{M}, [\text{Ph}_2\text{N.NO}] = 2.62 \times 10^{-4}\text{M}, [\text{KCNS}] = 4.9 \times 10^{-3}\text{M}$$

$$[\text{NH}_2\text{SO}_3\text{H}] = 2.46 \times 10^{-2}\text{M}$$

| $10^4 k_o \text{ sec}^{-1}$ | $k_o^{-1} \text{ sec}$ | $10^4 [\text{Ph}_2\text{NH}] \text{ M}$ |
|-----------------------------|------------------------|---|
| 11.7 | 855 | 1.41 |
| 7.7 | 1299 | 2.82 |
| 6.1 | 1639 | 4.22 |
| 5.6 | 1786 | 5.62 |
| 4.4 | 2280 | 7.03 |

$$\text{Slope} = 2.37723 \times 10^6, \quad \text{Intercept} = 5.686 \times 10^2, \quad r = 0.988$$

$$k^{-1}/k_3 = 102.8$$

TABLE 17 (Hydroxylamine)

$$[\text{H}_2\text{SO}_4] = 0.56\text{M}, [\text{Ph}_2\text{N.NO}] = 2.62 \times 10^{-4}\text{M}, [\text{KCNS}] = 4.9 \times 10^{-3}\text{M}$$

$$[\text{NH}_3\text{OH HSO}_4^-] = 0.151\text{M}$$

| $10^4 k_o \text{ sec}^{-1}$ | $k_o^{-1} \text{ sec}$ | $10^6 [\text{Ph}_2\text{NH}] \text{ M}$ |
|-----------------------------|------------------------|---|
| 14.2 | 705 | 5.9 |
| 13.2 | 760 | 11.8 |
| 12.6 | 794 | 17.7 |
| 11.8 | 848 | 23.6 |
| 11.4 | 880 | 29.5 |

$$\text{Slope} = 7.42373 \times 10^6, \quad \text{Intercept} = 6.66 \times 10^2, \quad r = 0.996$$

$$k_{-1}/k_3 = 1683.2$$

It is thus apparent that the order of trap reactivity is $\text{HN}_3 > \text{NH}_2\text{SO}_3\text{H} > \text{NH}_2\text{OH}$ as was obtained previously,^{19,23} for reaction with N-methyl-N-nitrosoaniline. Since the step $\text{NOSCN} + \text{X} \longrightarrow \text{products}$ is common to both nitrosamines one would expect the k_3 values to be invariant also. Hence:-

$$\frac{(k_{-1})_{\text{DPA}}}{(k_3)_{\text{DPA}}} \times \frac{(k_3)_{\text{NMA}}}{(k_{-1})_{\text{NMA}}} = \frac{(k_{-1})_{\text{DPA}}}{(k_{-1})_{\text{NMA}}}$$

The k_{-1}/k_3 ratios were found to be 280, 26 and 18 for HN_3 , sulphamic acid and hydroxylamine, respectively. The poor agreement is probably due to the effect of protonation upon the concentration of 'active' amine and trap since it is held¹³⁹ that nitrosyl halides react only with the unprotonated forms of such species. Williams has allowed for this in the denitrosation of N-methyl-N-nitrosoaniline where the competition for NOY occurs between X and N-methylaniline (NMA). The corrected k_{-1}/k_3 ratios are given by:-¹⁹

$$\left(\frac{k_{-1}}{k_3} \right)' = \frac{k_{-1}}{k_3} \cdot \frac{h_o}{K_{\text{NMA}}} \cdot \left[\frac{1}{1 + h_o / K_x} \right]$$

A knowledge of the various pK_{BH^+} values is thus necessary. For water as solvent these are readily available, except for the N-protonation of sulphamic acid. However, for mixed methanol-water solvent they

are not, and this therefore prevents the calculation of true $(k_{-1}/k_3)'$ ratios in the case of N-nitrosodiphenylamine. As a result the calculation of the true, trap-invariant $(k_{-1})'$ DPA: $(k_{-1})'$ NMA ratio is impossible. All that can be inferred from the present set of results is that k_{-1} is always largest for diphenylamine thereby indicating that the dominant factor is the different basicities of the two product amines.

However, unless the same nucleophile has been used in the denitrosation of both nitrosamines it may be unreasonable to expect constancy of the (k_{-1}) DPA / (k_{-1}) NMA ratios over all the trap species used. This is because plots of k_o versus [Halide] are curved (see Figure 4) and it is to be expected that the degree of curvature will be a function of the nucleophilicity of the halide. In other words the tendency towards zero-order behaviour in [Halide] will be most pronounced at low concentrations for iodide. Strict comparisons between the two sets of results should therefore be made only when the same concentration of the same nucleophile has been used in the denitrosation of both nitrosamines. In the present case thiocyanate has been used in the $\text{Ph}_2\text{N.NO}$ reaction and Br^- , Cl^- and H_2O in the PhNMe.NO reaction.

3.6 Comparison with N-ethyl-N-nitrosourethane:

It has been demonstrated that N-nitrosodiphenylamine, like other N-alkyl-N-nitrosoanilines, undergoes fast initial proton transfer followed by rate-determining cleavage of the N - N bond, except at high nucleophile concentrations. On the other hand, N-nitrosamides undergo slow initial protonation regardless of nucleophile concentration.^{33,34,37} In this section it is shown that N-nitrosourethanes, not surprisingly, follow the latter pattern of behaviour.

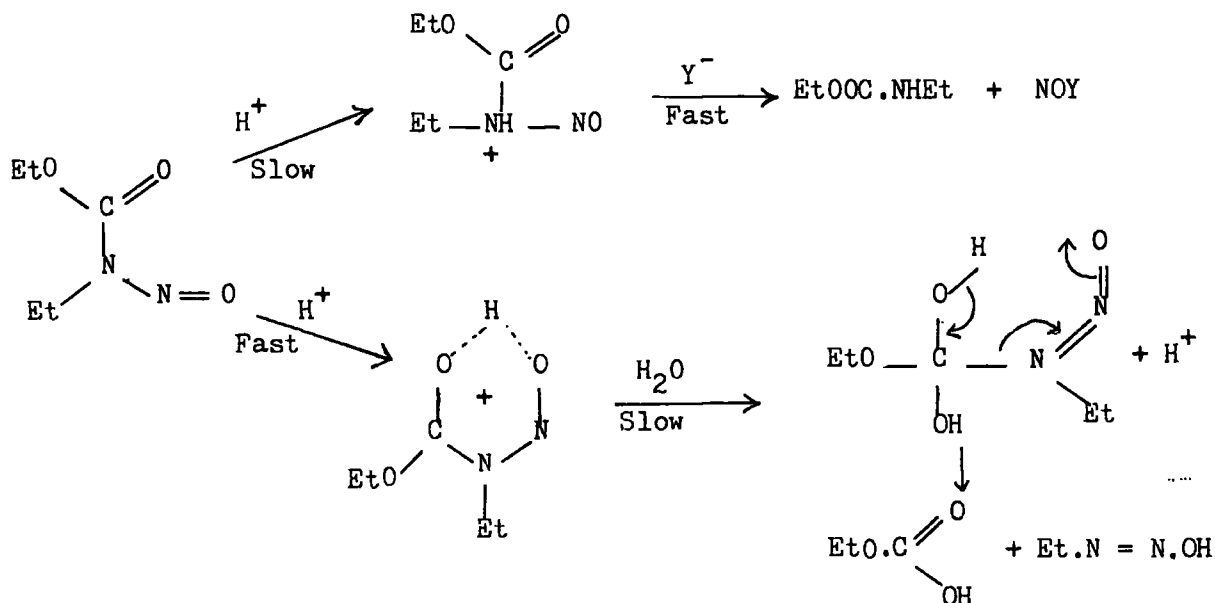
Evidence to support this view comes from the observation that k_0 for the decomposition of N-ethyl-N-nitrosourethane is independent of such factors as $[N_3^-]$, $[Cl^-]$, $[Br^-]$ and [ethylurethane]. The results are shown in Table 18 for reaction in 1.51M sulphuric acid with $[NNEU] = 1.75 \times 10^{-4} M$ initially. It is apparent that the decomposition is rapid even in the absence of added azide or nucleophile when $k_0 = 6.9 \times 10^{-3} \text{ sec}^{-1}$. Furthermore, the yield of nitrous acid under such conditions is not quantitative. Direct determination of nitrous acid was carried out spectrophotometrically at 370 nm for several 'runs' at 'infinite' time. The yield was found to be $68 \pm 3\%$ of the maximum theoretical.

TABLE 18

| $10^3 k_0 \text{ sec}^{-1}$ | IN PRESENCE OF |
|-----------------------------|-------------------------------------|
| 7.0 | $2.2 \times 10^{-3} M \text{ HN}_3$ |
| 7.5 | 5.5 " " |
| 7.5 | 8.7 " " |
| 7.3 | 10.9 " " |
| 7.5 | $8.2 \times 10^{-2} M \text{ Cl}^-$ |
| 7.3 | 16.3 " " |
| 8.6 | 24.5 " " |
| 7.6 | 32.7 " " |
| 7.4 | $8.3 \times 10^{-2} M \text{ Br}^-$ |
| 7.7 | 16.6 " " |
| 7.5 | $8.6 \times 10^{-3} M \text{ EU}$ |

$$\text{mean } 10^3 k_0 = 7.43 \pm 0.06 \text{ sec}^{-1} \quad (\text{EU} = \text{N-ethylurethane})$$

The reaction therefore appears to resemble those of the N-nitrosamides in which denitrosation is accompanied by deamination.^{33,34} These are thought to occur via separate pathways and an analogous scheme is shown below:-



N-methyl-N-nitrosotoluene-4-sulphonamide under similar conditions only gives quantitative denitrosation.³⁷

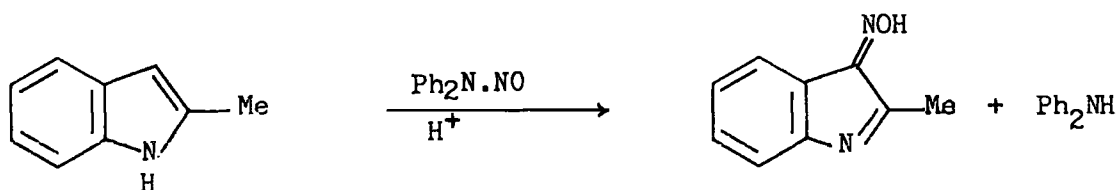
Further details of the acid hydrolysis of N-nitrosourethanes have as yet to be elucidated.

CHAPTER FOUR

Diazotization with N - nitrosodiphenylamine

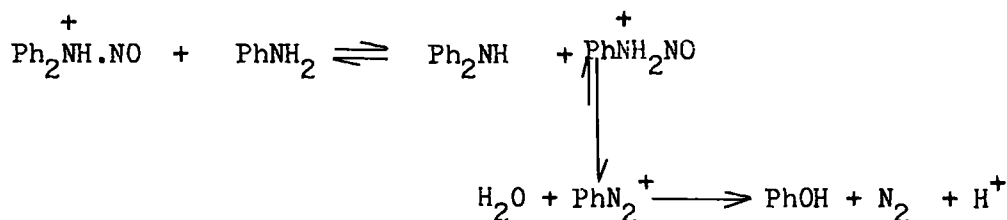
N-methylaniline over N_3^- is not evident for nitrosation by $NOCl$.

It was also noted that aniline itself could be diazotized by N-nitrosodiphenylamine in either hydrochloric or perchloric acid. In the former catalysis by chloride was observed thereby implying that Cl^- and $PhNH_2$ compete for direct reaction with the $Ph_2NH.NO$. In the latter only catalysis by $PhNH_2$ was observed since the ClO_4^- ion is too weakly nucleophilic to compete. (Nitrosyl perchlorate is completely ionised even in the solid state whereas nitrosyl chloride is covalent). It was therefore suggested that under favorable conditions aniline may react directly with N-nitrosodiphenylamine. Similar behaviour was reported for the reaction with 2-methylindole.



4.2 Diazotization of Aniline:

The reaction between N-nitrosodiphenylamine and N-methylaniline is complicated by its reversibility and only initial rates ($< 7\%$) were measured by Challis & Osborne.³⁸ In order to avoid this difficulty the present work focuses attention upon the reaction with aniline where one would expect the intermediate primary nitrosamine to react rapidly and irreversibly to give the diazonium ion and its subsequent solvolysis products.



The reaction was carried out in sulphuric acid to avoid complication by halide catalysis since HSO_4^- is believed to be too weak a nucleophile to react directly with the protonated form of the nitrosamine.

Aniline is theoretically capable of reacting either directly or indirectly with N-nitrosodiphenylamine and it is therefore necessary to distinguish kinetically between the two possibilities. Fortunately this can be achieved by carrying out the reaction in the presence of azide at or above the limiting concentration established in section 3.1 when k_0 is independent of trap concentration. It can be assumed that at this limit increasing the aniline concentration would have no effect upon k_0 if the aniline were merely acting as a trap. On the other hand, at the limit:-

$$k_0 = k_1 K h_0 [Y]$$

so that if the aniline were to behave as a nucleophile (Y), and react directly with the nitrosamine, one would expect a linear dependence of k_0 upon aniline concentration.

The results for reaction at two acidities are shown in Tables 19 and 20. The experimental plots of $\log(a - x)$ versus t used to calculate k_0 were good straight lines at low aniline concentration. However, at the highest aniline concentrations used the plots began to curve late in the reaction. In these cases the initial rate method was used. It is thus apparent that the reaction can be significantly reversible at high aniline concentrations.

TABLE 19 : (Low Acidity)

$$[\text{H}_2\text{SO}_4] = 0.60\text{M}, \quad [\text{Ph}_2\text{N.NO}] = 1.62 \times 10^{-4}\text{M}, \quad [\text{NaN}_3] = 0.16\text{M}$$

| $10^4 k_o \text{ sec}^{-1}$ | $10^3 [\text{PhNH}_3^+] \text{ M}$ |
|-----------------------------|------------------------------------|
| 12.6 | 2.8 |
| 14.5 | 8.1 |
| 21.6 | 16.7 |
| 27.4 | 31.9 |
| 39.1 | 56.4 |

TABLE 20 : (High Acidity)

$$[\text{H}_2\text{SO}_4] = 1.16\text{M}, \quad [\text{Ph}_2\text{N.NO}] = 1.62 \times 10^{-4}\text{M}, \quad [\text{NaN}_3] = 0.16\text{M}$$

| $10^4 k_o \text{ sec}^{-1}$ | $10^3 [\text{PhNH}_3^+] \text{ M}$ |
|-----------------------------|------------------------------------|
| 20.8 | 2.6 |
| 25.3 | 8.7 |
| 30.5 | 16.4 |
| 39.4 | 35.4 |
| 51.7 | 53.0 |

At the acidities used in these experiments the aniline is extensively protonated ($\text{pK} = 4.6$) and it seems reasonable to assume that the reaction involves the protonated form. If reaction does proceed via the free amine the slopes of the graphs of k_o versus $[\text{PhNH}_2]$ predict that aniline would then be too reactive relative to its Pearson¹⁰⁷ 'n'

value by a factor of $\sim 10^3$. This seems unlikely. Thus the k_0 values are plotted against $[\text{PhNH}_3^+]$ and the results shown in Table 21 where slope = k_1Kh_0 and the intercepts correspond to denitrosation by the solvent.

TABLE 21

| ACIDITY | LOW | HIGH |
|-----------|----------------------|----------------------|
| SLOPE | 4.9×10^{-2} | 5.9×10^{-2} |
| INTERCEPT | 1.2×10^{-3} | 2.0×10^{-3} |
| 'r' | 0.995 | 0.997 |

As an approximation it has again been assumed that the azide is completely protonated and the values of h_0 have been interpolated from the data of Robertson & Dunford¹⁰⁰ for the corresponding residual sulphuric acid concentrations. These were found to be 0.74 and 1.95 at low and high $[\text{H}_2\text{SO}_4]$, respectively. The corresponding k_1K values were then calculated to be 6.6×10^{-2} and 3.0×10^{-2} , and as can be seen the agreement is not particularly good with a mean value of $(4.8 \pm 1.8) \times 10^{-2}$.

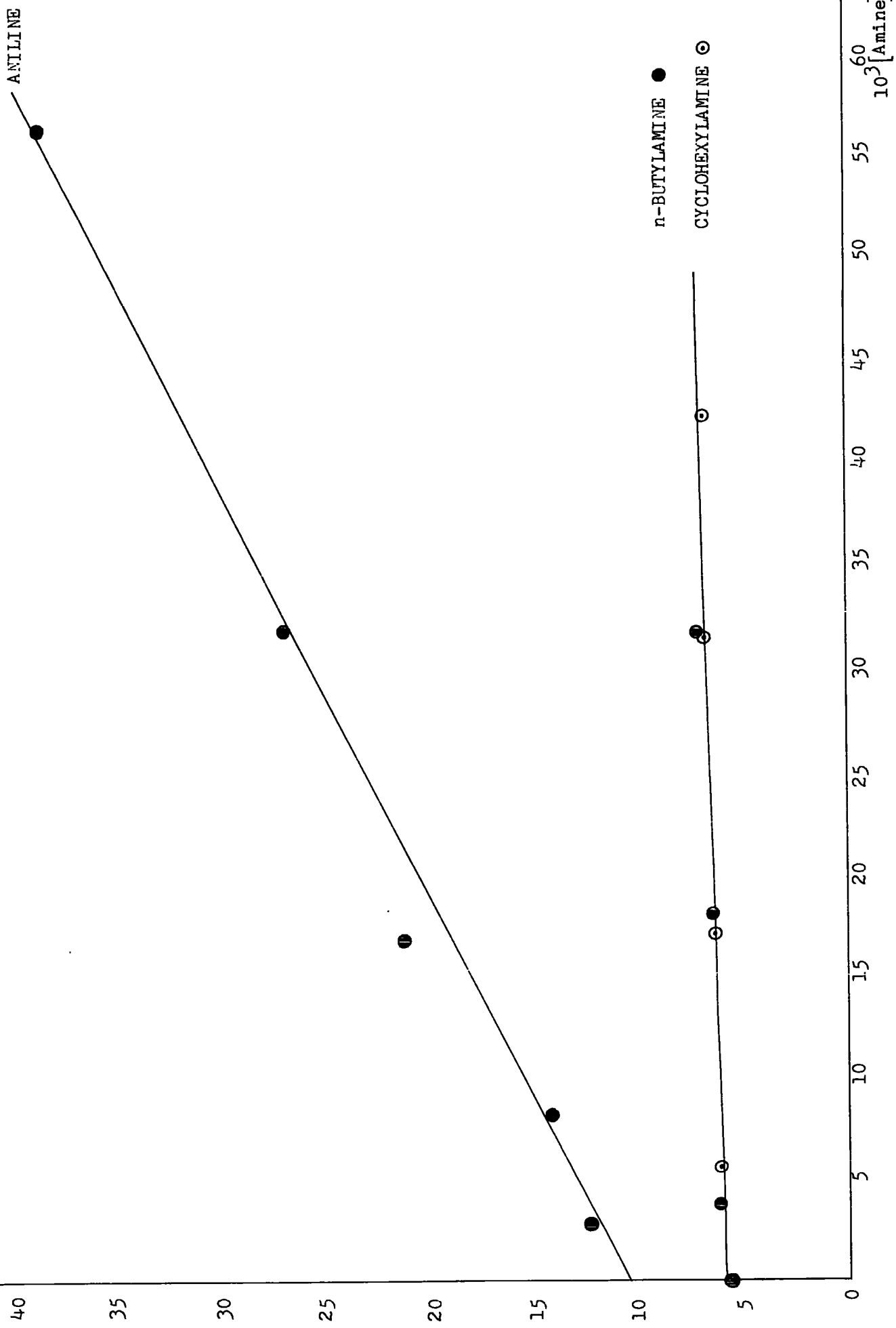
However, the $2 + \log k_1K$ value of 0.68 corresponds to a Pearson 'n' value of approximately 4.6 (see figure 3) which is comparable to that of chloride (4.4), but significantly less than those of bromide (5.8) and thiocyanate (6.7). This probably accounts for the fact that Cl^- catalysis is unimportant in the corresponding reaction with N-methylaniline whereas catalysis by Br^- and SCN^- is observed.³⁸

Williams¹¹⁸ has examined the aniline reaction over a wider range of acidity and obtained linear plots of k_o versus Aniline in each case, with the slopes and intercepts increasing with increasing acidity. The intercept values correspond to solvent-catalysed denitrosation and would therefore be expected to increase as the concentration of $\text{Ph}_2\text{NH}\cdot\text{NO}^+$ increases. The increasing slopes suggest PhNH_3^+ as the reactive species for if free PhNH_2 were responsible one would expect, as a first approximation, that the slopes be independent of acidity since the concentrations of $\text{Ph}_2\text{NH}\cdot\text{NO}^+$ and PhNH_2 would simultaneously increase and decrease with increasing acidity.

The rather large 'n' value of 4.6 is therefore somewhat surprising since one would hardly expect a protonated amino group to be very nucleophilic. However, it is conceivable that the aromatic π -electrons could constitute such a 'reagent'. It will be recalled that all of the substrates involved in the direct reaction with N-nitrosodiphenylamine, i.e. aniline, N-methylaniline and 2-methylindole, possess benzenoid character. Thus although reaction is envisaged as occurring between two positively charged species this in itself should not deter reaction if proton loss to the solvent is largely complete in the transition state.

The hypothesis was tested by replacing aniline by the aliphatic substrates n-butylamine and cyclohexylamine, the latter bearing a formal similarity to the aromatic amine. Both are stronger bases than aniline and are virtually 100% protonated in the acidic solution employed. In both cases $[\text{H}_2\text{SO}_4] = 0.60\text{M}$, $[\text{Ph}_2\text{N}\cdot\text{NO}] = 3.12 \times 10^{-4}\text{M}$ and $[\text{NaN}_3] = 0.16\text{M}$. The results are set out in the tables overleaf

FIGURE 8: k_o VERSUS [AMINE]



and the plots of k_0 versus [Amine] drawn in Figure 8 along with that for aniline at the same acidity.

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{n-BuNH}_2] \text{ M}$ |
|-----------------------------|------------------------------------|
| 5.7 | 0 |
| 6.1 | 3.76 |
| 6.4 | 17.90 |
| 7.0 | 31.83 |

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{CHA}] \text{ M}$ |
|-----------------------------|-------------------------------|
| 5.7 | 0 |
| 6.2 | 5.61 |
| 6.3 | 17.01 |
| 6.7 | 31.51 |
| 6.7 | 42.38 |

CHA = cyclohexylamine

It can clearly be seen that the direct reaction appears to be a property of the aromatic system since the two aliphatic amines are virtually inert under the same conditions. At this stage the exact role of the π -system is unclear but it would seem that the formation of a π -complex of some sort plays a part in the reaction.

Concrete evidence for the existence of such π -complexes is rather lacking at the present time. For example, studies of the gas-phase ion-molecule reactions between NO^+ and aromatic species such as benzene, toluene and pyridine have been made,¹⁴⁰ and complex formation proposed. However, the lower limit bonding energy suggested that they were of the σ -type. The controversy surrounding the π - σ debate has been more fully discussed in section 1.6.

That diazotization had indeed taken place in the reaction between aniline and N-nitrosodiphenylamine was confirmed by coupling the diazonium ion with 2-naphthol-3,6-disulphonic acid after complete reaction. Spectrophotometric determination of the azo-dye ($\lambda_{\text{max}} = 485 \text{ nm}$) indicated yields of PhN_2^+ of $\geq 70\%$ of the maximum theoretical.

4.3 Substituent Effects on the Diazotization Reaction:

An analogous scheme to the one above was proposed for the diazotization of aniline by H_2NO_2^+ in 3M perchloric acid on the basis of ring substituent effects.⁴³ Similar substituent effects are observed in the reaction between aniline and N-nitrosodiphenylamine.

The results are set out in Tables 22 - 25. In each case $[\text{Ph}_2\text{N.NO}] = 2.0 \times 10^{-4}\text{M}$, $[\text{NaN}_3] = 0.17\text{M}$ and $[\text{H}_2\text{SO}_4] = 0.53\text{M}$, so that $h_0 = 0.62$.

TABLE 22

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{p-Chloroaniline}] \text{ M}$ |
|-----------------------------|---|
| 11.3 | 9.6 |
| 14.0 | 19.1 |
| 17.3 | 28.7 |
| 18.4 | 38.3 |
| 19.1 | 47.9 |

TABLE 23

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{p-Toluidine}] \text{ M}$ |
|-----------------------------|---------------------------------------|
| 41.0 | 10.1 |
| 58.7 | 20.3 |
| 68.0 | 30.4 |
| 77.9 | 40.6 |
| 87.0 | 50.7 |

TABLE 24

| $10^4 k_o \text{ sec}^{-1}$ | $10^3 [\text{m-Toluidine}] \text{ M}$ |
|-----------------------------|---------------------------------------|
| 17.8 | 10.6 |
| 22.5 | 19.7 |
| 26.0 | 30.4 |
| 31.0 | 43.7 |
| 34.7 | 60.0 |

TABLE 25

| $10^4 k_o \text{ sec}^{-1}$ | $10^3 [\text{m-Anisidine}] \text{ M}$ |
|-----------------------------|---------------------------------------|
| 19.3 | 6.2 |
| 32.2 | 12.1 |
| 50.9 | 19.3 |
| 63.2 | 23.4 |
| 64.8 | 31.0 |

Good first-order plots of $\log (a-x)$ versus t were obtained in all cases except *m*-methoxyaniline for which the initial rate method was used. From the values of the slope k_1K values were calculated and are shown in Table 26.

TABLE 26

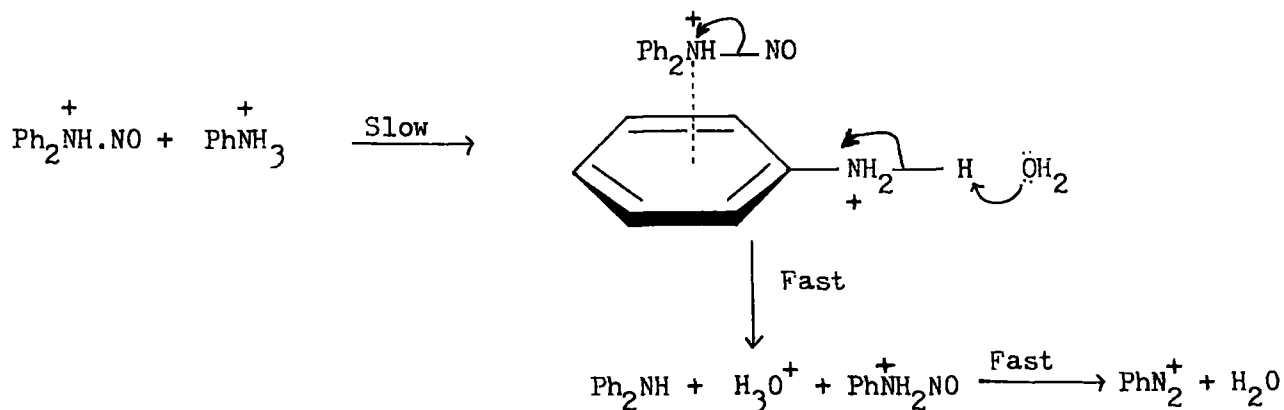
| ANILINE | Slope | k_1K | r |
|----------------|-----------------------|-----------------------|-------|
| <i>p</i> - Cl | 2.1×10^{-2} | 3.3×10^{-2} | 0.962 |
| <i>p</i> - Me | 11.0×10^{-2} | 17.4×10^{-2} | 0.989 |
| <i>m</i> - Me | 3.4×10^{-2} | 5.6×10^{-2} | 0.991 |
| <i>m</i> - OMe | 19.8×10^{-2} | 32.5×10^{-2} | 0.965 |

The results can be expressed relative to the k_1K value for aniline of 4.8×10^{-2} and then compared with the data of Ridd and co-workers.⁴³

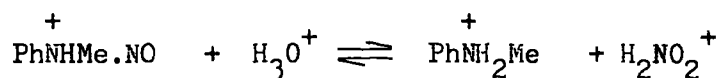
TABLE 27

| | Ph_2NHNO^+ Reaction | H_2NO_2^+ Reaction |
|---------|-------------------------------------|------------------------------------|
| AMINE | $(k_1K)_x / (k_1K)_H$ | $(k_1K)_x / (k_1K)_H$ |
| H | 1.0 | 1.0 |
| p - Cl | 0.7 | 0.2 |
| m - Me | 1.2 | 6.8 |
| p - Me | 3.6 | 7.4 |
| m - OMe | 6.8 | 18.6 |

Whilst the two sets of results do not parallel each other exactly there are notable similarities. Firstly, the order of reactivity is the same in both cases and secondly, a meta - OMe substituent brings about a significant rate enhancement. The latter has been taken to emphasise the importance of N - H bond breaking in the transition state since m-Me and m-OMe should have approximately the same effect upon the π - electron density but different effects upon the acidity of the amino protons. The respective $\text{p}K_{\text{BH}^+}$ values for the anilines are 4.7 (m-Me), 4.2 (m-OMe) and 4.6 (H).¹⁴¹ Thus it is argued⁴³ that the N-X bond is relatively weak in the transition state.



Thus, the assumption that proton loss from the transition state is largely complete in order to facilitate reaction between two positively charged molecules seems to be borne out by experiment. Further support for the validity of such a reaction comes from the study of the denitrosation of N-methyl-N-nitrosoaniline in sulphuric acid²¹ where the reaction:-

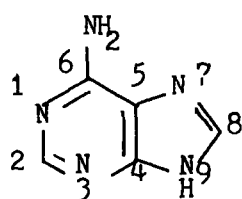


is believed to be important at high acidities.²⁰ The reverse of this reaction is analogous to the above diazotization scheme.

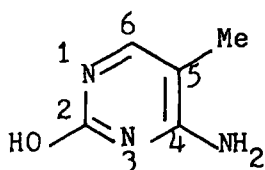
4.4 Reaction with Adenine and 5 - methylcytosine:

It is well known that many aromatic secondary nitrosamines are carcinogenic whereas nitrous acid itself, although mutagenic, is not unless ingested with secondary amines.^{142,143} Nitrous acid is believed to exert its mutagenic effect by reacting with resting DNA so that mutations result in subsequent DNA replications. These are thought to be due to the deamination of adenine, guanine and cytosine in the parent DNA, the resulting products, hypoxanthine, xanthine and uracil respectively, having different pairing properties from the parent bases. Since N-nitrosodiphenylamine is particularly effective in the diazotization of aniline it is of interest to determine whether or not it exhibits enhanced reactivity over nitrous acid in the deamination of the above DNA bases.

The aniline runs were therefore duplicated using adenine (6-amino-purine) and 5-methylcytosine (4-amino-2-hydroxy-5-methylpyrimidine).

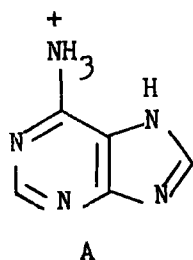


Adenine

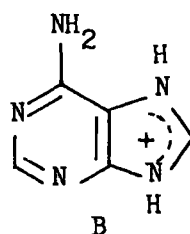


5 - methylcytosine

These bases are only slightly soluble in water because of the extensive hydrogen bonding in the solids but are quite soluble in sulphuric acid. However, the position of protonation is unresolved. For example, for adenine protonation is thought to occur either at N(1) or at the amino group. Evidence has been presented for both cases, e.g. for adenosine n.m.r. indicates protonation at N(1)¹⁴⁴ but the fluorescence spectrum¹⁴⁵ of protonated adenine favors either A or B below.



A



B

with A being preferred on theoretical grounds.

However, whatever the site of protonation, neither adenine nor 5-methylcytosine reacts directly with N-nitrosodiphenylamine. The results are shown in Tables 28 and 29 with $[\text{H}_2\text{SO}_4] = 1.30\text{M}$, $[\text{Ph}_2\text{N.NO}] = 2.0 \times 10^{-4}\text{M}$, and $[\text{NaN}_3] = 0.17\text{M}$.

TABLE 28

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [\text{Adenine}] \text{ M}$ |
|-----------------------------|-----------------------------------|
| 22.1 | 3.9 |
| 21.6 | 5.2 |
| 21.4 | 11.9 |
| 20.0 | 17.1 |
| 19.9 | 20.2 |

TABLE 29

| $10^4 k_0 \text{ sec}^{-1}$ | $10^3 [5\text{-methylcytosine}] \text{ M}$ |
|-----------------------------|--|
| 22.1 | 3.5 |
| 18.5 | 5.3 |
| 22.2 | 9.1 |
| 21.8 | 12.8 |
| 21.8 | 15.9 |

As can be seen k_0 is independent of the concentration of either base (within experimental error), the mean value of k_0 being $(21.1 \pm 0.4) \times 10^{-4} \text{ sec}^{-1}$ which is the rate constant for denitrosation by the solvent at this acidity.

Thus, the DNA bases appear to exhibit 'aliphatic' reactivity towards N-nitrosodiphenylamine in preferring indirect nitrosation via H_2NO_2^+ etc.. The difference in carcinogenicity between secondary nitrosamines and nitrous acid is therefore probably not due to any enhanced deamination by the nitrosamines. The type of π -electron donation envisaged for aniline may not be favorable for purines and

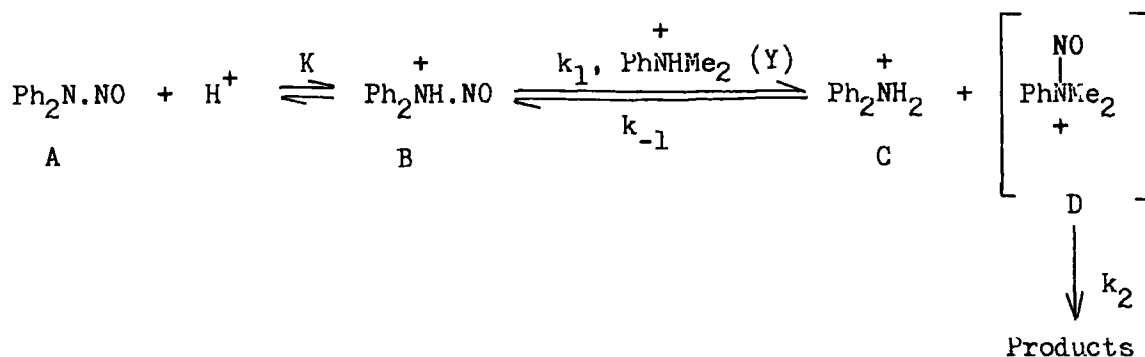
pyrimidines since the electronegative ring nitrogen atoms would be expected to cause an electron deficiency in the centre of the ring. Protonation at ring nitrogen would further enhance this effect. Support for this view comes from the observation that the 2,4 and 6 positions in the pyrimidine ring are not amenable to standard electrophilic aromatic substitution.¹⁴⁶

4.5 Nitrosation of N,N - dimethylaniline:

The rearrangement of N-nitrosodiphenylamine in the presence of N,N-dimethylaniline has been reported to yield some para-C-nitroso-N,N-dimethylaniline and this was taken as evidence of the intermolecularity of the Fischer-Hepp rearrangement.⁵ (see section 1.2). However, it would appear from the results with aniline in section 4.2 that the nitrosation of N,N - dimethylaniline is likely to follow a similar mechanism.

Reaction was again carried out in sulphuric acid containing the limiting concentration of sodium azide where it can be assumed that complete protonation of the N,N - dimethylaniline ($pK_{BH} + = 5.15$) occurs. However, unlike the case with aniline, simple first-order kinetics were not observed, the curvature of plots of $\log(a - x)$ versus t indicating a significant degree of reversibility in the reaction. The method used to circumvent this difficulty is as follows:-

On the basis of experience with the direct nitrosation of aniline it was assumed 'a priori' that direct reaction occurs also for N,N - dimethylaniline, and the following scheme was proposed.



where D is some derivative of Y though not necessarily exactly as drawn above. If D is assumed to be highly reactive it's steady-state concentration can easily be calculated.

$$\begin{aligned}
 k_1 [B] [Y] &= k_{-1} [C] [D] + k_2 [D] \\
 &= [D] (k_{-1} [C] + k_2) \\
 \therefore [D] &= \frac{k_1 [B] [Y]}{(k_{-1} [C] + k_2)}
 \end{aligned}$$

But,

$$\text{rate} = -\frac{d[A]}{dt} = k_2 [D] = \frac{k_1 k_2 [B] [Y]}{(k_{-1} [C] + k_2)}$$

Furthermore, if A is assumed to behave as a Hammett base one can write $[B] = K h_0 [A]$ so that:-

$$-\frac{d[A]}{dt} = \frac{k_1 k_2 K h_0 [A] [Y]}{(k_{-1} [C] + k_2)}$$

At time $t = 0$, $[A] = a$, $[C] = 0$

" " $t = t$, $[A] = (a-x)$, $[C] = x$

Hence, at $t = 0$ we see that $\text{rate} = k_1 K h_0 [A] [Y]$ which allows direct calculation of $k_1 K$ from the initial rate. However, since the

determination of initial rates is open to quite large errors the following technique is preferred:-

At $t > 0$ one can write

$$-\frac{d[A]}{dt} = \frac{k_1 k_2 K h_o [Y] (a-x)}{(k_{-1}x + k_2)}$$

but $x = [a - (a-x)]$ so that:-

$$-\frac{d[A]}{dt} = \frac{k_1 k_2 K h_o [Y] (a-x)}{k_2 + k_{-1} [a - (a-x)]} = \frac{k_1 k_2 K h_o [Y] (a-x)}{(k_2 + k_{-1}a) - k_{-1} (a-x)}$$

This leaves $(a-x)$ as the only time dependent variable on the right hand side of the equation which can now be seen to be hyperbolic in form.

Thus $-dt/d[A]$ should be a linear function of $1/(a-x)$ since:-

$$-\frac{dt}{d[A]} = \frac{(k_2 + k_{-1}a)}{k_1 k_2 K h_o [Y] (a-x)} - \frac{k_{-1}}{k_1 k_2 K h_o [Y]}$$

and such double reciprocal plots were indeed found to be linear for the present reaction. However, the determination of $-dt/d[A]$ by drawing tangents to the experimental curve of $[A]$ versus t is susceptible to large errors even with the use of suitable mirror devices. Hence the following procedure was adopted.

If we assume that the reaction can be represented by an observed first-order rate constant k_o then we can write:-

$$-\frac{d[A]}{dt} = k_o (a-x) = \frac{k_1 k_2 K h_o [Y] (a-x)}{(k_2 + k_{-1}a) - k_{-1} (a-x)}$$

$$\text{i.e. } k_0 = \frac{k_1 k_2 K h_0 [Y]}{(k_2 + k_{-1} a) - k_{-1} (a-x)}$$

$$\text{so that } k_0^{-1} = - \frac{k_{-1} (a-x)}{k_1 k_2 K h_0 [Y]} + \frac{(k_2 + k_{-1} a)}{k_1 k_2 K h_0 [Y]}$$

$$\text{where } k_0 = 1/t. \ln (a/a-x).$$

Hence, for each run a graph of k_0^{-1} versus $(a-x)$ should be linear with slope = $-k_{-1}/k_1 k_2 K h_0 [Y]$ and intercept = $(k_2 + k_{-1} a) / k_1 k_2 K h_0 [Y]$

Furthermore, it can be seen that:-

$$\frac{\text{Intercept}}{\text{Slope}} = - (k_2/k_{-1} + a)$$

$$\text{and } k_1 K h_0 = - \frac{k_{-1}}{k_2} \times \frac{1}{\text{Slope}} \times \frac{1}{[Y]}$$

The runs were carried out by weighing amounts of pure N,N-dimethylaniline into each flask and following the disappearance of the absorption due to N-nitrosodiphenylamine at 310 nm ($\epsilon = 5619.8$). The factor $(\text{Abs}_t = \text{Abs}_{00})$ was converted to $(a-x)$ in concentration units by dividing by ϵ , and $(\text{Abs}_0 - \text{Abs}_{00}) / \epsilon$ equated with a . The solvent was sulphuric acid (1.37M) containing sodium azide (0.16M). In fact four runs were performed varying the concentration of N,N-dimethylaniline, i.e. $[Y]$, each time.

The results are shown in Tables 30 - 33.



TABLE 30

| k_o^{-1} (sec) | $10^5(a-x)M$ |
|------------------|--------------|
| 376 | 7.1 |
| 424 | 6.3 |
| 457 | 5.6 |
| 482 | 5.0 |
| 502 | 4.6 |
| 511 | 4.1 |
| 519 | 3.7 |
| 531 | 3.4 |
| 550 | 3.1 |
| 560 | 2.9 |

TABLE 31

| k_o^{-1} (sec) | $10^5(a-x) M$ |
|------------------|---------------|
| 235 | 5.2 |
| 266 | 4.3 |
| 275 | 3.5 |
| 288 | 2.9 |
| 304 | 2.5 |
| 316 | 2.2 |
| 321 | 1.8 |
| 325 | 1.6 |
| 331 | 1.3 |
| 340 | 1.2 |

TABLE 32

| k_o^{-1} (sec) | $10^5(a-x)M$ |
|------------------|--------------|
| 154 | 5.0 |
| 162 | 4.2 |
| 169 | 3.6 |
| 176 | 3.1 |
| 183 | 2.7 |
| 185 | 2.3 |
| 189 | 2.0 |
| 191 | 1.7 |
| 195 | 1.5 |
| 200 | 1.4 |

TABLE 33

| k_o^{-1} (sec) | $10^5(a-x) M$ |
|------------------|---------------|
| 127 | 4.5 |
| 138 | 3.7 |
| 148 | 3.1 |
| 154 | 2.6 |
| 160 | 2.2 |
| 164 | 1.9 |
| 168 | 1.6 |
| 171 | 1.4 |
| 177 | 1.2 |
| 181 | 1.1 |

They are all good straight lines with correlation coefficients in excess of $|-0.99|$. The values of the slope, intercept, k_2/k_{-1} and k_1K thus calculated are shown in Table 34. For these runs $h_o = 2.63$ as obtained from the data of Robertson & Dunford.¹⁰⁰ The mean values are as follows:-

$$(k_2/k_{-1}) = (8.7 \pm 0.9) \times 10^{-5}$$

$$k_1K = 0.32 \pm 0.05$$

A typical graph is shown in Figure 9 with the data from Table 33.

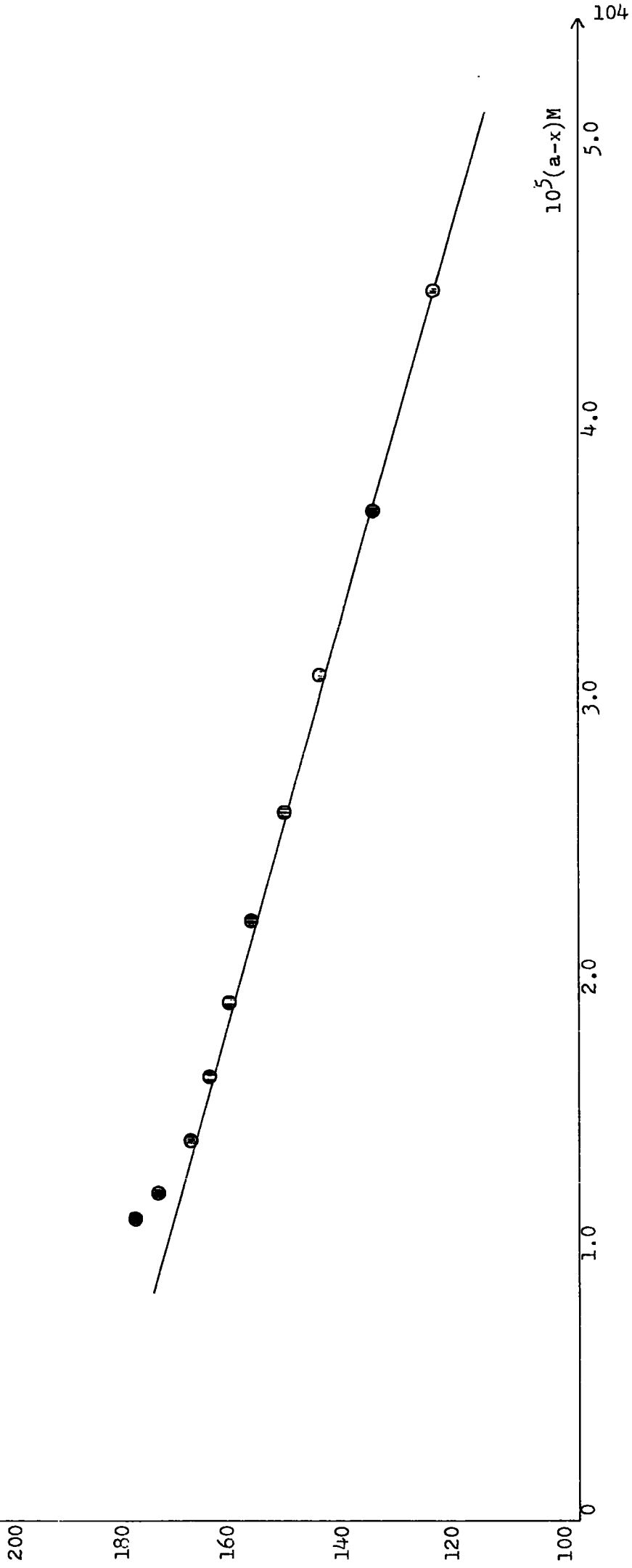
TABLE 34

| $10^3 [Y] M$ | $10^5 a.m.$ | 10^6 SLOPE | 10^2 INTERCEPT | $10^5(k_2/k_{-1})$ | k_1Kh_o | k_1K |
|--------------|-------------|--------------|------------------|--------------------|-----------|--------|
| 2.6 | 8.3 | -4.059 | 6.77 | 8.38 | 1.13 | 0.43 |
| 5.1 | 6.8 | -2.489 | 3.66 | 7.90 | 1.00 | 0.38 |
| 10.8 | 6.1 | -1.220 | 2.14 | 11.44 | 0.66 | 0.25 |
| 15.5 | 5.7 | -1.507 | 1.94 | 7.17 | 0.60 | 0.23 |

The k_1K value of 0.32 thus obtained is comparable to that of m-methoxyaniline (0.32) obtained in section 4.3. This treatment therefore yields results of the correct order of magnitude and would indicate that N,N - dimethylaniline does in fact undergo direct reaction with N-nitrosodiphenylamine, being one of the more reactive anilines studied.

FIGURE 9: k_0 VERSUS $(a - x)$

$r = -0.995$



However, no para-C-nitroso isomers, whether of Ph_2NH or PhNMe_2 , could be detected spectrophotometrically in any of the reaction solutions. It seems likely that the reversibility of the reaction ($k_{-1} \sim 10^4 k_2$) prevents the build up of p-ON-C₆H₄NMe₂ and that the $\text{Ph}_2\text{NH}\cdot\text{NO}$ is simultaneously denitrosated by the solvent so that ultimately the ' NO^+ ' is lost by reaction with HN_3 . Tertiary amines can also be cleaved by nitrous acid.¹⁴⁷



and a similar process may operate in the nitrosation of PhNMe_2 . The reaction is thus probably more complex than has been assumed here. It is also likely that the early identification of p-ON-C₆H₄NMe₂ by Houben⁵ was made possible by the use of alcoholic rather than aqueous acidic media. Johal¹² has shown that in alcoholic HCl the denitrosation of PhNMeNO and $\text{Ph}_2\text{N}\cdot\text{NO}$ occurs rapidly (within minutes) without any rearrangement but on standing overnight the same solutions gave good yields of rearrangement product. It therefore appears that the mechanism could well be different in the two types of solvent. The involvement of alkyl nitrites (RONO) in the alcoholic rearrangement has not yet been investigated thoroughly, but could well be important.

Finally, it is of interest to recall that the proposed scheme for the direct nitrosation of N,N - dimethylaniline by N-nitroso-diphenylamine gives the equation:-

$$k_o = \frac{k_1 k_2 K h_o [Y]}{k_2 + k_{-1} [C]}$$

For N,N - dimethylaniline it was found that $k_{-1} > k_2$ which results in

curved first-order plots. With aniline, however, one would expect $k_2 > k_{-1}$ which reduces the rate equation to:-

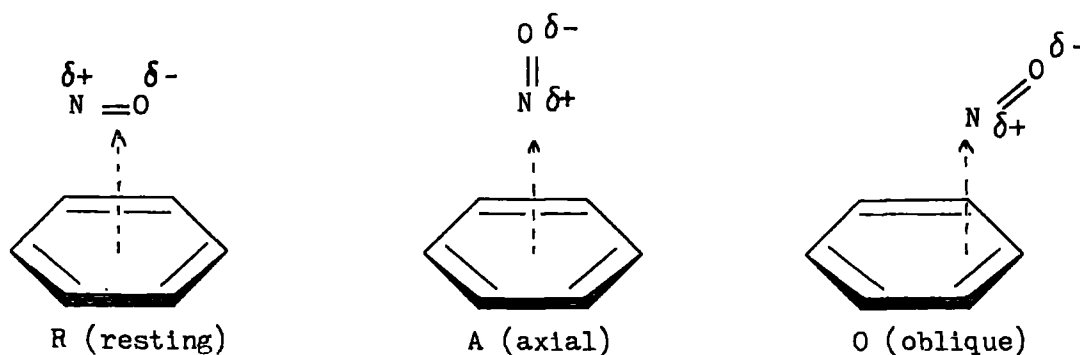
$$k_o = k_1 K h_o [Y]$$

so that one would expect reasonable first-order behaviour and a linear dependence of k_o upon $[Y]$ as outlined in section 4.2.

4.6 Consequences for Fischer-Hepp Rearrangement

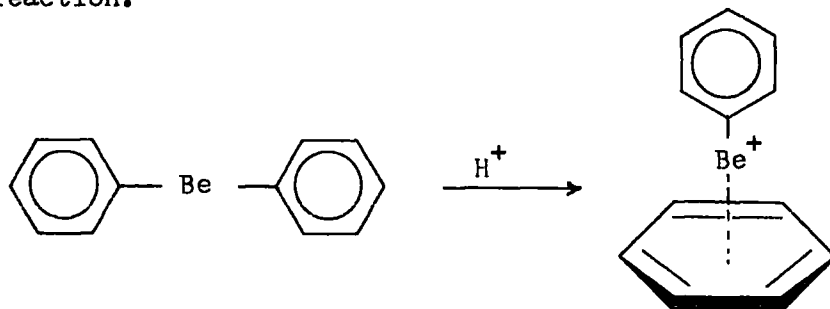
In section 1.6 the Fischer-Hepp rearrangement was discussed in terms of generalized perturbation theory and π - complexes between $ArNHR$ and NO^+ were proposed to account for the intramolecular nature of the reaction in aqueous solution. The results of this chapter suggest another possibility, namely direct reaction between the protonated nitrosamine and its product of denitrosation via a π - complex. Since both donor and acceptor are structurally very similar one would expect degenerate orbital-controlled reaction and predominantly para-substitution.

However, the major difference between the two types of π - complex is the larger size of the organic nitrosating agent compared with NO^+ . What effect this has on the geometry of the π - complex is uncertain. The scheme in section 4.2 has the acceptor lying over the centre of the donor benzene ring. There are several alternatives, however, and consideration of the simple case with NO^+ shows that there are in fact three types of orientation with respect to the benzene ring.¹⁴⁸



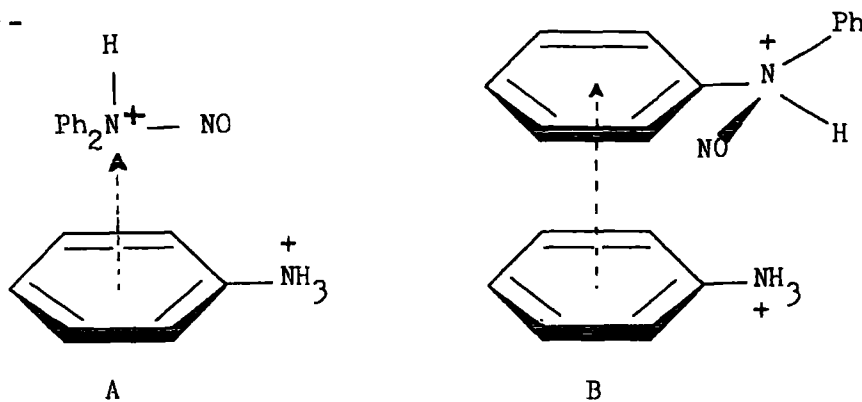
Model R gives the maximum orbital overlap but suffers from dipole- π electron repulsion so that the partially negative oxygen is repelled as in model O. It is further argued that model A is in fact least likely since the π -electron density is lowest in the centre of the ring.¹⁴⁸ Support for this comes from the X-ray diffraction pattern of the complex $\text{Ag}^+ \cdot \text{Bz} \cdot \text{ClO}_4^-$ which shows that the silver ion lies off-centre with respect to the ring.¹⁴⁹

However, MINDO calculations for the π -complex formed from benzene and BeH^+ indicate that maximum stability is obtained when the beryllium has six nearest neighbours, i.e. when it lies over the 6-fold symmetry axis of the ring, and evidence has been obtained for the reaction:¹⁵⁰

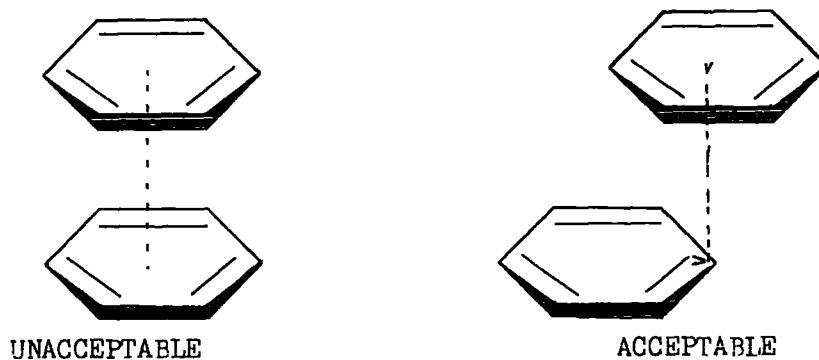


The exact conformation of the benzene- NO^+ π -complex is therefore unclear at the present time.

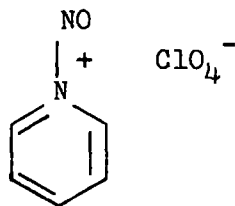
Likewise, it is not yet clear how the π -complex formed from $\text{Ph}_2\text{NH}^+\text{NO}$ and aniline achieves maximum stability. Two possible arrangements are:-

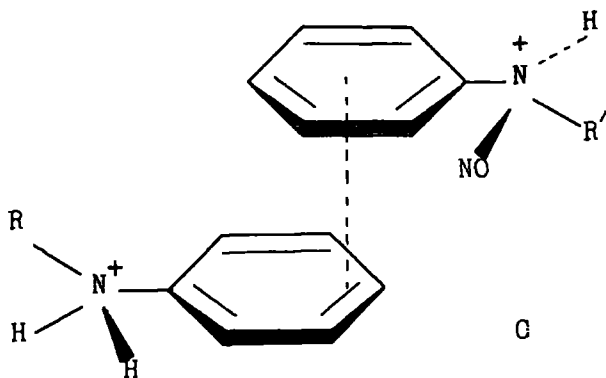


However, the tetrahedral arrangement around the amino nitrogen in the nitrosamine would be expected to hinder model A. Furthermore, model B offers maximum degeneracy in the acceptor-donor interaction. It has been pointed out, however, that models having benzene rings superimposed with their 6-fold axes coincident have zero-overlap integral and are therefore untenable.¹⁵¹



The geometry of the $\text{Ph}_2\text{NH}\cdot\text{NO} - \text{PhNH}_3$ π -complex is therefore probably unsymmetrical in having the staggered ring conformation. What influence this would have on the steric interactions in such complexes is unclear. For example, although model B appears likely for aniline (to account for the observed diazotization) with staggered rings, the introduction of N-alkyl groups into the aniline may result in severe steric crowding so that the preferred geometry becomes as in model C. This may well account for exclusive para-C-nitrosation in the reaction of $\text{Ph}_2\text{N}\cdot\text{NO}$ and PhNMe_2 in alcoholic HCl. The Fischer-Hepp rearrangement then becomes the special case with $\text{R} = \text{R}'$. If this is the case then one would expect an induction period for the actual rearrangement during which the concentration of PhNH_2R builds up through denitrosation. This scheme also predicts no Fischer-Hepp rearrangement for N-nitrosopyridinium salts.





since π -complex formation is hindered by the positive ring nitrogen (cf. purines and pyrimidines, section 4.4).

This type of mechanism for rearrangement had earlier been ruled out by Williams^{10,14} since direct reactions between N-methyl-N-nitrosoaniline and aniline was not observed. However, the range of aniline concentrations was not large ($1-5 \times 10^{-2}M$) and reaction was carried out in 3.05M hydrochloric acid where competition by Cl^- would seriously hinder the direct diazotization. In the present case the aniline was varied in concentration from $2 - 60 \times 10^{-3}M$ and the reaction conducted in 0.60M sulphuric acid to avoid competition from other nucleophiles. It may well prove useful to re-examine the reaction between PhNMeNO and aniline under the conditions used here.

S E C T I O N T H R E E

CHAPTER FIVE

Diazotization with Nitrosyl Bromide

5.1 Introduction:

Results are presented here for a detailed examination of the kinetics of diazotization for a range of ring substituted anilines in aqueous sulphuric acid ($\sim 0.2M$) containing sodium nitrite (varying from amine to amine in the range $0.5 - 5.0 \times 10^{-4}M$), and potassium bromide (over the range $0.01 - 0.08M$) where the effective nitrosating agent is thought to be nitrosyl bromide.⁸⁰ In each case the total amine concentration was always in at least twenty-fold excess over the corresponding total nitrous acid concentration. This ensures pseudo-first order behaviour. In practice good first-order behaviour in nitrous acid was always observed both from the linearity of plots of $\log(a-x)$ versus t and from the constancy of the observed rate-constant k_o upon doubling the initial sodium nitrite concentration. This rate-constant is defined by:-

$$- d [HNO_2] / dt = k_o [HNO_2]$$

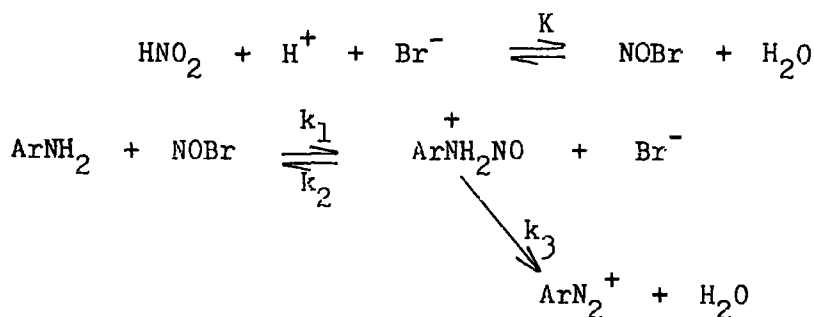
where $[HNO_2]$ corresponds to the total 'nitrite' concentration. Reaction via N_2O_3 was therefore ruled out since otherwise a second-order dependence upon nitrous acid would be observed.⁹⁰ The values of k_o remained unchanged on doubling the acidity at any one bromide concentration which further rules out reaction via the nitrous acidium ion.⁸⁵ In all cases k_o was found to be directly proportional to the total amine concentration.

The rate measurements were carried out using a 'Canterbury' stopped flow spectrophotometer at $25^\circ C$ and the effect of varying both $[Br^-]$ and $[Amine]$ upon k_o was observed. Each quoted value of k_o

is in fact the mean of five separate determinations with a standard deviation of $\pm 2\%$ or less. In view of the instability of the product diazonium ions extensive use was made of the Guggenheim method for first-order reactions.¹⁵² Details of the experimental technique and the methods used to calculate k_0 and the attendant errors will be found in Chapter 7.

5.2 The Steady-State Treatment

The scheme of Hughes & Ridd⁹⁰ shown in section 2.3 can be taken as the basis for a more detailed model.



Assuming $\overset{+}{\text{ArNH}_2\text{NO}}$ to behave as a reactive intermediate permits the use of the stationary state approximation. Here it is therefore assumed that $[\overset{+}{\text{ArNH}_2\text{NO}}]$ remains constant during the course of the reaction so that:-

$$\begin{aligned} \text{Rate of formation of } \overset{+}{\text{ArNH}_2\text{NO}} &= \text{Rate of destruction of } \overset{+}{\text{ArNH}_2\text{NO}} \\ k_1 [\text{ArNH}_2] [\text{NOBr}] &= k_2 [\overset{+}{\text{ArNH}_2\text{NO}}] [\text{Br}^-] + k_3 [\overset{+}{\text{ArNH}_2\text{NO}}] \\ &= [\overset{+}{\text{ArNH}_2\text{NO}}] (k_2 [\text{Br}^-] + k_3) \end{aligned}$$

$$\therefore [\overset{+}{\text{ArNH}_2\text{NO}}] = \frac{k_1 [\text{ArNH}_2] [\text{NOBr}]}{(k_2 [\text{Br}^-] + k_3)}$$

$$\text{But, Rate} = \frac{d[\text{ArN}_2^+]}{dt} = k_3 [\overset{+}{\text{ArNH}_2\text{NO}}]$$

so that,
$$\text{Rate} = \frac{k_1 k_3 [\text{ArNH}_2] [\text{NOBr}]}{(k_2 [\text{Br}^-] + k_3)}$$

However,
$$[\text{NOBr}] = K [\text{HNO}_2] [\text{H}^+] [\text{Br}^-]$$

$$\text{Rate} = \frac{k_1 k_3 [\text{ArNH}_2] K [\text{HNO}_2] [\text{H}^+] [\text{Br}^-]}{(k_2 [\text{Br}^-] + k_3)}$$

and since the observed rate-constant has been defined as $-\frac{d[\text{HNO}_2]}{dt} = k_o [\text{HNO}_2]$ one can write:-

$$k_o = \frac{k_1 k_3 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]}{(k_2 [\text{Br}^-] + k_3)}$$

The value of K for the formation of NOBr is known⁹⁶ and has a value of $5.1 \times 10^{-2} \text{ mol}^{-2} \text{ dm}^6$ at 25°C.

Two limiting conditions can be envisaged. Firstly $k_3 \gg k_2 [\text{Br}^-]$ when the rate equation reduces to:-

$$k_o = k_1 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]$$

and secondly $k_2 [\text{Br}^-] \gg k_3$ when:-

$$k_o = \frac{k_1 k_3 K \cdot [\text{ArNH}_2] [\text{H}^+]}{k_2}$$

The first predicts that at constant acidity and bromide concentration k_o will be a linear function of $[\text{ArNH}_2]$ and the second that at high bromide concentration k_o will become independent of $[\text{Br}^-]$

Note that no allowance has been made for activity effects which would tend to increase the calculated k_1 values somewhat. It is felt that these effects will be small in the dilute reaction conditions and

that applying the approximate Debye-Hückel corrections would lead to greater error.

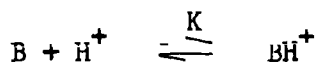
5.3 Limiting Case $k_3 \gg k_2 [\text{Br}^-]$

This is the 'normal' situation where the ArNH_2NO^+ intermediate reacts rapidly and irreversibly to give the diazonium ion. The condition is obviously best satisfied at low bromide concentration. Since:-

$$k_0 = k_1 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]$$

values of k_1 can be calculated from the slope of a graph of k_0 versus $[\text{ArNH}_2]$. The fact that the observed rate-constants are larger for those anilines carrying electron-withdrawing substituents argues in favour of reaction between NOBr and the unprotonated amine since at any one acidity there will be proportionally more free base present than in the case of the more basic amines. Indeed the results only make sense when interpreted in this way.

The experimental results for seven amines are shown in Tables 36 - 42 where the k_0 values are displayed against the total added amine concentration and the corresponding concentration of unprotonated amine. The slopes are calculated by a least-squares procedure (see chapter ?) and refer to k_0 versus free base concentration. The concentrations of free base are calculated as follows:-



$$[\text{BH}^+] = K [\text{B}] [\text{H}^+]$$

$$\begin{aligned} [\text{B}]_{\text{TOT}} &= [\text{B}] + [\text{BH}^+] \\ &= [\text{B}] + K [\text{B}] [\text{H}^+] \\ &= [\text{B}] (1 + K [\text{H}^+]) \end{aligned}$$

so that:-
$$[B] = \frac{[B]_{\text{tot}}}{(1 + K [H^+])}$$

where $K = \frac{1}{K_{\text{BH}^+}} = 10^{\text{pK}_{\text{BH}^+}}$. The values of pK_{BH^+} have been obtained from Perrin,¹⁴¹ and for convenience are listed in Table 35.

TABLE 35

| ANILINE | pK_{BH^+} (25°C) |
|-------------------|----------------------------------|
| p-Ome | 5.357 |
| p-Me | 5.084 |
| H | 4.596 |
| m-Ome | 4.204 |
| p-Cl | 3.982 |
| p-COOH | 2.42 |
| p-NO ₂ | 1.019 |

In the following Tables [Amine] refers to the total added amine and [ArNH₂] to the concentration of free base.

TABLE 36; ANILINE

| $10^2 k_o \text{ sec}^{-1}$ | 10^3 [Amine] M | 10^7 [ArNH ₂] M |
|-----------------------------|------------------|-------------------------------|
| 0 | 0 | 0 |
| 16.0 | 5.46 | 3.46 |
| 23.4 | 8.74 | 5.54 |
| 33.2 | 12.01 | 7.61 |
| 42.1 | 15.29 | 9.69 |

TABLE 37: m - ANISIDINE

| $k_o \text{ sec}^{-1}$ | $10^3 [\text{Amine}] \text{ M}$ | $10^7 [\text{ArNH}_2] \text{ M}$ |
|------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 0.524 | 5.02 | 6.82 |
| 0.830 | 8.03 | 10.91 |
| 1.05 | 11.04 | 15.00 |
| 1.35 | 14.06 | 19.11 |

TABLE 38: p - ANISIDINE

| $10^2 k_o \text{ sec}^{-1}$ | $10^3 [\text{Amine}] \text{ M}$ | $10^8 [\text{ArNH}_2] \text{ M}$ |
|-----------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 1.38 | 1.15 | 1.05 |
| 2.05 | 1.85 | 1.69 |
| 2.80 | 2.54 | 2.33 |
| 3.89 | 3.23 | 2.96 |

TABLE 39: p - TOLUIDINE

| $10^2 k_o \text{ sec}^{-1}$ | $10^4 [\text{Amine}] \text{ M}$ | $10^8 [\text{ArNH}_2] \text{ M}$ |
|-----------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 1.37 | 6.80 | 1.33 |
| 1.98 | 10.88 | 2.13 |
| 2.91 | 14.96 | 2.93 |
| 3.55 | 19.04 | 3.74 |

TABLE 40: p-AMINO BENZOIC ACID

| $k_o \text{ sec}^{-1}$ | $10^3 [\text{Amine}] \text{ M}$ | $10^5 [\text{ArNH}_2] \text{ M}$ |
|------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 3.04 | 3.04 | 2.60 |
| 4.63 | 4.87 | 4.17 |
| 5.77 | 6.70 | 5.74 |
| 6.88 | 8.53 | 7.31 |

TABLE 41: p-CHLOROANILINE

| $k_o \text{ sec}^{-1}$ | $10^2 [\text{Amine}] \text{ M}$ | $10^6 [\text{ArNH}_2] \text{ M}$ |
|------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 2.24 | 1.08 | 2.01 |
| 2.60 | 1.71 | 3.18 |
| 2.62 | 2.36 | 4.39 |
| 3.80 | 3.00 | 5.58 |

TABLE 42: p-NITROANILINE

| $k_o \text{ sec}^{-1}$ | $10^3 [\text{Amine}] \text{ M}$ | $10^4 [\text{ArNH}_2] \text{ M}$ |
|------------------------|---------------------------------|----------------------------------|
| 0 | 0 | 0 |
| 4.00 | 2.05 | 3.53 |
| 4.88 | 2.66 | 4.58 |
| 5.61 | 3.48 | 5.99 |

Values of k_1 can then be obtained from plots of k_o versus ArNH_2 since $\text{Slope} = k_1 K [\text{H}^+] [\text{Br}^-]$. A modified least squares procedure has been used to calculate the 'best' slope because the origin is

unambiguously fixed and the line must pass through this point. The relevant acidity and bromide data are shown in Table 43 along with the values calculated for the slope and k_1 .

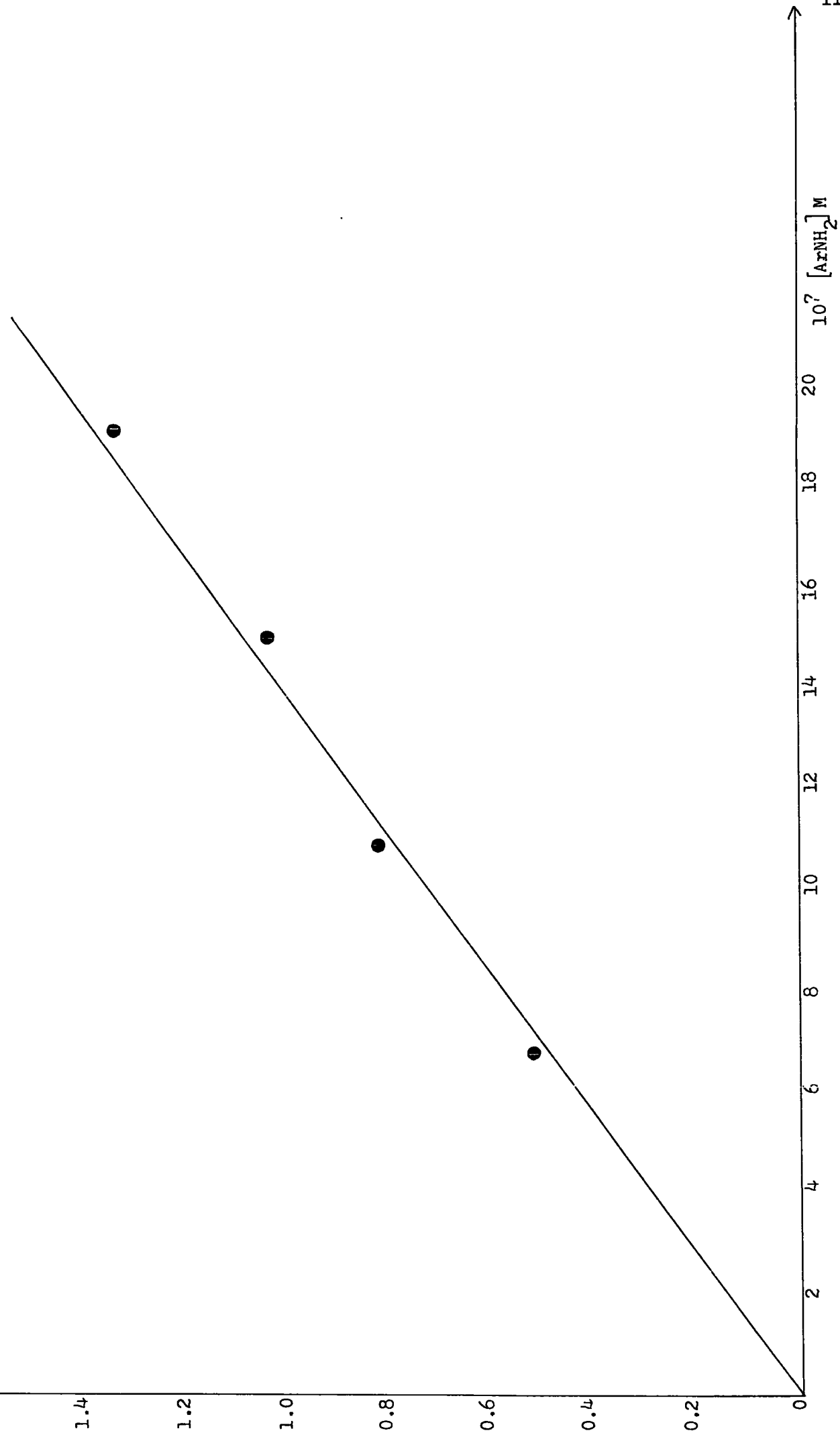
TABLE 43

| ANILINE | $10^4[\text{NaNO}_2] \text{ M}$ | $10^2[\text{Br}^-] \text{ M}$ | $[\text{H}^+] \text{ M}$ | 10^{-5} Slope | $10^{-9} k_1 \cdot 1 \text{ mol}^{-1} \text{ sec}^{-1}$ |
|-------------------|---------------------------------|-------------------------------|--------------------------|-------------------------|---|
| p-Ome | 2.0 | 1.56 | 0.48 | 12.646 | 3.31 |
| p-Me | 4.0 | 1.56 | 0.42 | 9.641 | 2.88 |
| m-Ome | 0.5 | 1.56 | 0.46 | 7.169 | 1.96 |
| H | 3.0 | 1.29 | 0.40 | 4.348 | 1.65 |
| p-Cl | 5.0 | 1.55 | 0.56 | 7.044 | 1.59 |
| p-COOH | 1.5 | 1.54 | 0.44 | 1.001 | 0.29 |
| p-NO ₂ | 0.5 | 1.51 | 0.46 | 0.101 | 0.03 |

A typical graph is shown in Figure 10.

The theoretical treatment of Smoluchowski¹⁵³ predicts a value of k of $\sim 7 \times 10^9 \text{ l. mole}^{-1} \text{ sec}^{-1}$ for the diffusion-controlled bimolecular encounter of uncharged reactants in water at 25°C and it can be seen that the k_1 values tend towards this limit. Furthermore the effect of substituents upon k_1 can be seen to be more marked for those amines with $\text{pK}_{\text{BH}^+} < 4$. This is no doubt due to the influence of the diffusion limit upon the relative reactivities of the more basic amines and this leads to curvature in the Bronsted plot of $\log k_1$ versus pK_{BH^+} . This matter will be discussed in connection with the k_1 values for the corresponding NOCl reactions in Chapter 6. The data of Schmid⁹⁶ for the NOBr reaction is rather incomplete, the only quoted result being that for aniline with $k_1 = 3.2 \times 10^9 \text{ l. mole}^{-1} \text{ sec}^{-1}$. The present value is somewhat smaller than this but the general agreement is quite good.

FIGURE 10: k_o VERSUS [p-TOLUIDINE]



The order with respect to nitrous acid was in each case checked at the lowest amine concentration by doubling or halving the original concentration of sodium nitrite used, with $[H^+]$ and $[Br^-]$ held constant at the values shown in Table 43. The results are shown in Table 44.

TABLE 44

| ANILINE | $10^4 [NaNO_2] M$ | $k_o \text{ sec}^{-1}$ | $10^4 [NaNO_2] M$ | $k_o \text{ sec}^{-1}$ |
|-------------------|-------------------|------------------------|-------------------|------------------------|
| p-OMe | 2.0 | 1.38×10^{-2} | 4.0 | 1.71×10^{-2} |
| p-Me | 4.0 | 1.37×10^{-2} | 2.5 | 1.40×10^{-2} |
| m-OMe | 0.5 | 0.524 | 1.2 | 0.547 |
| H | 3.0 | 0.16 | 7.2 | 0.17 |
| p-Cl | 5.0 | 2.24 | 2.5 | 1.71 |
| p-COOH | 1.5 | 3.04 | 2.5 | 3.07 |
| p-NO ₂ | 0.5 | 4.0 | 1.0 | 3.8 |

As can be seen no significant changes in k_o were recorded so that the reaction is first-order in nitrous acid.

Likewise the effect of acidity was examined at the lowest amine concentration with all else held constant as in Table 43. The results are shown in Table 45.

TABLE 45

| ANILINE | $[H^+] M$ | $k_o \text{ sec}^{-1}$ | $[H^+] M$ | $k_o \text{ sec}^{-1}$ |
|-------------------|-----------|------------------------|-----------|------------------------|
| p-OMe | 0.48 | 1.38×10^{-2} | 0.85 | 1.62×10^{-2} |
| p-Me | 0.42 | 1.37×10^{-2} | 0.76 | 1.63×10^{-2} |
| m-OMe | 0.46 | 0.524 | 0.75 | 0.538 |
| H | 0.40 | 0.16 | 0.67 | 0.16 |
| p-Cl | 0.56 | 2.2 | 0.74 | 2.4 |
| p-COOH | 0.44 | 3.04 | 0.78 | 3.24 |
| p-NO ₂ | 0.40 | 4.0 | 0.74 | 4.1 |

Again it can be seen that k_0 is independent of the acidity (within experimental error).

5.4 Limiting Case $k_2 [\text{Br}^-] \gg k_3$

This is the situation where the reversibility of ArNH_2NO formation competes with the process leading to the diazonium ion. The steady state model predicts that at sufficiently high bromide concentration k_0 becomes independent of $[\text{Br}^-]$ and the rate-equation then takes the form:-

$$k_0 = \frac{k_1 k_3 K}{k_2} [\text{ArNH}_2] [\text{H}^+]$$

from which the ratio k_2/k_3 can be calculated using the k_1 values from the preceding section. However, this limit was not reached with any of the amines studied. The results are drawn up in Tables 46 - 52.

It can be seen that the graphs of k_0 versus $[\text{Br}^-]$ resolve into two groups:

- (a) For those amines with $\text{pK}_{\text{BH}^+} > 4.0$ the graphs appear linear.
- (b) For those amines with $\text{pK}_{\text{BH}^+} < 4.0$ the graphs exhibit curvature.

The curvature is most marked for the powerfully electron withdrawing groups - COOH and - NO₂.

TABLE 46: p-ANISIDINE

$$[\text{ArNH}_2] = 1.05 \times 10^{-8} \text{M}; [\text{H}^+] = 0.48 \text{M}$$

| $10^2 k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|-----------------------------|--------------------------------|
| 0 | 0 |
| 1.38 | 1.56 |
| 2.43 | 3.12 |
| 3.41 | 4.68 |
| 5.08 | 6.24 |
| 6.16 | 7.80 |

TABLE 47: p-TOLUIDINE

$$[\text{ArNH}_2] = 1.33 \times 10^{-8} \text{M}; [\text{H}^+] = 0.42 \text{M}$$

| $10^2 k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|-----------------------------|--------------------------------|
| 0 | 0 |
| 1.37 | 1.56 |
| 2.36 | 3.12 |
| 2.88 | 4.68 |
| 4.73 | 6.24 |
| 5.50 | 7.80 |

TABLE 48: m-ANISIDINE

$$[\text{ArNH}_2] = 6.82 \times 10^{-7} \text{M}; [\text{H}^+] = 0.46 \text{M}$$

| $k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|------------------------|--------------------------------|
| 0 | 0 |
| 0.503 | 1.56 |
| 0.773 | 2.49 |
| 1.028 | 3.43 |
| 1.185 | 4.36 |
| 1.405 | 5.30 |
| 1.591 | 6.23 |

TABLE 49: p-NITROANILINE

$$[\text{ArNH}_2] = 3.53 \times 10^{-4} \text{M}; [\text{H}^+] = 0.40 \text{M}$$

| $k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|------------------------|--------------------------------|
| 0 | 0 |
| 4.0 | 1.51 |
| 5.9 | 3.02 |
| 7.9 | 4.53 |
| 8.4 | 6.04 |

TABLE 50: p-AMINO BENZOIC ACID

$$[\text{ArNH}_2] = 2.60 \times 10^{-5} \text{M}; [\text{H}^+] = 0.44 \text{M}$$

| $k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|------------------------|--------------------------------|
| 0 | 0 |
| 3.04 | 1.54 |
| 5.47 | 3.08 |
| 7.15 | 4.62 |
| 8.64 | 6.16 |
| 9.87 | 7.70 |

TABLE 51: p-CHLOROANILINE

$$[\text{ArNH}_2] = 2.01 \times 10^{-6} \text{M}; [\text{H}^+] = 0.56 \text{M}$$

| $k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|------------------------|--------------------------------|
| 0 | 0 |
| 2.24 | 1.55 |
| 3.6 | 3.10 |
| 5.22 | 4.65 |
| 6.1 | 6.21 |
| 7.6 | 7.75 |

TABLE 52: ANILINE

$$[\text{ArNH}_2] = 3.46 \times 10^{-7} \text{M}; \quad [\text{H}^+] = 0.40 \text{M}$$

| $10^2 k_o \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ |
|-----------------------------|--------------------------------|
| 0 | 0 |
| 10.9 | 1.04 |
| 16.0 | 1.29 |
| 22.2 | 1.81 |
| 26.8 | 2.33 |
| 28.2 | 2.59 |
| 29.3 | 2.85 |
| 33.5 | 3.11 |
| 39.1 | 3.37 |
| 45.1 | 3.61 |
| 50.1 | 4.13 |
| 55.2 | 4.64 |

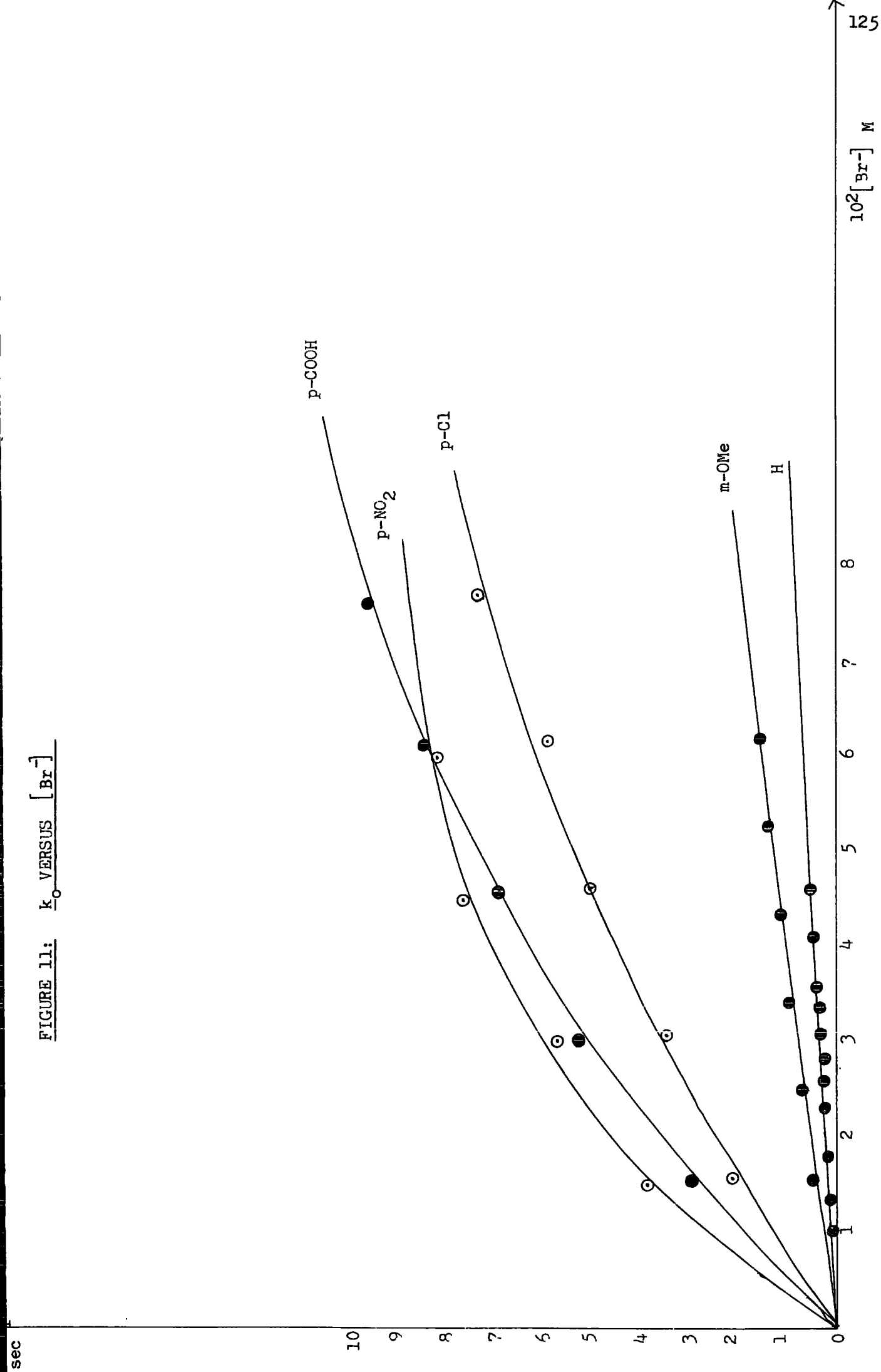
The graphs are shown in Figure 11 except for p-Me and p-OMe for which the slopes are smaller than that for aniline. The lines cannot be conveniently represented on the same scale.

With reference to the reaction scheme outlined in section 5.2, one might speculate on how an electron-withdrawing group should affect the values of k_1 , k_2 and k_3 relative to those for aniline.

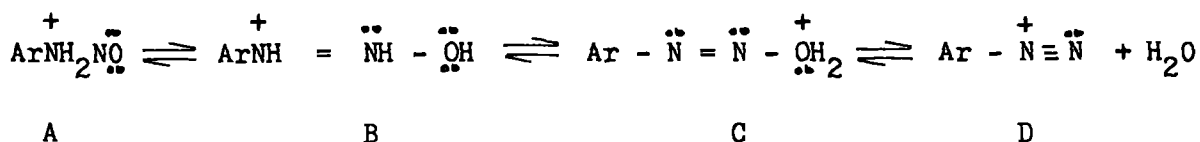
(a) It should decrease k_1 by making the amino lone-pair less available for attack by the electrophilic NOBr.

(b) It should increase k_2 for the same reason since the nucleophilic Br^- now attacks.

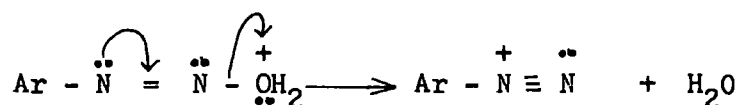
FIGURE 11: k_0 VERSUS $[Br^-]$



As an approximation one might expect these effects to cancel so that the overall effect will be largely due to that upon k_3 . However, the effect on k_3 is not clear-cut since this is a composite rate-constant representing a multi-stage process, viz:-



The effect on the formation of C from A would be expected to be small since the rate of proton loss from nitrogen will be enhanced whilst the rate of O-protonation will be retarded. These effects should cancel (approximately) so that the overall substituent effect will operate largely on the rate of formation of D from C. This will clearly be retarded by an electron withdrawing substituent since delocalisation of the amino lone-pair would retard the process:-



If this is so then k_3 (p-NO₂) < k_3 (p-COOH) < k_3 (p-Cl) < k_3 (H) < k_3 (m-OMe) < k_3 (p-Me) < k_3 (p-OMe). The limiting condition k_2 [Br⁻] \gg k_3 should therefore be satisfied at the lowest bromide concentration for p-nitroaniline, since k_2 will be largest and k_3 smallest for this substrate. This would explain the shapes of the curves in Figure 11 where that for p-nitroaniline tends to zero-order bromide dependence at the lowest bromide concentration. This aspect of the diazotization process will be discussed in more detail in section 6.3 where the k_2/k_3 ratios for both the NOBr and NOCl reactions will be compared.

5.5 Non-Limiting Conditions

The bromide concentrations of the preceding section failed to realise the limiting condition $k_2 [\text{Br}^-] \gg k_3$. It should therefore prove possible to treat the data according to the non-limiting rate equation:-

$$k_o = \frac{k_1 k_3 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]}{(k_2 [\text{Br}^-] + k_3)}$$

which is a hyperbolic curve. Written in the form,

$$1/k_o = 1/k_1 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-] + k_2/k_1 k_3 K [\text{ArNH}_2] [\text{H}^+]$$

it is evident that a straight line results when $1/k_o$ is plotted against $1/[\text{Br}^-]$. From the slopes of such plots values for k_1 can be obtained and compared with those obtained in section 5.3 from the plots of k_o versus $[\text{ArNH}_2]$. The intercepts yield the corresponding k_2/k_3 ratios.

The relevant data are listed below in Tables 53 - 59 and are compiled from the results of the preceding section.

TABLE 53: p- ANISIDINE

| $1/k_o$ sec | $1/[\text{Br}^-] \text{ M}^{-1}$ |
|-------------|----------------------------------|
| 72.46 | 64.10 |
| 41.15 | 32.05 |
| 29.32 | 21.37 |
| 19.68 | 16.03 |
| 16.23 | 12.82 |

TABLE 54: p-TOLUIDINE

| $1/k_0$ sec | $1/[Br^-] M^{-1}$ |
|-------------|-------------------|
| 72.99 | 64.10 |
| 42.37 | 32.05 |
| 34.72 | 21.37 |
| 21.14 | 16.03 |
| 18.18 | 12.82 |

TABLE 55: m-ANISIDINE

| $1/k_0$ sec | $1/[Br^-] M^{-1}$ |
|-------------|-------------------|
| 1.99 | 64.10 |
| 1.29 | 40.16 |
| 0.97 | 29.15 |
| 0.84 | 22.94 |
| 0.71 | 18.87 |
| 0.63 | 16.05 |

TABLE 56: p-NITROANILINE

| $1/k_0$ sec | $1/[Br^-] M^{-1}$ |
|-------------|-------------------|
| 0.25 | 66.22 |
| 0.17 | 33.11 |
| 0.13 | 22.07 |
| 0.12 | 16.56 |

TABLE 57: p-AMINOBENZOIC ACID

| $1/k_0$ sec | $1/[Br^-]$ M ⁻¹ |
|-------------|----------------------------|
| 0.33 | 64.93 |
| 0.18 | 32.47 |
| 0.14 | 21.64 |
| 0.12 | 16.23 |
| 0.10 | 12.99 |

TABLE 58: p-CHLOROANILINE

| $1/k_0$ sec | $1/[Br^-]$ M ⁻¹ |
|-------------|----------------------------|
| 0.45 | 64.52 |
| 0.28 | 32.26 |
| 0.19 | 21.50 |
| 0.16 | 16.10 |
| 0.13 | 12.90 |

TABLE 59: ANILINE

| $1/k_0$ sec | $1/[Br^-]$ M ⁻¹ |
|-------------|----------------------------|
| 9.17 | 96.15 |
| 6.25 | 77.52 |
| 4.50 | 55.25 |
| 3.73 | 42.92 |
| 3.55 | 38.61 |
| 3.41 | 35.09 |
| 2.98 | 32.15 |
| 2.56 | 29.67 |
| 2.22 | 27.70 |
| 2.00 | 24.21 |
| 1.81 | 21.55 |

The results presented in Table 60 have been calculated by the normal least squares procedure.

TABLE 60

| ANILINE | SLOPE | $10^{-9}k_1$ l.mole ⁻¹ sec ⁻¹ | INTERCEPT | k_2/k_3 l.mole ⁻¹ |
|-------------------|--------|---|-----------|--------------------------------|
| p-Ome | 1.0862 | 3.58 | 3.9694 | 3.65 |
| p-Me | 1.0444 | 3.36 | 7.3047 | 6.99 |
| m-Ome | 0.0282 | 2.22 | 0.1741 | 6.18 |
| H | 0.0784 | 1.81 | 0.2842 | 3.63 |
| p-Cl | 0.0061 | 2.84 | 0.0612 | 7.80 |
| p-COOH | 0.0044 | 0.39 | 0.0445 | 10.12 |
| p-NO ₂ | 0.0026 | 0.05 | 0.0762 | 27.42 |

In all cases $r > 0.99$. A typical graph is shown in Figure 12.

The k_1 values from both methods are collected together in Table 61 for convenience and it can be seen that the general agreement is quite good.

TABLE 61

| ANILINE | $10^{-9}k_1$ (a) | $10^{-9}k_1$ (b) |
|-------------------|------------------|------------------|
| p-Ome | 3.3 | 3.6 |
| p-Me | 2.9 | 3.4 |
| m-Ome | 2.0 | 2.2 |
| H | 1.7 | 1.8 |
| p-Cl | 1.6 | 2.8 |
| p-COOH | 0.3 | 0.4 |
| p-NO ₂ | 0.03 | 0.05 |

(a) From k_0 versus $[\text{ArNH}_2]$

(b) From k_0^{-1} versus $1/[\text{Br}^-]$

In view of the round-off errors introduced into the double-reciprocal plots it is thought that the values from method (a) are more accurate and confidence limits for these values are given in Chapter 7.

Discussion of the k_2/k_3 values will be found in Chapter 6 where the corresponding values for the NOCl reaction will also be given.

5.6 The Slow Process

For those anilines containing an electron withdrawing group ($-\text{NO}_2$, $-\text{Cl}$, and $-\text{COOH}$) a second, slower reaction was observed. This had quite different characteristics from the first in that, although it was first-order in total nitrous acid, it was first-order in $[\text{H}^+]$ and independent of both $[\text{Amine}]$ and $[\text{Br}^-]$.

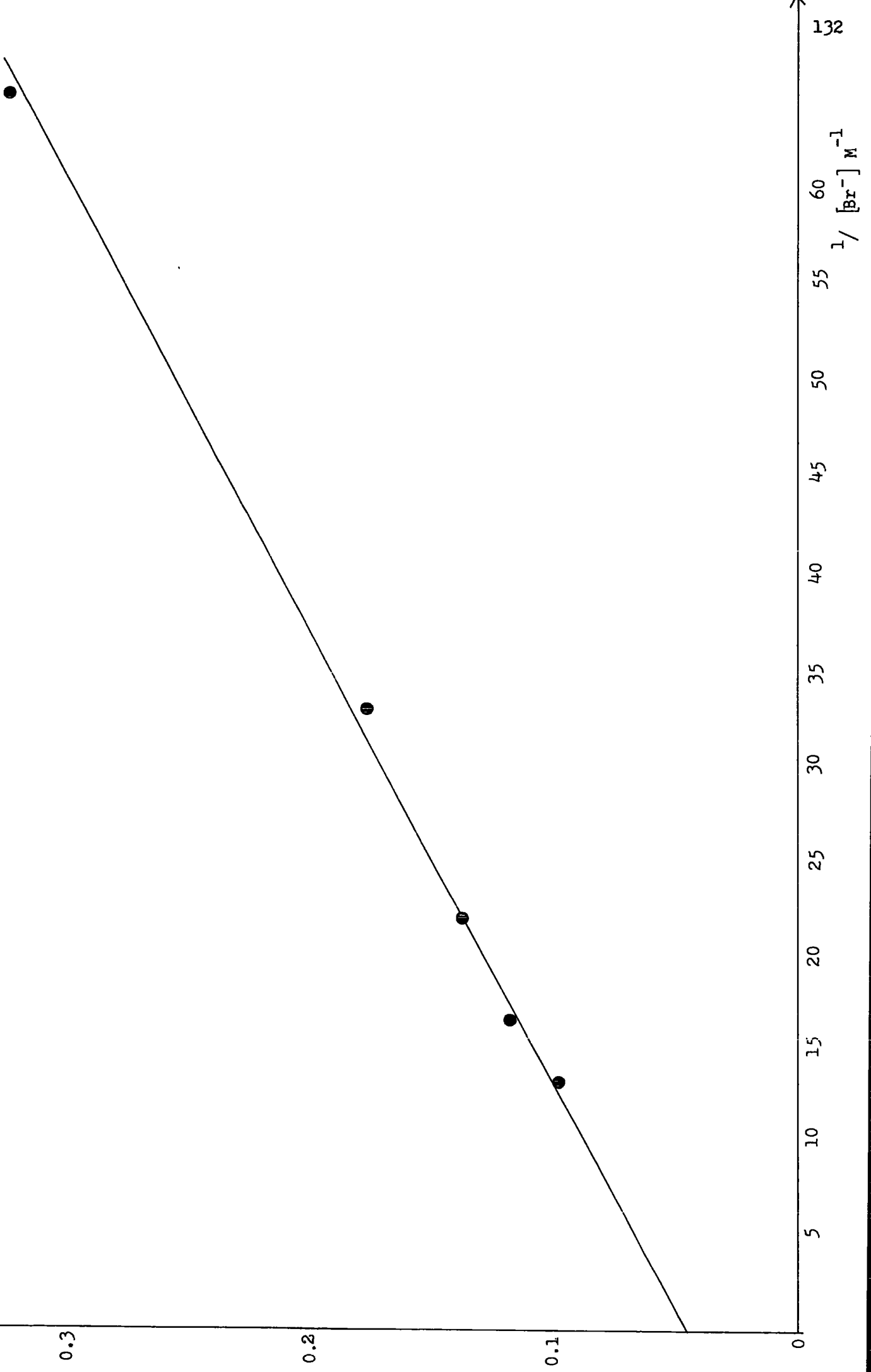
The results for p-chloroaniline and p-aminobenzoic acid are shown in Tables 62 and 63 although it must be borne in mind that the k_0 values are less accurate than those for the fast process since the absorbance changes during reaction are much smaller.

TABLE 62: p-CHLOROANILINE

$$[\text{H}^+] = 0.56\text{M}, \quad [\text{NaNO}_2] = 1.0 \times 10^{-3}\text{M}$$

| $10^2 k_0 \text{ sec}^{-1}$ | $10^2 [\text{Br}^-] \text{ M}$ | $10^2 k_0 \text{ sec}^{-1}$ | $10^6 [\text{ArNH}_2] \text{ M}$ |
|-----------------------------|--------------------------------|-----------------------------|----------------------------------|
| 0.71 | 1.55 | 0.71 | 2.01 |
| 0.82 | 3.10 | 0.72 | 3.22 |
| 0.94 | 4.65 | 0.75 | 4.42 |
| 0.90 | 6.20 | 0.81 | 5.64 |
| 0.98 | 7.75 | | |

FIGURE 12: k_o^{-1} VERSUS $1/[Br^-]$ FOR p-AMINOBENZOIC ACID



All amine runs carried out at 1.55×10^{-2} M bromide and all bromide runs at 2.01×10^{-6} free amine concentration.

$$k_o = (0.83 \pm 0.04) \times 10^{-2} \text{ sec}^{-1}$$

Halving the nitrite concentration gave $k_o = 0.79 \times 10^{-2} \text{ sec}^{-1}$ and with $[H^+] = 0.74$ M with all else as in first run $k_o = 1.4 \times 10^{-2} \text{ sec}^{-1}$.

TABLE 63: p-AMINOBENZOIC ACID

$$[H^+] = 0.44 \text{ M}, \quad [NaNO_2] = 1.5 \times 10^{-4} \text{ M}$$

| $10^2 k_o \text{ sec}^{-1}$ | $10^2 [Br^-] \text{ M}$ | $10^2 k_o \text{ sec}^{-1}$ | $10^5 [ArNH_2] \text{ M}$ |
|-----------------------------|-------------------------|-----------------------------|---------------------------|
| 12.0 | 1.54 | 12.0 | 2.63 |
| 12.8 | 3.08 | 11.3 | 4.22 |
| 12.7 | 4.62 | 13.0 | 5.81 |
| 12.1 | 6.16 | 11.3 | 7.39 |
| 14.1 | 7.70 | | |

All amine runs at 1.54×10^{-2} M bromide, and all bromide runs at 2.63×10^{-5} M free amine concentration.

$$k_o = (12.4 \pm 0.07) \times 10^{-2} \text{ sec}^{-1}$$

Doubling the nitrite concentration gave $k_o = 10.9 \times 10^{-2} \text{ sec}^{-1}$ and with $[H^+] = 0.78$ M with all else as in first run $k_o = 21.0 \times 10^{-2} \text{ sec}^{-1}$.

The corresponding slow process in the NOCl reaction was measured for p-nitroaniline. Here the reaction was carried out in hydrochloric acid with the following results:-

FIGURE 13:

k_o VERSUS $[HCl] f_{\pm}$ FOR p-NITROANILINE (Slow Process)

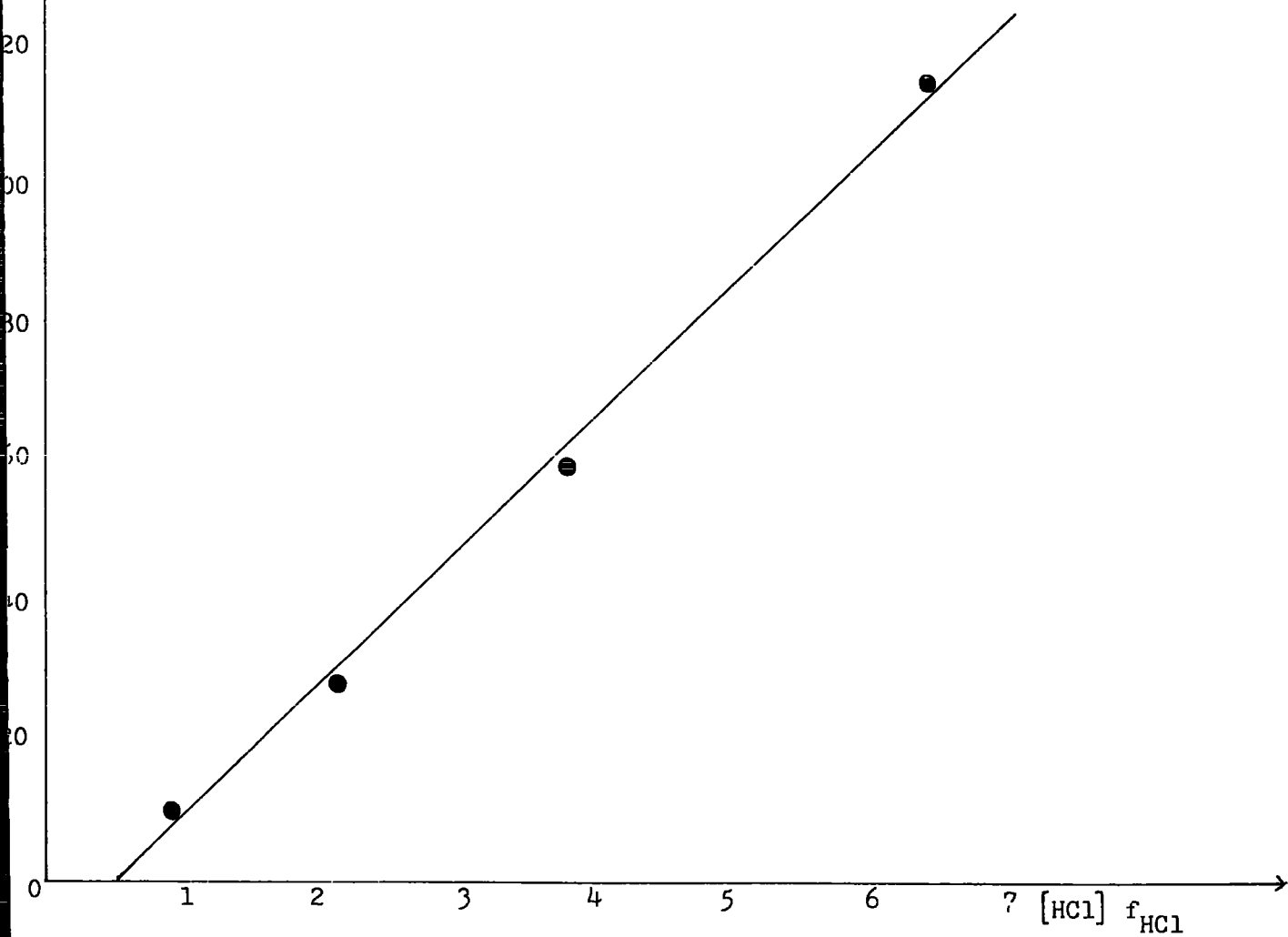


TABLE 64: p-NITROANILINE

$$[\text{NaNO}_2] = 7.8 \times 10^{-4} \text{ M}$$

| $10^2 k_0 \text{ sec}^{-1}$ | $[\text{HCl}] f_{\pm}$ |
|-----------------------------|------------------------|
| 9.6 | 0.94 |
| 28.8 | 2.14 |
| 60.5 | 3.83 |
| 116.0 | 6.46 |

The hydrochloric acid concentrations are such that activity effects cannot be ignored and f_{\pm} refers to the mean ionic activity coefficient of $[\text{HCl}]$. The values of $[\text{HCl}] f_{\pm}$ have been obtained from the data of section 6.2.

The graph is linear, as is shown in Figure 13, with $r = 0.998$. This suggests first-order behaviour in $[\text{HCl}]$ so that k_0 must be dependent upon either $[\text{H}^+]$ or $[\text{Cl}^-]$ but not on both. (N.B: poorer correlation exists between k_0 and $[\text{H}^+][\text{Cl}^-] f_{\pm}^2$). The results for the NOBr reaction would indicate a first-order dependence upon $[\text{H}^+]$.

The nature of this slower process is unknown. However, it seems reasonable to assume that it is either (a) en route to ArN_2^+ or (b) some irreversible reaction of ArN_2^+ . Fortunately a distinction can be made between these two alternatives by the replacement of the nitrite in one of the runs by the same concentration of ArN_2^+ . Then, if the reaction involves ArN_2^+ in, for example, coupling with ArN_2^+ or substitution of N_2 by Br^- , the same absorbance changes should still be observed.

The preparation of a solution for which the diazonium ion concentration is known reasonably accurately necessitates the preparation and handling of the dry salt. For this reason p-chlorophenyldiazonium hydrogen sulphate was chosen because of its relative stability towards

explosion and its high solubility in water, (the BF_4^- and PF_6^- salts, although more stable, are only slightly soluble in water). Furthermore, the HSO_4^- anion would not be expected to compete with either p-chloroaniline or bromide for reaction with the diazonium ion. The preparative method used is due to Piercey & Ward¹⁵⁴ (see chapter ?).

In practice an accurately known aqueous solution of $\text{ArN}_2^+\text{HSO}_4^-$ was rapidly mixed with one containing H_2SO_4 , KBr and p-chloroaniline in concentrations such as to duplicate one of the original runs. The relevant data (after mixing equal volumes of the two solutions) are shown in Table 65. The original run showed a steady decrease in absorption at 354 nm and gave $k_0 = 0.82 \times 10^{-2} \text{ sec}^{-1}$. The duplicate, however, showed no absorbance change at this wavelength. A second duplicate was carried out, this time omitting the p-chloroaniline, to see if the reaction between ArN_2^+ and Br^- did occur. It was thought that the amine, which was present in ~ 20 times the concentration of the diazonium ion, may have masked any absorbance change due to the latter. However, again nothing was observed at 354 nm.

TABLE 65

| ORIGINAL | DUPLICATE |
|---|---|
| $[\text{NaNO}_2] = 5.0 \times 10^{-4} \text{ M}$ | $[\text{ArN}_2^+] = 5.5 \times 10^{-4} \text{ M}$ |
| $[\text{H}_2\text{SO}_4] = 0.28 \text{ M}$ | $[\text{H}_2\text{SO}_4] = 0.35 \text{ M}$ |
| $[\text{KBr}] = 3.10 \times 10^{-2} \text{ M}$ | $[\text{KBr}] = 3.02 \times 10^{-2} \text{ M}$ |
| $[\text{Amine}]_{\text{tot}} = 1.08 \times 10^{-2} \text{ M}$ | $[\text{Amine}]_{\text{tot}} = 1.08 \times 10^{-2} \text{ M}$ |

It therefore appears that the slower process is not some reaction of the diazonium cation but lies en route to its formation. This could well be the tautomerisation $\text{ArNH}_2\text{NO}^+ \rightleftharpoons \text{ArN}=\text{N}^+-\text{OH}_2$ which would account for the independence in halide ion concentration and the first-order behaviour in acid. Furthermore, the k_2/k_3 ratios suggest that the composite rate-constant for this process (k_3) is reduced by electron withdrawing substituents. Hence the observation of this step only in the case of p-Cl, p-COOH and p-NO₂ substrates.

CHAPTER SIX:

Diazotization with Nitrosyl Chloride

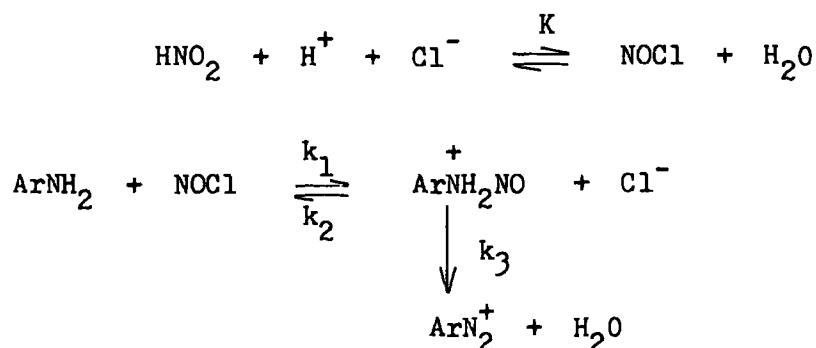
6.1 Introduction

The experimental procedure followed here is essentially the same as that for the NOBr reaction. However, the halide ion concentration varies over the range 1 - 5M and activity effects clearly cannot now be ignored. For this reason hydrochloric acid was used as the source of chloride and for which experimental mean activity coefficients are known with some accuracy.¹⁵⁵ The error introduced by no longer working at constant free amine concentration (as [HCl] varies) was felt to be less than that which would be introduced by using sulphuric acid containing potassium chloride for which activity coefficients could not be obtained.

Further problems arise from the fact that hydrochloric acid has a significant enthalpy of dilution. The acidic amine solution was therefore mixed with one of sodium nitrite in hydrochloric acid of the same strength. This avoids any temperature rise on mixing. However, such nitrite solutions rapidly deteriorate on standing so that small aliquots of aqueous nitrite solution were added to each HCl sample immediately prior to carrying out each reaction.

The reactions were again studied by means of stopped-flow spectrophotometry at 25°C and the effect of varying [HCl] upon the observed first-order rate constant k_0 was examined. Good first-order behaviour was always obtained with respect to total nitrous acid and total amine concentrations. Further details of the experimental method will be found in Chapter 7.

The plots of k_0 versus [HCl] were found to be curved. This is no doubt due to a combination of activity effects and the reversibility of the initial N-nitrosation. The reaction scheme is exactly analogous to that for the NOBr reaction, viz:-



with a value for K of 1.14×10^{-3} (ref.95). This is smaller than the corresponding equilibrium constant for NOBr formation and explains why bromide has the greater bulk catalytic effect despite the greater electrophilicity of NOCl as compared to NOBr . Again reaction is regarded as proceeding via the unprotonated amine. Application of the steady-state approximation then leads to the equation:-

$$k_o = \frac{k_1 k_3 K [\text{ArNH}_2] [\text{H}^+] [\text{Cl}^-] f_{\pm}^2}{(k_2 [\text{Cl}^-] f_{\pm}^2 + k_3)}$$

where f_{\pm} represents the mean ionic activity coefficient for the hydrochloric acid solution.¹⁵⁵ This is analogous to the equation deduced by Woppmann and Sofer¹⁵⁶ for the diazotization of aniline in methanolic hydrochloric acid.

Thus,

$$1/k_o = 1/k_1 K [\text{ArNH}_2] [\text{H}^+] [\text{Cl}^-] f_{\pm}^2 + k_2/k_1 k_3 K [\text{ArNH}_2] [\text{H}^+]$$

so that, for the seven amines studied, k_1 values can be obtained from the slopes of plots of $1/k_o$ versus $1/[\text{Cl}^-] f_{\pm}^2$. The intercepts then yield the corresponding k_2/k_3 ratios.

6.2 Evaluation of values for k_1 and k_2/k_3 :

The results are set out in Tables 66 - 72 where again [Amine] refers to total added amine concentration, and $[\text{ArNH}_2]$ to the concentration of free base. The values of f_{\pm} are interpolated from the data of Robertson & Stokes.¹⁵⁵

TABLE 66: ANILINE

$$[\text{Amine}] = 7.70 \times 10^{-3}\text{M}, \quad [\text{NaNO}_2] = 2.5 \times 10^{-4}\text{M}$$

| $k_0 \text{ sec}^{-1}$ | [HCl] M | f_{\pm} | $1/k_0 \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|------------------------|---------|-----------|---------------------|-----------------------------|
| 0.33 | 1.01 | 0.810 | 3.03 | 1.51 |
| 0.90 | 2.08 | 1.025 | 1.11 | 0.46 |
| 1.87 | 3.07 | 1.334 | 0.53 | 0.18 |
| 3.31 | 4.08 | 1.790 | 0.30 | 0.08 |
| 3.89 | 5.25 | 2.555 | 0.26 | 0.03 |

TABLE 67: p-ANISIDINE

$$[\text{Amine}] = 1.98 \times 10^{-3}\text{M}, \quad [\text{NaNO}_2] = 9.2 \times 10^{-5}\text{M}.$$

Same HCl data as aniline.

| $10^2 k_0 \text{ sec}^{-1}$ | $1/k_0 \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|-----------------------------|---------------------|-----------------------------|
| 4.2 | 23.81 | 1.51 |
| 12.2 | 8.20 | 0.46 |
| 35.9 | 2.78 | 0.18 |
| 71.7 | 1.39 | 0.08 |
| 114.2 | 0.88 | 0.03 |

TABLE 68: m-ANISIDINE

$$[\text{Amine}] = 1.01 \times 10^{-3} \text{M}, \quad [\text{NaNO}_2] = 4.8 \times 10^{-4} \text{M}$$

Same HCl data as aniline

| $k_o \text{ sec}^{-1}$ | $1/k_o \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|------------------------|---------------------|-----------------------------|
| 0.15 | 6.67 | 1.51 |
| 0.45 | 2.22 | 0.46 |
| 0.86 | 1.16 | 0.18 |
| 1.39 | 0.72 | 0.08 |
| 2.94 | 0.34 | 0.03 |

TABLE 69: p-TOLUIDINE

$$[\text{Amine}] = 2.21 \times 10^{-3} \text{M}, \quad [\text{NaNO}_2] = 1.6 \times 10^{-4} \text{M}$$

Same HCl data as aniline

| $10^2 k_o \text{ sec}^{-1}$ | $1/k_o \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|-----------------------------|---------------------|-----------------------------|
| 5.95 | 16.81 | 1.51 |
| 21.0 | 4.76 | 0.46 |
| 48.0 | 2.08 | 0.18 |
| 98.7 | 1.01 | 0.08 |
| 144.0 | 0.69 | 0.03 |

TABLE 70: p-CHLOROANILINE

$$[\text{Amine}] = 2.06 \times 10^{-3} \text{M}, \quad [\text{NaNO}_2] = 2.0 \times 10^{-4} \text{M}$$

| $k_o \text{ sec}^{-1}$ | $[\text{HCl}] \text{ M}$ | f_{\pm} | $1/k_o \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|------------------------|--------------------------|-----------|---------------------|-----------------------------|
| 0.32 | 1.13 | 0.830 | 3.12 | 1.28 |
| 0.81 | 2.08 | 1.025 | 1.23 | 0.46 |
| 1.54 | 2.96 | 1.295 | 0.65 | 0.20 |
| 2.73 | 3.86 | 1.673 | 0.37 | 0.09 |
| 3.27 | 4.90 | 2.296 | 0.31 | 0.04 |

FIGURE 14: $\frac{1}{k_o}$ VERSUS $\frac{1}{[Cl^-]_{f \pm}^2}$ FOR p-CHLOROANILINE

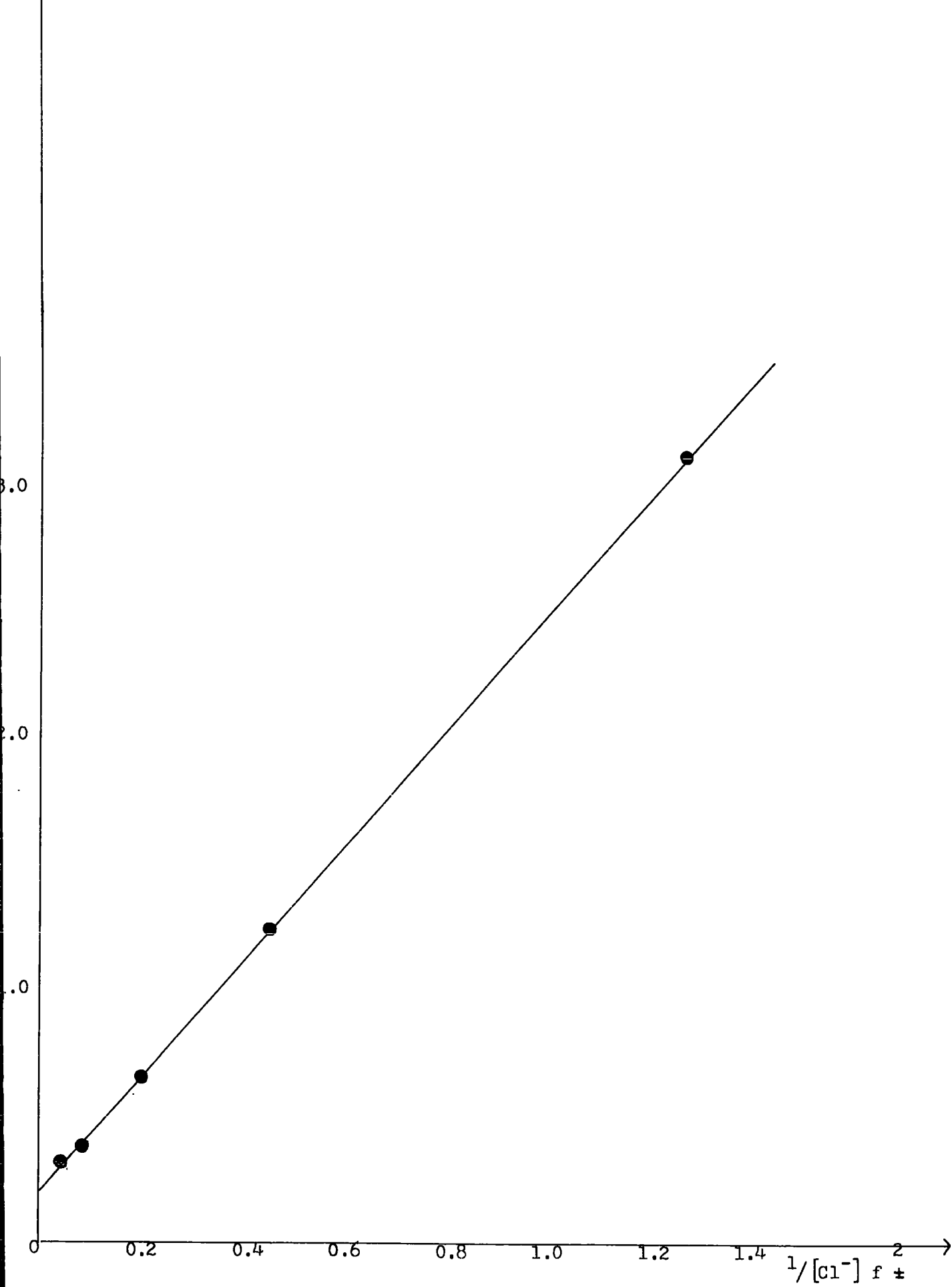


TABLE 71: p-AMINOBENZOIC ACID

$$[\text{Amine}] = 2.01 \times 10^{-3}\text{M}, \quad [\text{NaNO}_2] = 9.9 \times 10^{-5}\text{M}$$

Same HCl data as p-chloroaniline

| $k_o \text{ sec}^{-1}$ | $1/k_o \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|------------------------|---------------------|-----------------------------|
| 5.6 | 0.18 | 1.28 |
| 11.3 | 0.09 | 0.46 |
| 15.2 | 0.07 | 0.20 |
| 19.7 | 0.05 | 0.09 |

TABLE 72: p-NITROANILINE

$$[\text{Amine}] = 1.04 \times 10^{-3}\text{M}, \quad [\text{NaNO}_2] = 6.7 \times 10^{-5}\text{M}$$

same HCl data as p-chloroaniline

| $k_o \text{ sec}^{-1}$ | $1/k_o \text{ sec}$ | $1/[\text{Cl}^-] f_{\pm}^2$ |
|------------------------|---------------------|-----------------------------|
| 8.4 | 0.119 | 1.28 |
| 11.5 | 0.087 | 0.46 |
| 13.8 | 0.072 | 0.20 |
| 14.5 | 0.069 | 0.09 |
| 15.2 | 0.066 | 0.04 |

The graphs are all linear with values of $r > 0.99$. A typical example is shown in Figure 14.

Values of k_1 and k_2/k_3 have been calculated from the slopes and intercepts, respectively, by using the mean values for $[\text{H}^+]$ and $[\text{ArNH}_2]$ and the results are shown in Table 73. The units for k_1 and k_2/k_3 are $1.\text{mole}^{-1}.\text{sec}^{-1}$ and $1.\text{mole}^{-1}$, respectively.

TABLE 73

| AMINE | mean $[H^+]$ M | mean $[ArNH_2]$ M | Slope | $10^{-9}k_1$ | Intercept | k_2/k_3 |
|-------------------|----------------|-----------------------|--------|--------------|-----------|-----------|
| p-OMe | 3.10 | 2.81×10^{-9} | 15.638 | 6.44 | 0.343 | 0.02 |
| p-Me | 3.10 | 5.88×10^{-9} | 10.988 | 4.38 | 0.104 | 0.01 |
| m-OMe | 3.10 | 2.04×10^{-8} | 4.204 | 3.30 | 0.322 | 0.08 |
| H | 3.10 | 6.30×10^{-8} | 1.887 | 2.38 | 0.193 | 0.10 |
| p-Cl | 2.99 | 7.18×10^{-8} | 2.286 | 1.79 | 0.190 | 0.08 |
| p-COOH | 2.99 | 2.55×10^{-6} | 0.106 | 1.08 | 0.043 | 0.40 |
| p-NO ₂ | 2.99 | 3.23×10^{-5} | 0.043 | 0.21 | 0.065 | 1.50 |

Again it can be seen that the k_1 values approach the diffusion controlled limit. The trend will be discussed in section 6.5 where more accurate k_1 values will be presented.

6.3 Significance of the k_2/k_3 ratios:

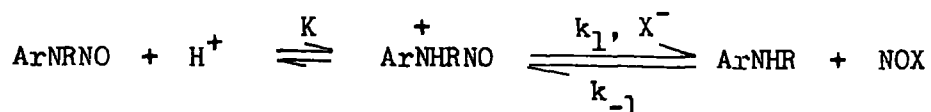
For convenience the results for the NOBr and NOCl reactions have been drawn up in Table 74. For both reactions the general trend is toward larger ratios for the more weakly basic amines. Assuming k_3 to be the same in both cases allows calculation of k_2 (NOBr) : k_2 (NOCl) ratios. The results are not in good agreement because of the approximate nature of the method used to calculate the original k_2/k_3 ratios. However, in all cases it can be seen that k_2 (Br⁻) > k_2 (Cl⁻) as would be expected since bromide is more efficient than chloride in the halide catalysed denitrosation of secondary nitrosamines. For example, with N-methyl-N-nitrosoaniline the ratio k (Br⁻) : k (Cl⁻) is ~ 50 (ref.14) and with N-nitrosodiphenylamine it is ~ 25 (see section 3.2).

TABLE 74

| AMINE | (k_2/k_3) NOBr | (k_2/k_3) NOCl | $k_2(\text{Br}^-)/k_2(\text{Cl}^-)$ |
|-------------------|------------------|------------------|-------------------------------------|
| p-OMe | 3.65 | 0.02 | 182.5 |
| p-Me | 6.99 | 0.01 | 699.0 |
| m-OMe | 6.18 | 0.08 | 77.2 |
| H | 3.63 | 0.10 | 36.3 |
| p-Cl | 7.80 | 0.08 | 97.5 |
| p-COOH | 10.12 | 0.40 | 25.3 |
| p-NO ₂ | 27.42 | 1.50 | 18.3 |

The effect of ring substituents upon the k_2/k_3 ratios is towards larger values for those amines carrying electron withdrawing substituents with factors of ~ 10 and 10^2 covering the range for the bromide catalysed and chloride catalysed reactions, respectively, and this reflects the greater selectivity shown by the substrates (i.e. ArNH_2NO) towards denitrosation by the weaker nucleophile. The denitrosation of secondary nitrosamines is also enhanced by electron withdrawing ring substituents but with only a factor of 6 covering the range from p-OMe to p-NO₂.²¹ The reason for the smaller substituent effect in the latter reaction is not clear-cut but may be rationalised as follows:-

Consider the case of electron-withdrawing substituents. In the simple denitrosation process these operate to enhance the rate of the actual nucleophilic substitution but also reduce the concentration of ArNHRNO by virtue of their effect upon the pK_{BH^+} of the nitrosamine.



These effects therefore conflict and result in a small overall substituent effect on the product k_1K . In the diazotization process such substituents operate to increase k_2 (i.e. the denitrosation of the primary nitrosamine) and to reduce k_3 (see section 5.4). These opposing effects are magnified in the ratio k_2/k_3 , and a larger overall substituent effect results. For electron releasing substituents the effects are in the opposite direction. However, the separate effects always conflict in the product k_1K and co-operate in the ratio k_2/k_3 .

It is now apparent that the N-nitrosation of anilines can become significantly reversible at high halide concentration, particularly for those amines carrying the more powerful electron-withdrawing groups. In section 2.3 it was suggested that the k_1 values for the N-nitrosation of anilines, as measured by an indirect procedure, did not approach the diffusion-controlled limit. However, for those anilines for which the reversibility of the nitrosation step is important, the relative k_1 values thus obtained are not necessarily the true values but the composite $k_1k_3 / (k_2 [X^-] + k_3)$ values. This leads to a wider range of apparent rate-constants than would be obtained if the reversibility were unimportant. It was precisely this large range of reactivity from p-OMe to p-NO₂ that was taken as evidence against diffusion-control.⁹⁷ Once again the existence of good Hammett correlations can be seen to be fortuitous (see critique in section 3.2).

Finally, it should be noted that in the bromide catalysed reaction the k_2/k_3 ratios are all greater than unity which implies that $k_2 > k_3$ for all seven amines and that reversibility is always important. For the chloride catalysed reaction the opposite is generally true. Again

this reflects the greater catalytic effect of bromide in the denitrosation of the primary nitrosamines. The indirect procedure⁹⁷ involved measurements of the diazotization under catalysis by both bromide, and the more powerful nucleophile thiocyanate, so that the reversibility of the reactions should always be kinetically significant, even for those amines carrying electron-donating substituents.

6.4 Correction of the k_1 values:

The k_1 values of section 6.2 have been calculated by using the mean values of $[H^+]$ and $[ArNH_2]$. However, it would be better to avoid this if possible and allow for the variation of $[ArNH_2]$ with acidity.

$$k_o^{-1} = 1/k_1 K [ArNH_2] [H^+] [Cl^-] f_{\pm}^2 + k_2/k_1 k_3 K [ArNH_2] [H^+]$$

However, the intercepts of the graphs of k_o^{-1} versus $1/[Cl^-] f_{\pm}^2$ are known from the analysis of section 6.2 so that we can write:-

$$k_1 = 1 / (k_o^{-1} - \text{Intercept}) K [ArNH_2] [H^+] [Cl^-] f_{\pm}^2$$

and calculate values of k_1 for each acidity. This also allows the estimation of standard errors for the k_1 values. The free base concentrations are calculated as in section 5.3, and again are represented by the symbol $[ArNH_2]$. The corresponding total amine concentrations are represented by $[Amine]$. The results are shown in Tables 75 - 81.

Mean values of the rate-constant for each amine have been calculated according to $\bar{x} = \sum x_i/n$ where n = number of estimates. The standard error of the mean is then given by $\sigma_x/n^{1/2}$ where σ_x is the standard deviation of the data from the mean and is given by:-

TABLE 75: ANILINE

$$[\text{Amine}] = 7.70 \times 10^{-3} \text{M}, \text{ Intercept} = 0.193$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $[\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{ s}^{-1}$ |
|------------------------|--------------------------|-----------------------------|---------------------------|--|
| 3.03 | 1.01 | 1.933×10^{-7} | 0.6627 | 2.39 |
| 1.11 | 2.08 | 9.385×10^{-8} | 2.1853 | 2.24 |
| 0.53 | 3.07 | 6.358×10^{-8} | 5.4632 | 2.44 |
| 0.30 | 4.08 | 4.784×10^{-8} | 13.0727 | 3.21 |
| 0.26 | 5.25 | 3.718×10^{-8} | 34.2721 | 1.96 |

$$k_1 = (2.4 \pm 0.2) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 76: p-ANISIDINE

$$[\text{Amine}] = 1.98 \times 10^{-3} \text{M}; \text{ Intercept} = 0.343$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^9 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{ s}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|--|
| 23.81 | 1.01 | 8.617 | 0.6627 | 6.48 |
| 8.20 | 2.08 | 4.184 | 2.1853 | 5.87 |
| 2.78 | 3.07 | 2.835 | 5.4632 | 7.57 |
| 1.39 | 4.08 | 2.133 | 13.0727 | 7.36 |
| 0.88 | 5.25 | 1.658 | 34.2721 | 5.48 |

$$k_1 = (6.5 \pm 0.4) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 77: m-ANISIDINE

$$[\text{Amine}] = 1.01 \times 10^{-3} \text{M}, \text{ Intercept} = 0.322$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^8 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{ s}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|--|
| 6.67 | 1.01 | 6.251 | 0.6627 | 3.30 |
| 2.22 | 2.08 | 3.036 | 2.1853 | 3.35 |
| 1.16 | 3.07 | 2.057 | 5.4632 | 3.03 |
| 0.72 | 4.08 | 1.548 | 13.0727 | 2.67 |
| 0.34 | 5.25 | 1.203 | 34.2721 | 22.53* |

* = omitted.

$$k_1 = (3.1 \pm 0.2) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 78: p-AMINO BENZOIC ACID

$$[\text{Amine}] = 2.01 \times 10^{-3} \text{M}; \text{ Intercept} = 0.043$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^6 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{ s}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|--|
| 0.18 | 1.13 | 6.740 | 0.7785 | 1.08 |
| 0.09 | 2.08 | 3.667 | 2.1853 | 1.12 |
| 0.07 | 2.96 | 2.578 | 4.9640 | 0.86 |
| 0.05 | 3.86 | 1.978 | 10.8039 | 1.52 |

$$k_1 = (1.1 \pm 0.1) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 79: p-TOLUIDINE

$$[\text{Amine}] = 2.21 \times 10^{-3} \text{M}; \text{ Intercept} = 0.104$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^9 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \cdot 1. \text{mole}^{-1} \text{sec}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|---|
| 16.81 | 1.01 | 18.033 | 0.6627 | 4.35 |
| 4.76 | 2.08 | 8.756 | 2.1853 | 4.73 |
| 2.08 | 3.07 | 5.933 | 5.4632 | 4.46 |
| 1.01 | 4.08 | 4.464 | 13.0727 | 4.07 |
| 0.69 | 5.25 | 3.469 | 34.2721 | 2.40 |

$$k_1 = (4.0 \pm 0.4) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 80: p-CHLOROANILINE

$$[\text{Amine}] = 2.06 \times 10^{-3} \text{M}; \text{ Intercept} = 0.190$$

| $k_o^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^8 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{sec}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|---|
| 3.12 | 1.13 | 19.000 | 0.7785 | 1.79 |
| 1.23 | 2.08 | 10.322 | 2.1853 | 1.80 |
| 0.65 | 2.96 | 7.254 | 4.9640 | 1.79 |
| 0.37 | 3.86 | 5.562 | 10.8039 | 2.10 |
| 0.31 | 4.90 | 4.382 | 25.8309 | 1.32 |

$$k_1 = (1.8 \pm 0.1) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

TABLE 81: p-NITROANILINE

$$[\text{Amine}] = 1.04 \times 10^{-3} \text{M}; \text{Intercept} = 0.065$$

| $k_0^{-1} \text{ sec}$ | $[\text{H}^+] \text{ M}$ | $10^5 [\text{ArNH}_2] \text{ M}$ | $[\text{Cl}^-] f_{\pm}^2$ | $10^{-9} k_1 \text{ l.mole}^{-1} \text{ sec}^{-1}$ |
|------------------------|--------------------------|----------------------------------|---------------------------|--|
| 0.119 | 1.13 | 8.122 | 0.7785 | 0.23 |
| 0.087 | 2.08 | 4.575 | 2.1853 | 0.19 |
| 0.072 | 2.96 | 3.258 | 4.9640 | 0.26 |
| 0.069 | 3.86 | 2.517 | 10.8039 | 0.21 |
| 0.066 | 4.90 | 1.993 | 25.8309 | 0.35 |

$$\therefore k_1 = (0.25 \pm 0.03) \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

$$\sigma_x = \left[\frac{n \sum x_i^2 - (\sum x_i)^2}{n(n-1)} \right]^{\frac{1}{2}}$$

(n-1) weighting has been used so that σ measures the dispersion of the data about the mean.

6.5 Comparison of k_1 values for the NOCl and NOBr reactions:

In section 5.3 k_1 values for the NOBr reaction were calculated from the slopes of plots of k_0 versus $[\text{ArNH}_2]$ by virtue of the linear relationship:-

$$k_0 = k_1 K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]$$

However, in the form $k_1 = k_0 / K [\text{ArNH}_2] [\text{H}^+] [\text{Br}^-]$ this allows the calculation of k_1 at each free base concentration. The mean value of k_1 and the corresponding standard error can then be calculated for each

amine in a manner exactly analogous to that used in the preceding section for the k_1 values in the NOCl reaction. The relevant data can be found in section 5.3 (Tables 36 - 43).

The results for both reactions are presented in Table 82, the units of k_1 being $\text{l.mole}^{-1} \text{sec}^{-1}$.

TABLE 82

| ANILINE | $(10^{-9})k_1$ NOBr | $(10^{-9})k_1$ NOCl |
|-------------------|---------------------|---------------------|
| p-OMe | 3.30 ± 0.08 | 6.5 ± 0.4 |
| p-Me | 2.92 ± 0.07 | 4.0 ± 0.4 |
| m-OMe | 2.00 ± 0.05 | 3.1 ± 0.2 |
| H | 1.68 ± 0.03 | 2.4 ± 0.2 |
| p-Cl | 1.8 ± 0.3 | 1.8 ± 0.1 |
| p-COOH | 0.30 ± 0.02 | 1.1 ± 0.1 |
| p-NO ₂ | 0.029 ± 0.002 | 0.25 ± 0.03 |

As can be seen the precision is greater for the NOBr values. This reflects the round-off error in the double-reciprocal method used to evaluate the NOCl values.

The results for the NOCl reaction can be compared with the k_1 values obtained by Schmid & co-workers for reaction in 0.2M hydrochloric acid,^{94,95} with p-anisidine ($k_1 = 3.0 \times 10^9 \text{l.mole}^{-1} \text{sec}^{-1}$), aniline ($k_1 = 2.6 \times 10^9 \text{l.mole}^{-1} \text{sec}^{-1}$) and p-chloroaniline ($k_1 = 1.9 \times 10^9 \text{l.mole}^{-1} \text{sec}^{-1}$). Although the comparison is limited to these three amines it can be seen that in general the agreement is quite good.

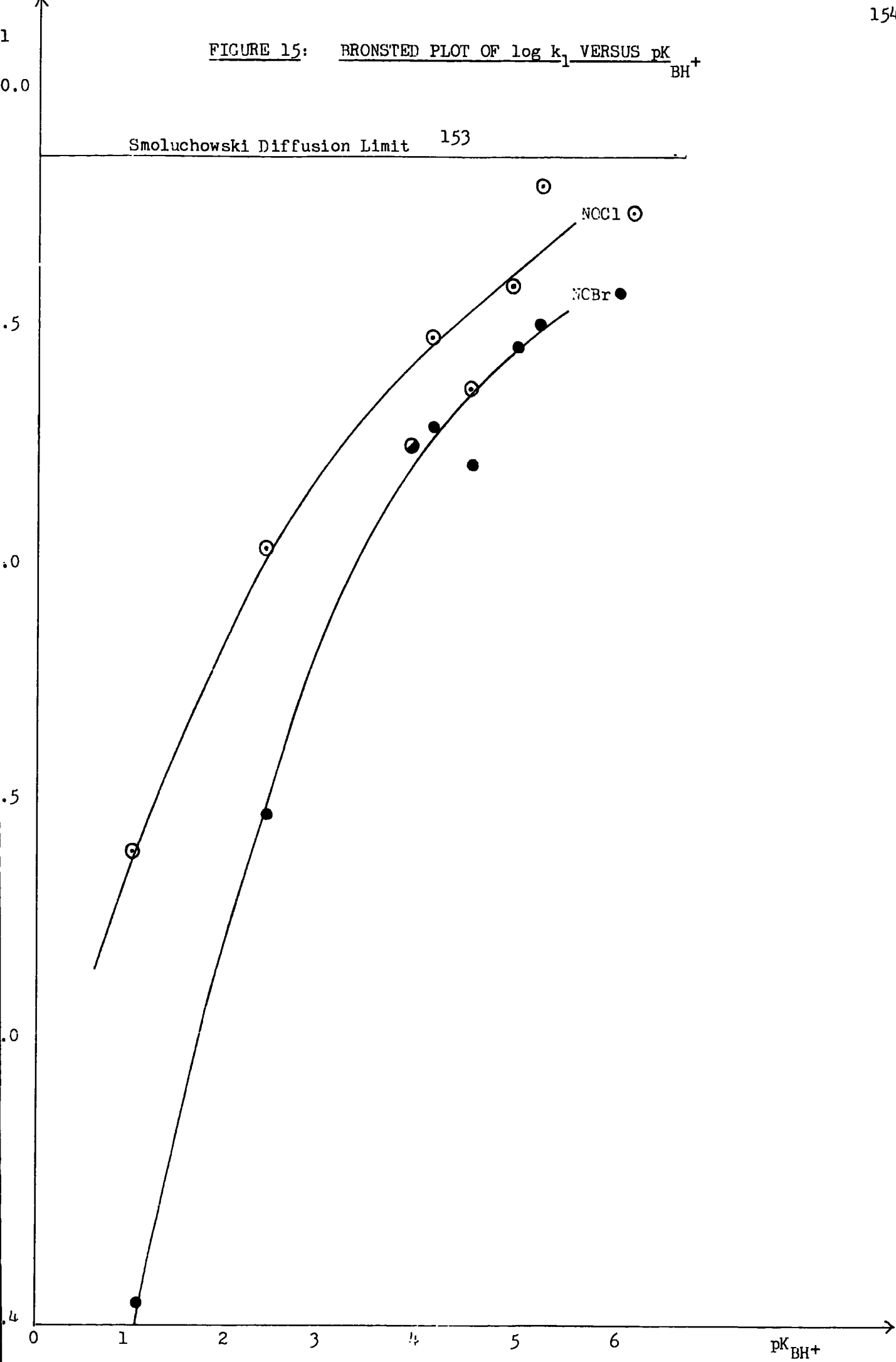
The data for both the NOCl and NOBr reactions are presented in Figure 15 as a function of pK_{BH^+} (values from ref.141) where it can be seen that k_1 values level off as the diffusion-controlled limit ($7.4 \times 10^9 \text{ l.mole}^{-1} \text{ sec}^{-1}$) is approached. At low pK_{BH^+} it is clear that NOCl is significantly more reactive than NOBr as would be expected from simple electronegativity considerations. This compares with the results of Woppmann & Sofer¹⁵⁶ for the diazotization of aniline in methanolic hydrochloric and hydrobromic acids where the k_1 values were found to be approximately 10^2 units below the diffusion-controlled limit with NOCl ~ 3 x more reactive than NOBr. Similar behaviour has been observed in the electrophilic addition of nitrosyl halides to alkenes in aqueous solution,¹⁵⁷ and more recently in the halide-catalysed nitrosation of the hydrazonium ion $(NH_2NH_3)^+$.¹⁵⁸

The numerical data for the Brønsted plot are shown in Table 83.

TABLE 83

| AMINE | pK_{BH^+} | $(\log k_1) \text{ NOCl}$ | $(\log k_1) \text{ NOBr}$ |
|-------------------|-------------|---------------------------|---------------------------|
| p-OMe | 5.357 | 9.81 ± 0.03 | 9.52 ± 0.01 |
| p-Me | 5.084 | 9.60 ± 0.04 | 9.47 ± 0.01 |
| m-OMe | 4.204 | 9.49 ± 0.02 | 9.30 ± 0.01 |
| H | 4.596 | 9.38 ± 0.04 | 9.22 ± 0.01 |
| p-Cl | 3.982 | 9.26 ± 0.02 | 9.26 ± 0.08 |
| p-COOH | 2.42 | 9.04 ± 0.04 | 8.48 ± 0.03 |
| p-NO ₂ | 1.019 | 8.40 ± 0.06 | 7.46 ± 0.03 |

FIGURE 15: BRONSTED PLOT OF $\log k_1$ VERSUS pK_{BH^+}



CHAPTER SEVEN

Experimental Technique

7.1. Preparation & Purification of Materials

N-nitrosodiphenylamine was prepared from diphenylamine and sodium nitrite by the usual procedure¹⁵⁹ and recrystallized from AnalaR methanol. Stock solutions were made up in AnalaR methanol for use in the kinetic runs. p-Nitroso-N,N-dimethylaniline was likewise prepared from N,N-dimethylaniline and sodium nitrite for use as reference material in the spectrophotometric determination of products from the reaction between N-nitrosodiphenylamine and N,N-dimethylaniline (section 4.5).

p-Chlorophenyldiazonium hydrogen sulphate was prepared from p-chloroaniline and nitrosonium hydrogen sulphate by the method of Piercey & Ward,¹⁵⁴ viz:-

Fuming 100% nitric acid ($d = 1.5$; 10 cm^3) was placed in a flask and continuously cooled by a circulating jacket of cold water. Dry sulphur dioxide was then bubbled through the nitric acid until it appeared quite solid. The crude yellow product was filtered at the pump on a sintered glass funnel, washed with the minimum volume of glacial acetic acid necessary to remove the coloration, and finally washed with dry carbon tetrachloride (molecular seive). The nitrosonium hydrogen sulphate thus obtained as hygroscopic, white crystals was used immediately in the preparation of the diazonium salt.

p-chloroaniline (1.0 gm; 0.008 mole) was dissolved in glacial acetic acid (5 cm^3) and added dropwise, with stirring, to a solution of nitrosonium hydrogen sulphate (1.2 gm; 0.009 mole) in glacial acetic acid (7 cm^3) contained in an ice-bath. Upon solidification (AcOH m.pt = 16.6°C) the mixture was removed from the ice-bath and allowed to attain room temperature (~ 30 mins.). Pure, dry diethyl ether (50 cm^3) was

then added slowly, with stirring, and cooling in ice, until the product was precipitated in crystalline form. This was filtered, dissolved in glacial acetic acid (5 cm^3) and reprecipitated by a further quantity of ether (50 cm^3). The final product, p-chlorophenyldiazonium hydrogen sulphate, was filtered at the pump, washed with ether ($5 \times 20 \text{ cm}^3$) and allowed to dry in the funnel whilst air was drawn through.

An accurately weighed sample of the dry diazonium salt (0.0262 gm) was dissolved in ice-cold distilled water (100 cm^3) so that $[\text{ArN}_2^+]$ = $1.1 \times 10^{-3} \text{ M}$. After mixing with an equal volume of an aqueous solution of sulphuric acid containing potassium bromide and p-chloroaniline this concentration was therefore reduced to $5.5 \times 10^{-4} \text{ M}$ (see Table 65). The remaining solid diazonium salt was destroyed by dissolution in water.

All amines used in this study were obtained commercially. Aniline and its -NMe₂, m-Me and m-OMe derivatives were purified by distillation under reduced pressure and stored under nitrogen. The p-Cl, p-COOH and p-NO₂ derivatives and diphenylamine were purified by recrystallization from aqueous ethanol, and the p-Me and p-OMe derivatives by vacuum sublimation. In each case the m.pt or b.pt agreed with the literature value.¹⁶⁰

The commercial inorganic materials (NaN₃, NaNO₂, NaCl, KBr, KCNS, KI, SC(NH₂)₂, NH₂SO₃H and NH₃OH HSO₄⁻) were generally used without further purification, except for drying in either the oven or over KOH pellets as and when appropriate, and volumetric stock solutions made up in distilled water.

Commercial samples of N-ethylurethane, N-ethyl-N-nitrosourethane, adenine, 5-methylcytosine, MeOH, MeOD, D₂O, D₂SO₄, HCl and H₂SO₄ were used without further purification.

In general AnalaR grade materials were employed where available.

7.2 Denitrosation of N-nitrosodiphenylamine: experimental details

The kinetics of the process were studied by means of UV-visible spectrophotometry. The instrument used was a conventional double-beam recording spectrophotometer (Pye-Unicam SP 8000) possessing facilities for both temperature control of the cell-block, and delayed repeat scan by auto timer. Reactions were carried out at 31.0°C (for comparison with earlier work from this laboratory) in 1 cm. silica cells by the addition of a small aliquot (usually 1.00 cm³) of stock nitrosamine solution to an aqueous sulphuric acid solution containing all the other reagents (so that total volume usually 32.0 cm³). The cells, one containing the reaction mixture and one the solvent, were placed in the sample and reference beams, respectively, and maintained at 31.0°C for the duration of the reaction by water pumped through the cell-block from a thermostat bath.

The rate constants were calculated from absorption measurements at 310 nm due to the nitrosamine, (see the example below). For the slower runs ($k_0 < 1 \times 10^{-3} \text{ sec}^{-1}$) it proved more convenient to scan a suitable wavelength range at regular time intervals (usually 450 to 250 nm). In such cases the existence of good isosbestic points supported the idea that a simple A → B process was occurring. Good first-order behaviour was usually obtained except in some cases (catalysis by p-anisidine) where the initial rate was determined.

With 1 cm cells the relationship between absorbance and concentration is simply $A = \epsilon C$ (where ϵ = molar absorptivity). This linearity

permits the use of absorbance measurements directly in the calculation of the rate-constants instead of the actual reactant concentrations. With A_o = initial absorbance, A_{oo} = final absorbance, R = reactant and P = product, then for a first-order reaction:-

$$[P]_t = [R]_o - [R]_t$$

$$[R]_o = [P]_{oo}$$

$$[R]_{oo} = [P]_o$$

so that:

$$A_o = \epsilon_R [R]_o$$

$$\begin{aligned} A_t &= \epsilon_R [R]_t + \epsilon_P [P]_t \\ &= \epsilon_R [R]_t + \epsilon_P ([R]_o - [R]_t) \end{aligned}$$

$$A_{oo} = \epsilon_P [P]_{oo} = \epsilon_P [R]_o$$

Therefore:-

$$(A_t - A_{oo}) = \epsilon_R [R]_t - \epsilon_P [R]_t$$

$$\therefore [R]_t = \frac{(A_t - A_{oo})}{(\epsilon_R - \epsilon_P)}$$

But for a first-order reaction:-

$$\ln [R]_t = -k_o t + \ln [R]_o$$

↓
constant

$$\therefore \ln \left[\frac{(A_t - A_{oo})}{(\epsilon_R - \epsilon_P)} \right] = -k_o t + \text{const.}$$

and if $(\epsilon_R - \epsilon_P)$ remains constant during the reaction this simplifies to:-

$$\ln [A_t - A_{oo}] = -k_o t + \text{const.}$$

Thus a plot of $\log_e [A_t - A_{oo}]$ versus time should be linear with slope = $-k_o$.

The 'infinity' value A_{∞} was determined in each case after a period of ten half-lives since this corresponds to $>99\%$ reaction. The disappearance of absorbance with time (A_t) was generally followed for at least two half-lives.

The following example is given for the reaction of N-nitrosodiphenylamine ($1 \times 10^{-4}M$) in sulphuric acid (0.25M) containing sodium azide (0.16M) and potassium bromide (0.104M). Values for k_0 have been calculated at each time from $k_0 = \frac{1}{t} \ln \left[\frac{(A_0 - A_{\infty})}{(A_t - A_{\infty})} \right]$ and the standard error computed from the standard deviation. (see Table 84).

This gives:

$$k_0 = (4.14 \pm 0.02) \times 10^{-3} \text{ sec}^{-1}$$

TABLE 84: $A_{\infty} = 0.311$

| t (sec) | A_t | $10^3 k_0 \text{ sec}^{-1}$ |
|---------|-------|-----------------------------|
| 0 | 0.857 | |
| 30 | 0.792 | 4.22 |
| 60 | 0.734 | 4.25 |
| 90 | 0.687 | 4.14 |
| 120 | 0.641 | 4.20 |
| 150 | 0.605 | 4.13 |
| 180 | 0.573 | 4.08 |
| 210 | 0.542 | 4.10 |
| 240 | 0.517 | 4.06 |
| 270 | 0.492 | 4.09 |
| 300 | 0.471 | 4.09 |

For this particular run 2.0 cm³ of methanolic stock N-nitrosodiphenylamine (3.1 x 10⁻³M) was added rapidly to an acidic solution of NaN₃ and KBr made up from 7.0 cm³ of stock KBr solution (0.2564M), 5.0 cm³ of stock NaN₃ solution (1.059M), 13.0 cm³ of distilled water and 5.0 cm³ of sulphuric acid (~1.5M) so that the total volume of the reaction mixture was 32.0 cm³. This technique permits the variation of [Br⁻], whilst maintaining all else at constant concentration, by the addition of more or less stock KBr solution and adjusting the corresponding water content so that the total volume equals 32.0 cm³.

However, aniline and its derivatives were generally weighed directly into the reaction solutions. The following example refers to the reaction of N-nitrosodiphenylamine (2 x 10⁻⁴M) with m-toluidine (4.37 x 10⁻²M) in sulphuric acid (0.53M) containing sodium azide (0.17M). Again, 'instantaneous' values of k_o have been calculated from $k_o = 1/t \cdot \ln [(A_o - A_{oo}) / (A_t - A_{oo})]$, and the standard error computed.

TABLE 85: A_{oo} = 0.292

| t (sec) | A _t | 10 ³ k _o sec ⁻¹ |
|---------|----------------|--|
| 0 | 0.788 | |
| 30 | 0.744 | 3.10 |
| 60 | 0.704 | 3.10 |
| 90 | 0.668 | 3.08 |
| 120 | 0.633 | 3.12 |
| 150 | 0.605 | 3.07 |
| 180 | 0.579 | 3.04 |
| 210 | 0.552 | 3.08 |
| 240 | 0.529 | 3.08 |
| 270 | 0.505 | 3.13 |
| 300 | 0.488 | 3.09 |

This gives: $k_0 = (3.09 \pm 0.01) \times 10^{-3} \text{ sec}^{-1}$

The actual run was carried out by dissolving 0.1498 gm of m-toluidine in an aqueous mixture of sulphuric acid (20.0 cm^3 ; 0.84M), stock sodium azide (5.0 cm^3 ; 1.094M) and distilled water (5.0 cm^3) and starting the reaction by the rapid addition of stock N-nitrosodiphenylamine (2.0 cm^3 ; $3.18 \times 10^{-3}\text{M}$).

The details of the solvent-isotope measurements are shown below:-

(a) Low [Halide]

| H | D |
|---|---|
| H_2SO_4 in H_2O (20.0cm^3 ; 0.971M) | D_2SO_4 in D_2O (20.0cm^3 ; 0.992M) |
| $\text{Ph}_2\text{N.NO}$ in MeOH (2.0cm^3 ; $4.0 \times 10^{-3}\text{M}$) | $\text{Ph}_2\text{N.NO}$ in MeOD (2.0cm^3 ; $5.0 \times 10^{-3}\text{M}$) |
| NaN_3 in H_2O (5.0cm^3 ; 1.017M) | NaN_3 in D_2O (5.0cm^3 ; 1.016M) |
| NaCl in H_2O (4.0cm^3 ; 3.104M) | NaCl in D_2O (4.0cm^3 ; 3.106M) |
| H_2O (1.0cm^3) | D_2O (1.0cm^3) |

$$k_H = 11.9 \times 10^{-3} \text{ sec}^{-1}$$

$$k_D = 24.3 \times 10^{-3} \text{ sec}^{-1}$$

$$\therefore k_D/k_H = 2.04$$

(b) High [Halide]

| H | D |
|---|--|
| H ₂ SO ₄ in H ₂ O (5.0cm ³ ; 0.80M) | D ₂ SO ₄ in D ₂ O (2.0cm ³ ; 0.992M) |
| Ph ₂ N.NO in MeOH (2.0cm ³ ; 3.09 x 10 ⁻³ M) | Ph ₂ N.NO in MeOD (0.5cm ³ ; 5.0 x 10 ⁻³ M) |
| NaN ₃ in H ₂ O (5.0cm ³ ; 1.059M) | NaN ₃ in D ₂ O (2.5cm ³ ; 1.016M) |
| KBr in H ₂ O (19.0cm ³ ; 0.259M) | KBr in D ₂ O (9.5cm ³ ; 0.261M) |
| H ₂ O (1.0cm ³) | D ₂ O (1.5cm ³) |

$$k_H = 4.6 \times 10^{-3} \text{ sec}^{-1}$$

$$k_D = 3.7 \times 10^{-3} \text{ sec}^{-1}$$

$$\therefore k_D/k_H = 0.80$$

Note that in (b) the concentration of bromide is 0.15M in both H₂O and D₂O and this corresponds to the early plateau region of Figure 4. Using a slightly higher value for [Br⁻] would take us further into this region and should lower k_D/k_H somewhat. (see discussion in section 3.2)

For the reaction between N-nitrosodiphenylamine and aniline an approximate check was made upon the yield of diazonium ion by coupling the latter with a suitable reagent and measuring the absorbance at the wavelength of maximum absorption. The measurements were made using a Pye-Unicam SP.500 spectrophotometer.

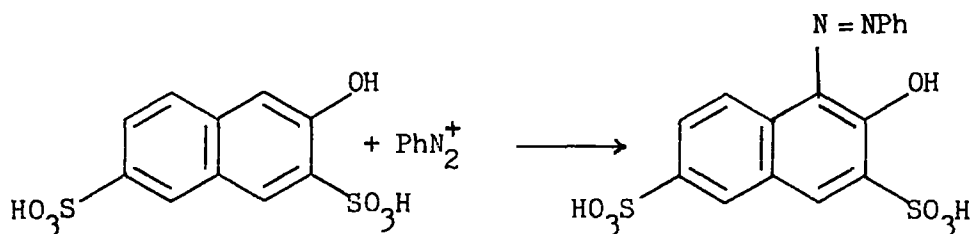
(a) Standard Solution:

3 grams of 2-naphthol-3,6-disulphonic acid were dissolved in 1 litre of sodium tetraborate solution (0.025M; 9.53 gm Na₂B₄O₇·10H₂O). Henceforward this will be referred to as "naphthol" solution.

A stock aqueous solution of sodium nitrite (1.0 cm^3 ; $5.43 \times 10^{-2} \text{ M}$) was added rapidly to an aqueous mixture of sulphuric acid (80.0 cm^3 ; 0.2 M) and aniline (1.0 cm^3 ; $1.79 \times 10^{-2} \text{ M}$) and a 1.0 cm^3 sample withdrawn and dumped into 20.0 cm^3 of the "naphthol" solution. Finally 1.0 cm^3 of this azo-dye solution was withdrawn after 30 minutes and diluted with 10.0 cm^3 of distilled water.

$$[\text{Azo-dye}]_{\text{max}} = [\text{ArN}_2^+]_{\text{max}} = [\text{PhNH}_2] = 9.45 \times 10^{-7} \text{ M}$$

since the maximum possible yield of diazonium ion is determined by the original aniline concentration (excess NaNO_2 was used), and the coupling takes place between 1 mole of aniline and 1 mole of "naphthol", i.e.:-



The wavelength of maximum absorption of the dye was found to be 340 nm (SP 8000). The absorbance at this wavelength was accurately determined on the SP 500 (using "naphthol" solution in the reference cell similarly diluted).

$$\text{Transmittance} = 7.75\% \quad \text{i.e.} \quad T = 7.75 \times 10^{-2}$$

$$\text{Absorbance} = \log_{10} (1/T) = 1.1106$$

Hence, since $A = \epsilon C$

$$\epsilon = 1.1106 / 9.45 \times 10^{-7} = 1.17 \times 10^6$$

(b) Reaction Solution:

0.2006 gm of aniline was dissolved in an aqueous mixture of sulphuric acid (20.0 cm^3 ; $\sim 0.7\text{M}$), stock NaN_3 (5.0 cm^3 ; 1.027M) and distilled water (5.0 cm^3). The reaction was started by the addition of methanolic N-nitrosodiphenylamine (2.0 cm^3 ; $5.0 \times 10^{-3}\text{M}$). At infinity (after 0.5 hr) a 1.0 cm^3 sample was withdrawn and dumped into 20.0 cm^3 of the "naphthol" solution. Finally a 1.0 cm^3 sample of this solution was diluted with 20.0 cm^3 of distilled water.

Here the aniline is in excess over the nitrosamine so that:-

$$[\text{Azo-dye}]_{\text{max}} = [\text{PhN}_2^+]_{\text{max}} = [\text{Ph}_2\text{N.NO}] = 7.09 \times 10^{-7}\text{M}$$

The transmittance at 340 nm was then determined as before.

$$T = 26.2\% = 0.262$$

$$\therefore \text{Absorbance} = 0.5817$$

Using the value of ϵ from (a) we then get:-

$$[\text{Azo-dye}] = 0.5817 / 1.17 \times 10^6 = 4.97 \times 10^{-7}\text{M}$$

Hence, the yield of diazonium ion is given by:-

$$\text{Yield} = \frac{4.97 \times 10^{-7}\text{M}}{7.09 \times 10^{-7}\text{M}} \times 100 = 70.1\%$$

It may therefore be concluded that the diazotization of aniline by N-nitrosodiphenylamine gives approximately 70% of the theoretical yield of diazonium ion. It seems reasonable to assume that during the reaction period some of the product will be lost through various side reactions such as solvolysis.

7.3 Denitrosation of N-ethyl-N-nitrosourethane:

These runs were carried out in exactly the same way as those of N-nitrosodiphenylamine, the rate of disappearance of the absorption at 250 nm being observed.

The following example refers to reaction in the absence of azide and other nucleophilic species. The reaction was started by the rapid addition of 1.0 cm³ of stock aqueous N-ethyl-N-nitrosourethane ($5.41 \times 10^{-3}M$) to 30 cm³ of aqueous sulphuric acid ($\sim 1.6M$). Again 'instantaneous' first-order rate constants have been calculated and the mean and standard error computed.

TABLE 86: $A_{\infty} = 0.020$

| t(sec) | A_t | $10^3 k_o \text{ sec}^{-1}$ |
|--------|-------|-----------------------------|
| 0 | 0.732 | |
| 15 | 0.669 | 6.18 |
| 30 | 0.612 | 6.15 |
| 45 | 0.553 | 6.43 |
| 60 | 0.512 | 6.16 |
| 75 | 0.466 | 6.24 |
| 90 | 0.420 | 6.41 |
| 105 | 0.380 | 6.49 |
| 120 | 0.340 | 6.66 |
| 135 | 0.305 | 6.78 |
| 150 | 0.272 | 6.92 |

$$\therefore 10^3 k_o = 6.44 \pm 0.09 \text{ sec}^{-1}$$

The k_o values quoted in section 3.6 were calculated from the slopes of plots of $\log_{10} (A_t - A_{\infty})$ versus t .

The yield of nitrous acid in the above reaction was determined directly from the absorbance of nitrous acid at 370 nm ($\epsilon = 55$). Runs were carried out exactly as above but using $3.90 \times 10^{-2} \text{M}$ stock N-ethyl-N-nitrosourethane. The maximum yield of nitrous acid is then theoretically $1.26 \times 10^{-3} \text{M}$.

Three separate determinations were made using the high sensitivity of the Beckmann model 25 spectrophotometer (0.1A absorbance scale).

- a) $A = 0.051 \therefore c = A/\epsilon = 0.93 \times 10^{-3} \text{M} \quad (74\%)$
 b) $A = 0.044 \therefore c = A/\epsilon = 0.80 \times 10^{-3} \text{M} \quad (63.5\%)$
 c) $A = 0.047 \therefore c = A/\epsilon = 0.85 \times 10^{-3} \text{M} \quad (67.5\%)$

$$\text{Mean yield} = 68 \pm 3\%$$

7.4 Diazotization by NOCl and NOBr; experimental details:

The kinetics of the processes were studied by means of a "Canterbury" stopped-flow spectrophotometer. The method involves the rapid mixing of two sample solutions A and B which are initially contained in two identical syringes driven by a single piston. On leaving the syringes the solutions (having identical flow velocities) enter the mixing cell where the reaction $A + B \rightarrow C$ takes place. The reaction mixture then enters a stopping syringe which arrests the flow and triggers the recording device at the observation point P. A beam of monochromatic light passes through the solution at this point and its intensity is converted into a proportional electrical signal which is then displayed on the storage oscilloscope. By flushing the system several times prior to making any measurements one obtains a situation in which the system after the mixing point is filled with the maximum possible product concentration. This is shown in the diagram overleaf (Figure 16).

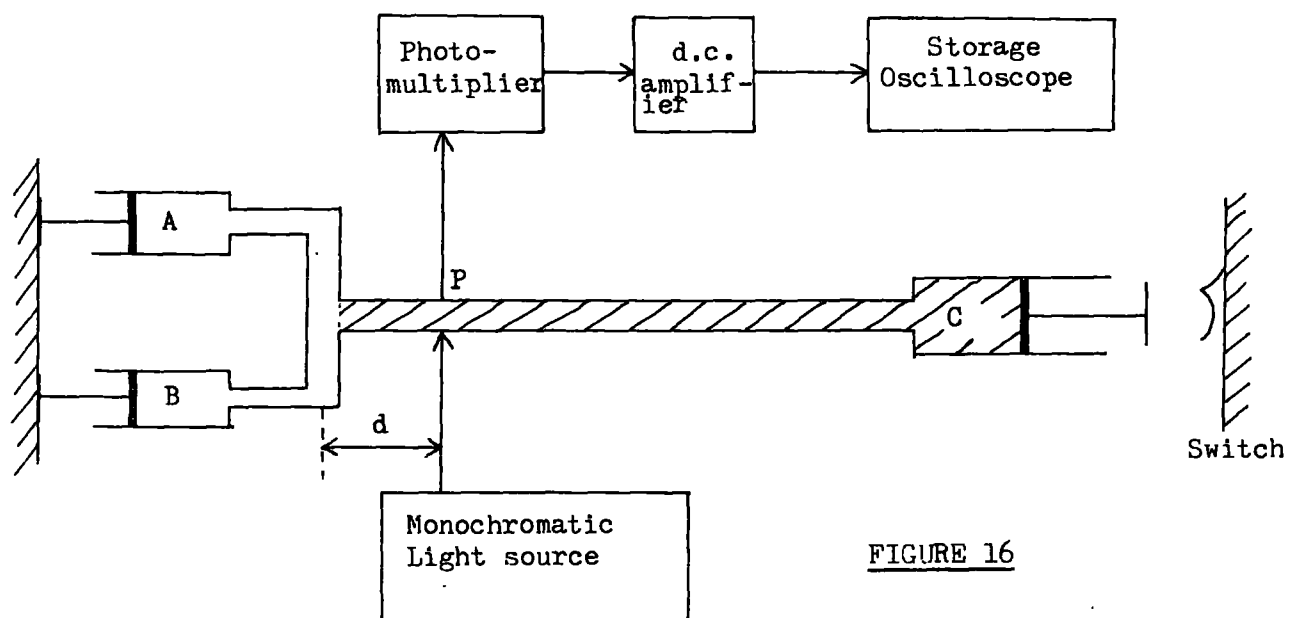


FIGURE 16

During a real run the solutions A & B mix and generate a small concentration of product ($[C]_{\min}$). This concentration is dependent upon the time taken for the mixture to traverse the distance from the mixing cell to P (d). Generally if $d \neq 0$ then $[C]_{\min} \neq 0$. This small concentration then displaces $[C]_{\max}$ at the point P where, after a short time, a stationary-state is set up since the product leaves this point as rapidly as it enters. When the stopping syringe halts the flow abruptly this stationary-state cannot be maintained at P and the recording device follows the reaction as it proceeds from $[C]_{\min}$ back to $[C]_{\max}$ (i.e. as it relaxes back to equilibrium).

If the observation being made at P is the monitoring of the product absorbance then, as the relaxation proceeds, the intensity of the light reaching the photomultiplier decreases. The oscilloscope display of voltage versus time then appears as shown diagrammatically in Figure 17.

The original equilibrium state at P ($[C]_{\max}$) can be regarded as having been perturbed by a concentration jump. If the perturbation is small the system will re-establish equilibrium by a first-order process irrespective of the kinetics of the forward and reverse reactions.¹⁶¹ It is then possible to analyse the relaxation time in terms of the rate-constants for the forward and reverse reactions. However, in the present case the exponential curve has been interpreted in terms of the pseudo first-order reaction between ArNH_2 and NO_x (k_0 ; section 5.2). This is made possible by the fact that the total amine concentration was always held in at least twenty-fold excess over the total 'nitrite' concentration.

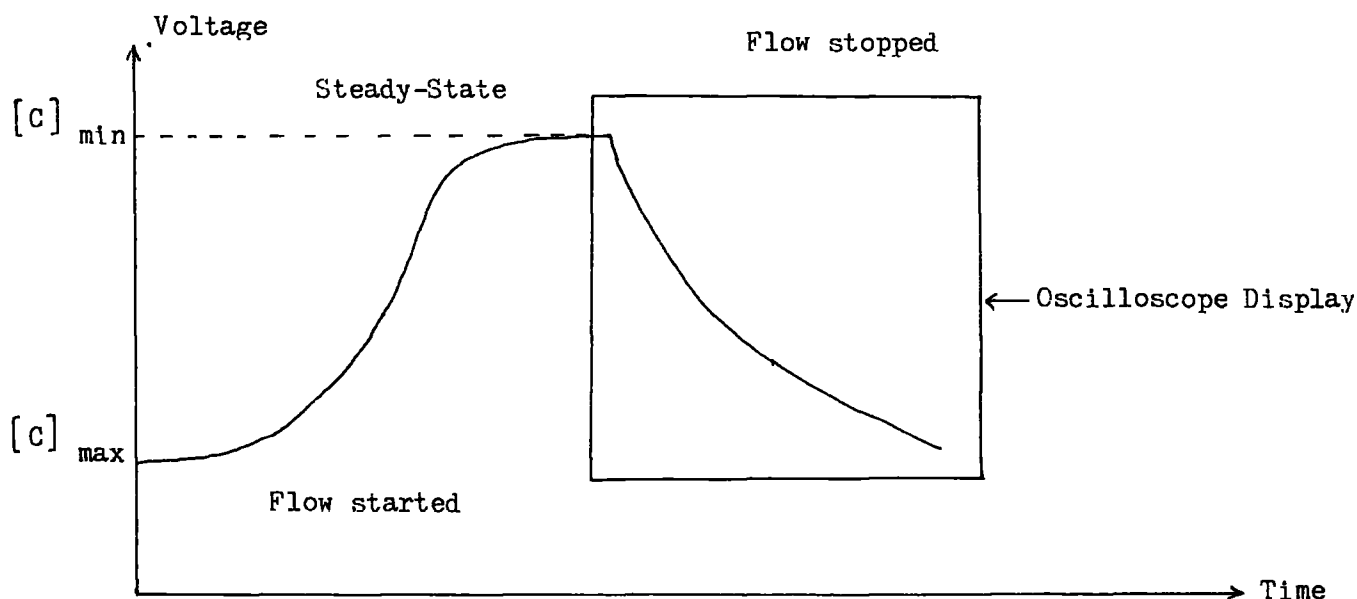


FIGURE 17

All measurements were carried out at 25°C by immersing the mixing cell in a thermostat bath at this temperature. The reactions were followed

by monitoring the increase in absorbance due to the formation of diazonium ion at the following wavelengths:-

TABLE 87

| ArN_2^+ | λ (nm) |
|-------------------|----------------|
| p-OMe | 340 |
| p-Me | 320 |
| m-OMe | 350 |
| H | 325 |
| p-COOH | 330 |
| p-Cl | 330 |
| p-NO ₂ | 390 |

where the influence of the absorption due to the corresponding ArNH_3^+ and ArNH_2 species is minimized.

Because of the instability of the infinity absorbance rate-constants were normally evaluated by means of the Guggenheim method for first-order reactions. Here readings are taken at times t_1, t_2, t_3 etc. and at times $(t_1 + \Delta), (t_2 + \Delta), (t_3 + \Delta)$ etc.. where Δ is a constant time increment of at least two half-lives. At time t_n the corresponding absorbance is A_n , and at $(t_n + \Delta)$ it is A'_n .

For a first-order reaction:-

$$[R]_t = [R]_0 e^{-kt}$$

so that: $(A_n - A_{\infty}) = (A_0 - A_{\infty}) e^{-kt_n}$

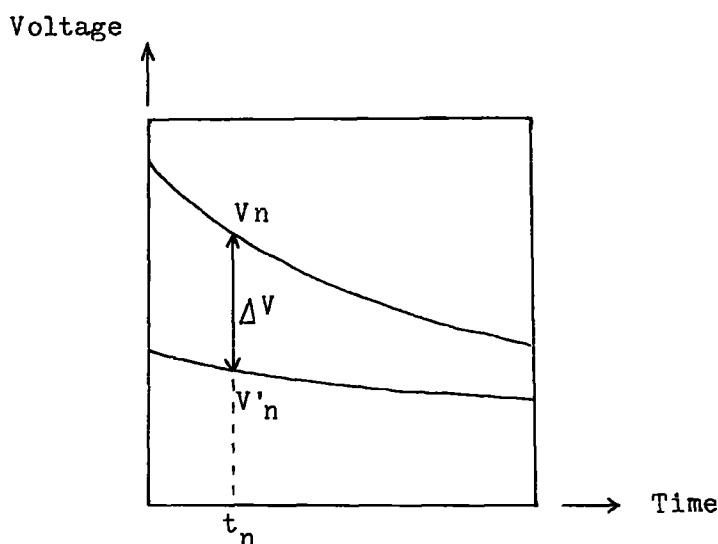
$$(A'_n - A_{\infty}) = (A_0 - A_{\infty}) e^{-k(t_n + \Delta)}$$

$$(A_n - A'_n) = (A_0 - A_{\infty}) e^{-kt_n} (1 - e^{-k\Delta})$$

$$\begin{aligned} \ln (A_n - A'_n) &= -kt_n + \ln [(A_0 - A_{\infty})(1 - e^{-k\Delta})] \\ &= -kt_n = \text{constant} \end{aligned}$$

Thus a plot of $\ln (A_n - A'_n)$ versus t_n should be linear with slope $-k$.

With the oscilloscope this is most easily achieved with two consecutive scans where the time taken between scans is negligible:-



and where a plot of $\log (\Delta V)$ versus t is linear and gives the rate-constant.

In general the runs were carried out by mixing equal volumes of the two solutions A & B. Owing to slight differences in procedure separate examples will be given for NOBr and NOCl.

a) Typical Run: NOBr reaction:

Nitrosyl bromide was generated 'in situ' by mixing an aqueous solution of NaNO_2 with an equal volume of diluted sulphuric acid containing the amine and KBr. Individual runs were repeated five times and the k_0

values quoted in the main text refer to the mean values.

The following data refers to the diazotization of m-anisidine in a single run.

Solution A consisted of sulphuric acid (24.0 cm^3 ; $\sim 0.9\text{M}$), stock aqueous KBr (1.0 cm^3 ; 1.558M), stock aqueous m-anisidine (11.0 cm^3 ; 0.1004M) and water (14.0 cm^3), so that the total volume was 50.0 cm^3 .

Solution B consisted of 1.0 l. of aqueous NaNO_2 ($1.0 \times 10^{-4}\text{M}$).

Titration of samples of solution A with standard sodium hydroxide using phenol red as indicator gave $[\text{H}^+] = 0.920\text{M}$. On mixing equal volumes of A & B the concentrations of all species are halved. This results in the values quoted in Tables 37 and 43.

Instantaneous rate-constants can be calculated according to:-

$$k_o = \frac{1}{t} \ln \frac{(\Delta V)_o}{(\Delta V)_t}$$

and the results are shown in Table 88.

TABLE 88

| t (sec) | ΔV | $k_o \text{ sec}^{-1}$ |
|---------|------------|------------------------|
| 0 | 5.05 | |
| 0.2 | 4.10 | 1.042 |
| 0.4 | 3.35 | 1.026 |
| 0.6 | 2.70 | 1.044 |
| 0.8 | 2.15 | 1.067 |
| 1.0 | 1.75 | 1.060 |
| 1.2 | 1.40 | 1.069 |
| 1.4 | 1.15 | 1.057 |
| 1.6 | 0.95 | 1.044 |
| 1.8 | 0.75 | 1.059 |
| 2.0 | 0.60 | 1.065 |

This gives: $k_o = 1.053 \pm 0.004 \text{ sec}^{-1}$

b) Typical Run: NOCl reaction:

Here NOCl was generated from NaNO_2 and HCl. Since the HCl solutions varied from 1 - 5 M mixing such solutions with aqueous nitrite during a run would lead to undesirable temperature changes. (see section 6.1). Hence the following general procedure was adopted.

Five stock solutions of hydrochloric acid were made up and, by titration against standard sodium hydroxide, found to be:-

| | | | |
|-----|-----|---|-------|
| HCl | 'A' | = | 1.12M |
| " | 'B' | = | 2.31M |
| " | 'C' | = | 3.41M |
| " | 'D' | = | 4.53M |
| " | 'E' | = | 5.83M |

The amine and nitrite were then made up in HCl of the same strength as follows:-

Solution A: 5.0 cm^3 stock aqueous amine + 45.0 cm^3 of HCl 'A'

Solution B: 5.0 cm^3 stock aqueous NaNO_2 + 45.0 cm^3 of HCl 'A'

and so on, variations in $[\text{Cl}^-]$ and $[\text{ArNH}_2]$ being achieved simply by changing the stock HCl solution. In practice everything would be set up 'ready to run' and only then would the 5.0 cm^3 of aqueous nitrite be added to the 45.0 cm^3 of acid. All runs would then be rapidly carried out in order to minimise the effects of deterioration, in the 'nitrous acid' solution.

For the more weakly basic amines it was found convenient to make up their stock solutions in dilute hydrochloric acid (HCl 'F' = 2.34M).

One would then use:-

A: 5.0 cm³ stock amine in HCl 'F' + 40.0 cm³ HCl 'A' + 5.0 cm³ H₂O

B: 5.0 cm³ stock NaNO₂ in H₂O + 40.0 cm³ HCl 'A' + 5.0 cm³ HCl 'F'.

and so on. This accounts for the slightly different values for [HCl] in Tables 70 - 72 as compared with Tables 66 - 69.

The following example refers to the diazotization of aniline in HCl 'E'. The two reactant solutions were made up thus:-

A: Stock aqueous PhNH₂ (5.0 cm³; 0.154M) + 45.0 cm³ HCl 'E'

B: Stock aqueous NaNO₂ (5.0 cm³; 5.0 x 10⁻³M) + 45.0 cm³ HCl 'E'

(see Table 66). Again all concentrations are halved on mixing. The instantaneous rate-constants are shown in Table 89:-

TABLE 89

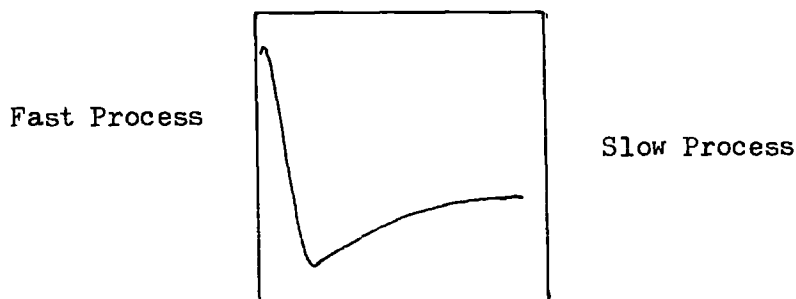
| t (sec) | ΔV | $k_o \text{ sec}^{-1}$ |
|---------|------------|------------------------|
| 0 | 3.35 | |
| 0.05 | 2.75 | 3.947 |
| 0.10 | 2.25 | 3.980 |
| 0.15 | 1.90 | 3.781 |
| 0.20 | 1.60 | 3.695 |
| 0.25 | 1.35 | 3.635 |
| 0.30 | 1.05 | 3.867 |
| 0.35 | 0.85 | 3.918 |
| 0.40 | 0.75 | 3.742 |
| 0.45 | 0.60 | 3.822 |
| 0.50 | 0.45 | 4.015 |

and this gives: $k_0 = 3.84 \pm 0.04 \text{ sec}^{-1}$

(N.B. Again the value of k_0 in Table 66 refers to the mean of five separate determinations).

The Slow Process

For those amines carrying electron-withdrawing substituents a second relaxation could be observed at the same wavelength as the main process. This was slower than the first process and by altering the time-base the oscilloscope display could be made to look like this:-



i.e. the slow process definitely follows that which we have taken to be the encounter between ArNH_2 and NOX . (This is one reason for unstable infinity values). The increase in voltage with time would also suggest destruction of the species responsible. Furthermore, the smaller voltage change in the slow process renders the evaluation of k_0 values susceptible to error.

Measurements were actually carried out for p-Cl, p-COOH (NOBr reaction) and p-NO₂ (NOCl reaction) anilines, (see section 5.6). A typical run is given for p-aminobenzoic acid (Table 90).

Solution A: H_2SO_4 (17.0 cm³; ~ 0.9M) + aq.KBr (1.0 cm³; 1.538M) + stock PAB in stock sulphuric acid (8.0 cm³; $6.1 \times 10^{-2}\text{M}$) + H_2O (24.0 cm³).

Solution B: aqueous NaNO_2 ($3.0 \times 10^{-4}\text{M}$)

Titration of solution A with standard sodium hydroxide gave

$$[\text{H}^+] = 0.88\text{M}.$$

Again all concentrations are halved on mixing. (see Tables 40 & 43).

TABLE 90

| t (sec) | Δv | $k_0 \text{ sec}^{-1}$ |
|---------|------------|------------------------|
| 0 | 1.25 | |
| 2.0 | 1.00 | 0.112 |
| 4.0 | 0.80 | 0.112 |
| 6.0 | 0.65 | 0.109 |
| 8.0 | 0.55 | 0.103 |
| 10.0 | 0.40 | 0.114 |
| 12.0 | 0.30 | 0.119 |
| 14.0 | 0.25 | 0.115 |

which gives: $k_0 = 0.112 \pm 0.002$

Although the internal precision is quite high the accuracy of such k_0 values is felt to be less than those of the fast process since the oscilloscope trace was subject to more noise, and duplicate runs did not agree so well. Nevertheless the existence of this process is intriguing and for a fuller discussion see section 5.6.

7.5 Treatment of Errors:

In general correlations between k_0 and other variables have been based on the principle of least squares. This minimizes the sum of the squares of the deviations from the line $y_1 = a + bx_1$.

$$\text{i.e.} \quad S = \sum (y_1 - a - bx_1)^2$$

and for a minimum $\partial S / \partial a$ and $\partial S / \partial b$ are set equal to zero.

$$\partial S / \partial a = -2 \sum (y_1 - a - bx_1) = 0$$

$$\partial S / \partial b = -2 \sum x_1 (y_1 - a - bx_1) = 0$$

Rearranging terms gives the so-called normal equations

$$(i) \quad \sum y_1 = na + b \sum x_1$$

$$(ii) \quad \sum x_1 y_1 = a \sum x_1 + b \sum x_1^2$$

$$\text{from which} \quad b = \frac{n \sum xy - \sum x \sum y}{n \sum x^2 - (\sum x)^2} = \text{'best' slope}$$

where n = total number of points.

The 'best' intercept 'a' can then be computed from the first normal equation.

The correlation coefficients quoted have been calculated from:-

$$r = \frac{n \sum xy - \sum x \sum y}{\left([n \sum x^2 - (\sum x)^2] [n \sum y^2 - (\sum y)^2] \right)^{\frac{1}{2}}}$$

However, in section 5.3 the plots of k_0 versus $[\text{ArNH}_2]$ must pass through the origin so that $a = 0$. Here, one minimizes:

$$Q = \sum (y_i - bx_i)^2$$

$$\therefore \frac{\partial Q}{\partial b} = 2 \sum x_i (y_i - bx_i) = 0$$

$$\therefore \sum x_i (y_i - bx_i) = 0$$

$$\sum xy - b \sum x_i^2 = 0$$

$$\therefore b = \frac{\sum xy}{\sum x_i^2} = \text{'best' slope.}$$

and the slopes have been calculated using this simpler form. (section 5.3).

Wherever feasible standard errors have been computed, e.g. in sections 6.4 and 6.5, from the theoretical expression for the linear relationship, (as in the calculation of 'instantaneous' rate-constants).

The theory of errors is discussed more fully in H.D. Young's "Statistical Treatment of Experimental Data"; McGraw-Hill (1962) and J.F. Ratcliffe's "Elements of Mathematical Statistics"; O.U.P. (1967) upon which the above treatment is based.

REFERENCES

1. W. Macmillen & T.H. Reade, J. Chem. Soc., 585, (1929)
2. E.C.S. Jones & J. Kenner, J. Chem. Soc., 711 (1932)
3. O. Fischer & E. Hepp, Ber. 19, 2991 (1886)
4. O. Fischer & P. Neber, 45, 1093, (1912)
5. J. Houben, Ber. 46, 3984, (1913)
6. P.W. Neber & H. Rauscher, Liebig's Annalen, 550, 182, (1942)
7. T.I. Aslapovskaya et alia, Reakts. Spasobnost. org. Soedineni, 5, 456, (1968)
8. T.D.B. Morgan & D.L.H. Williams, Chem. Comm., 1671 (1970)
9. T.D.B. Morgan & D.L.H. Williams, J.C.S. Perkin II, 74, (1972)
10. D.L.H. Williams, Tetrahedron, 31, 1343, (1975).
11. D.L.H. Williams, Int. J. Chem. Kinetics, 7, 215, (1975)
12. S.S. Johal, unpublished results, Durham University.
13. D.L.H. Williams & J.A. Wilson, J.C.S. Perkin II, 13, (1974)
14. I.D. Biggs & D.L.H. Williams, J.C.S. Perkin II, 107, (1975)
15. F.G. Soper, J. Phys. Chem., 31, 1192, (1927) & F.G. Soper & D.R. Pryde, J. Chem. Soc., 2761, (1927)
16. C.G. Swain & C.B. Scott, J. Am. Chem. Soc., 75, 141, (1953)
17. E. Kalatzis & J.H. Ridd, J. Chem. Soc. (B), 529, (1966)
18. B.C. Challis & J.H. Ridd, J. Chem. Soc., 5208, (1962)
19. D.L.H. Williams, J.C.S. Perkin II, 655, (1975).
20. I.D. Biggs & D.L.H. Williams, J.C.S. Perkin II, 601, (1976)
21. I.D. Biggs & D.L.H. Williams, J.C.S. Perkin II, 691, (1976)
22. D.L.H. Williams, Chem. Comm., 376, (1975)
23. D.L.H. Williams, J.C.S. Perkin II, 128, (1977)
24. K. Al-Mallah, P. Collings & G. Stedman, J.C.S. Dalton, 2469, (1974)
25. A.E. Werner, J. Chem. Soc., 101, 2180, (1912)
26. J.W. Dobereiner, Schweigger's Journal, 8, 239, (1812)
27. P.N. Magee & J.M. Barnes, Adv. Cancer Research, 10, 163, (1967)
28. B.A. Kihlman, in "Actions of Chemicals on Dividing Cells", p.77, Prentice-Hall (1966)
29. G. Hallett, unpublished results, Durham University.
30. R. Schoental & D.J. Rive, Biochem. J., 97, 466, (1965)
31. B.A. Kihlman, Exp. Cell Res., 20, 657, (1960)

.....

.....

32. ref. 28, page 185.
33. C.N. Berry & B.C. Challis, J.C.S. Perkin II, 1638, (1974)
34. B.C. Challis & S.P. Jones, J.C.S. Perkin II, 153, (1975)
35. R. Preusmann, R. Deutsch-Wenzel & G. Eisenbrand, Z.Krebsforsch, 84, 75, (1975)
36. D.L.H. Williams, unpublished results, Durham University.
37. D.L.H. Williams, J.C.S. Perkin II, 1838, (1976)
38. B.C. Challis & M.R. Osborne, J.C.S. Perkin II, 1526, (1973)
39. G. Stedman, J. Chem. Soc., 2949, (1959)
40. T.D.B. Morgan, D.L.H. Williams & J.A. Wilson, J.C.S. Perkin II, 473, (1973)
41. B.C. Challis, R.J. Higgins & A.J. Lawson, Chem. Comm., 1223 (1970)
42. W.J. Hickinbottom, J. Chem. Soc., 946, (1933)
43. E.C.R. de Fabrizio, E. Kalatzis & J.H. Ridd, J. Chem. Soc. (B), 533, (1966)
44. D. Dimitrov & F. Fratev, Compt. Rend., Acad. Bulgare. Sci., 16, 825, (1963)
45. Z.J. Allan et alia, Coll. Czech. Chem. Commun., 32, 1449, (1967)
46. A.D. Williamson et alia, J. Am. Chem. Soc., 97, 5714, (1975)
47. F. Basolo & R.G. Pearson, "Mechanisms of Inorganic Reactions", Ch.7, Wiley, (1958)
48. H.J. Shine, "Aromatic Rearrangements", p.231-235, Elsevier, Amsterdam, (1967)
49. H.J. Shine, in "International Review of Science", Org. Chem., series Two, Vol. 3, p.117, Butterworths, London (1976)
50. M.J.S. Dewar, in "The MO theory of Organic Chemistry", p. 392, McGraw-Hill, New York, (1969)
51. G. Klopman, in "Chemical Reactivity & Reaction Paths", p.55-165, Wiley, (1974)
52. Z.J. Allan, Tetrahedron Letters, 4225, (1971)
53. A.J. Kresge et alia, J. Am. Chem. Soc., 93, 6181, (1971)
54. B.T. Baliga, J. Org. Chem., 35, 2031, (1970)
55. L.P. Kappel et alia, Zhurnal Obschei Khimii, 45, 2734, (1975)
56. L.P. Kappel et alia, Zhurnal Obschei Khimii, 46, 2134, (1976)
57. S. Ehrenson, R.T.C. Brownlie & R.W. Taft, Prog. in Phys. Org. Chem., 10, 1 - 80, (1973)
58. B.C. Challis & J.H. Ridd, Proc. Chem. Soc., 245, (1960)
59. B. Nahlovsky & V. Chvalovsky, Coll. Czech. Chem. Commun., 33 3122, (1968)

.....

.....

60. H. Schmid & A. Maschka, Z. Phys. Chem. (B), 49, 171, (1941)
61. S.F.A. Kettle, "Coordination Compounds", p.48, Nelson, (1969)
62. D.V. Banthorpe, "Chemistry of the Amino Group", Ed. S. Patai,
Ch.10,Wiley Interscience (1968)
63. ref. 48 Chapter 3.
64. D.L.H. Williams, "Comprehensive Chemical Kinetics", Vol. 13, Ch.3.,
Elsevier, (1972)
65. J.F.J. Dippy & V. Moss, J. Chem. Soc., 2205, (1952)
66. ref. 48, p. p. 73.
67. E.D. Hughes & G.T. Jones, J. Chem. Soc., 2678 (1950)
68. D.V. Banthorpe, E.D. Hughes & D.L.H. Williams, J. Chem. Soc.,
5349, (1964)
69. J.H. Ridd & E.F.V. Scriven, Chem. Comm., 641, (1972)
70. G.A. Olah et alia, J. Am. Chem. Soc., 94, 7438, (1972)
71. A.C. Ling & F.H. Kendall, J. Chem. Soc. (B), 445, (1967)
72. J.H. Ridd, Quart. Rev. 418, (1961)
73. B.C. Challis, L.F. Larkworthy & J.H. Ridd, J. Chem. Soc., 5203 (1962)
74. H. Zollinger, "Azo & Diazo Chemistry", Ch. 2, Interscience, (1961)
75. E. Miller & H. Hais, Chem. Ber. 96, 570, (1963)
76. B.C. Challis & A.R. Butler, ref. 62, Ch. 6.
77. H. Schmid; Z. Electrochem., 42, 579, (1936)
78. T.W.J. Taylor, J. Chem. Soc., 1099, (1928)
79. T.W.J. Taylor & L.S. Price, J. Chem. Soc., 2052, (1929)
80. L.P. Hammett, "Physical Organic Chemistry", p. 294, McGraw-Hill,(1940)
81. E.D. Hughes, C.K. Ingold & J.H. Ridd, J. Chem. Soc., 65, (1958)
82. E.D. Hughes & J.H. Ridd, J. Chem. Soc., 70 (1958)
83. C.A. Bunton, D.R. Llewellyn & G. Stedman, J. Chem. Soc., 568, (1959)
84. L.F. Larkworthy, J. Chem. Soc., 3304, (1959)
85. E.D. Hughes, C.K. Ingold & J.H. Ridd, J. Chem. Soc., 83, (1958)
86. W.R. Angus & A.H. Leckie, Proc. Roy. Soc., A150, 615, (1935)
87. H.A.J. Schoutissen, J. Am. Chem. Soc., 58, 259, (1936)
88. H. Schmid, Z. Electrochem., 43, 626, (1937)
89. H. Schmid & G. Muhr, Ber. 70, 421, (1937)
90. E.D. Hughes & J.H. Ridd, J. Chem. Soc., 82, (1958)
91. H. Schmid & G. Muhr, Monatsh., 91, 1198, (1960)

.....

.....

92. H. Schmid & G. Muhr, *Monatsh.*, 93, 102, (1962)
93. H. Schmid, *Monatsh.*, 85, 424, (1954)
94. H. Schmid & C. Essler, *Monatsh.*, 88, 1110, (1957)
95. H. Schmid & E. Hallaba, *Monatsh.*, 87, 560, (1956)
96. H. Schmid & M.G. Foud, *Monatsh.*, 88, 631, (1957)
97. D.L.H. Williams, *J.C.S. Perkin II*, 502, (1977)
98. J.O. Edwards, *J. Am. Chem. Soc.*, 76, 1540, (1954)
99. K. Issleib & H. Bruchlos, *Z. Anorg. Allgem. Chem.*, 316, 1, (1962)
100. E.B. Robertson & H.B. Dunford, *J. Am. Chem. Soc.*, 86, 5082, (1964)
101. E.D. Hughes, C.K. Ingold & C.S. Patel, *J. Chem. Soc.*, 526, (1933)
102. J.N. Brønsted, *Z. Phys. Chem.*, 102, 169, (1922)
103. L.P. Hammett, *Chem. Rev.*, 17, 125, (1935)
104. O. Exner, "Progress in Phys. Org. Chem.", 10, 411, Wiley (1973)
105. J. Shorter, "Correlation Analysis in Organic Chemistry", p.105,
Oxford Chem.Series, (1973)
106. E. Heilbronner, in "Molecular Spectroscopy", p. 427, Heyden (1977)
107. R.G. Pearson, H. Sobel & J. Songstad, *J. Am. Chem. Soc.*, 90,
319, (1968)
108. A. Pross, "Advances in Phys. Org. Chem.", 14, 69, Academic Press (1977)
109. F.A. Long & J. Bigeleisen, *Trans. Faraday Soc.*, 55, 2077, (1959)
110. F.H. Westheimer, *Chem. Rev.* 61, 265, (1961)
111. S.J. Kuhn & J.S. McIntyre, *Can. J. Chem.*, 44, 105, (1966)
112. C.E. Looney, W.D. Philips & E.L. Reilly, *J. Am. Chem. Soc.*, 79,
6136, (1957)
113. J.T. D'Agostino & H.H. Jaffe, *J. Am. Chem. Soc.*, 92, 5160, (1970)
114. W.S. Layne, H.H. Jaffe & H. Zimmer, *J. Am. Chem. Soc.*, 85, 1816, (1963)
115. B.C. Challis & J.H. Ridd, *J. Chem. Soc.*, 5197, (1962)
116. C.H. Rochester, "Acidity Functions", p.80, Academic Press, (1970)
117. L. Zucker & L.P. Hammett, *J. Am. Chem. Soc.*, 65, 2779, 2785, 2791, (1939)
118. J.T. Thompson & D.L.H. Williams, *J.C.S. Perkin II*, 1932 (1977)
119. F.A. Long & M.A. Paul, *Chem. Rev.*, 57, 935, (1957)
120. J.F. Bunnett, *J. Am. Chem. Soc.*, 83, 4956, 4968, 4973, 4978, (1961)
121. R.J. Withey & E. Whalley, *Can. J. Chem.*, 41, 546, (1963)
122. N.V. Sidgwick, "Org. Chem. of Nitrogen", p.161, Clarendon Press,
Oxford, (1966)
123. J. Knop, *J. Am. Chem. Soc.*, 46, 263, (1924)

.....

.....

124. L.A. Kalashnikova et alia, Bull.Acad.Sci., USSR, 782, (1965)
125. L. Michaelis & S. Granick, J. Am. Chem. Soc., 65, 1747, (1943)
126. R.F. Milligan, J. Am. Chem. Soc., 72, 2775, (1950)
127. A. Kawamori et alia, J. Chem. Phys., 44, 4363, (1966)
128. V.E. Kholmogorev & E.V. Baranov., Opt.Spectr., 14, 440, (1963)
129. H. Wieland & St. Gambajarin, Ber. 39, 1499, (1906)
130. H. Wieland., Ber. 40, 4260, (1907); 41, 3478, (1908)
131. M.R. Das et alia, Proc. Indian Acad.Sci., 53A, 273, (1961)
132. A.G. Razuvaev et alia, J. Struct. Chem., 5, 278, (1964)
133. G.A. Razuvaev et alia, Doklady Chem., 169, 755, (1966)
134. H. Wieland, Ber. 46, 3296, (1913); 52, 886, (1919)
135. F. Kehrman et alia, Ber. 45, 2641, (1912); 55, 156, (1922)
136. A.D. Cross & R.A. Jones, "Practical I.R. Spectroscopy",
Butterworths, (1969)
137. G. Hallett, unpublished results, Durham University.
138. A. Lachman, Ber. 33, 1035, (1900)
139. B.C. Challis & J.H. Ridd, Proc. Chem. Soc., 173, (1961)
140. W. Schulz, H. Drost & H.D. Klotz, Org.Mass.Spectrom., 1, 391 (1968)
141. D.D. Perrin, "Dissociation Constants of Org. Bases", Supplement 1972,
Butterworths
142. H. Druckrey et alia, Arzneimittal Forsch., 13, 320, (1963)
143. ref. 28, p. 190 - 191.
144. C.D. & O. Jardetzky, J. Am. Chem. Soc., 82, 222, (1960)
145. Borresen, Acta.,Chem.Scand., 21, 2463, (1967)
146. I.T. Millar & H.D. Springall, "A Shorter Sidgwick", p.491,
Clarendon,Oxford (1969)
147. P.A.S. Smith & R.N. Lloepky, J. Am.Chem. Soc., 89, 1147, (1967)
148. R.S. Mulliken, J. Am. Chem. Soc., 74, 811, (1952)
149. H.G. Smith & R.E. Rundle, J. Am.Chem. Soc., 80, 5075, (1958)
150. P. von R. Schleyer, unpublished results, Durham Seminar, May, (1978)
151. R. Foster, "org. Charge Transfer Complexes", p.23, Academic Press (1969)
152. E.A. Guggenheim, Phil. Mag., 2, 538, (1926)
153. M.V. Smoluchowski, Physik. Z., 17, 557, 583 (1916) & Z.Phys.Chem.
92, 129, (1917)
154. M.R. Piercey & E.R. Ward, J. Chem. Soc., 3841, (1962)

.....

.....

155. R.A. Robertson & R.H. Stokes, "Electrolyte Solutions", p.491,
Butterworths, (1959)
156. A. Woppmann & H. Sofer, Monatsh, 103, 163, (1972)
157. J.R. Park & D.L.H. Williams, J.C.S. Perkin II, 691, (1976)
158. J.R. Perrott, C. Stedman & N. Uysal; J.C.S. Dalton, 2058, (1976)
159. A.I. Vogel, "Textbook of Practical Organic Chemistry", p.572-3,
Longmans, (1966)
160. "Handbook of Chemistry & Physics", 57th Edition, CRC Press (1976-77)
161. A.A. Frost & R.G. Pearson, "Kinetics & Mechanism", 2nd Edition,
p.280, Wiley (1961).

APPENDIX

1) Research Colloquia, Seminars and Lectures

1.1 1976 - 1977

a) University of Durham Chemistry Colloquia

Wednesday 20th October

Professor J.B. Hyne (University of Calgary), "New Research on an Old Element - Sulphur".

Wednesday 10th November

Dr. J.S. Ogden (Southampton University), "The Characterization of High Temperature Species by Matrix Isolation."

Wednesday 17th November

Dr. B.E.F. Fender (University of Oxford), "Familiar but Remarkable Inorganic Solids."

Wednesday 24th November

Dr. M.I. Page (Huddersfield Polytechnic), "Large and Small Rate Enhancements of Intramolecular Catalysed Reactions."

Wednesday 8th December

Professor A.J. Leadbetter (University of Exeter), "Liquid Crystals."

Wednesday 26th January

Dr. A. Davis (ERDR), "The Weathering of Polymeric Materials."

Wednesday 2nd February

Dr. M. Falk, (MRC Canada), "Structural Deductions from the Vibrational Spectrum of Water in Condensed Phases."

Wednesday 9th February

Professor R.O.C. Norman (University of York), "Radical Cations, Intermediates in Organic Reactions."

Wednesday 23rd February

Dr. G. Harris (University of St. Andrews), "Halogen Adducts of Phosphines and Arsines."

.....

.....

Friday 25th February

Professor H.T. Dieck (Frankfurt University), "Diazadienes - New Powerful Low-Valent Metal Ligands."

Wednesday 2nd March

Dr. F. Hibbert (Birkbeck College, London), "Fast Reaction Studies of Slow Proton Transfers Involving Nitrogen and Oxygen Acids."

Friday 4th March

Dr. G. Brink (Rhodes University, R.S.A.), "Dielectric Studies of Hydrogen Bonding in Alcohols."

Wednesday 9th March

Dr. I.O. Sutherland (Sheffield University), "The Stevens' Rearrangement: Orbital Symmetry and Radical Pairs."

Friday 18th March

Professor Hans Bock (Frankfurt University), "Photoelectron Spectra and Molecular Properties: A Vademecum for the Chemist."

Wednesday, 30th March

Dr. J.R. MacCallum (University of St. Andrews), "Photooxidation of Polymers."

Wednesday 20th April

Dr. D.M.J. Lilley (G.D. Searle, Research Div.), "Tails of Chromatin Structure - Progress towards a Working Model."

Wednesday 27th April

Dr. M.P. Stevens (University of Hartford), "Photocycloaddition Polymerisation."

Wednesday 4th May

Dr. G.C. Tabisz (University of Manitoba), "Collision Induced Light Scattering by Compressed Molecular Gases."

.....

Wednesday 11th May

Dr. R.E. Banks (UMIST), "The Reaction of Hexafluoropropene with Heterocyclic N-oxides."

Wednesday 18th May

Dr. J. Atwood (University of Alabama), "Novel Solution Behaviour of Anionic Organoaluminium Compounds: The Formation of Liquid Clathrates."

Wednesday 25th May

Professor M.M. Kreevoy (University of Minnesota), "The Dynamics of Proton Transfer in Solution."

Wednesday 1st June

Dr. J. McCleverty (University of Sheffield), "Consequences of Deprivation and Overcrowding on the Chemistry of Molybdenum and Tungsten."

Wednesday 6th July

Professor J. Passmore (University of Brunswick), "Adducts Between Group V Pentahalides and a Postscript on S_7I^+ ".

b) Durham University Chemical Society

Tuesday 19th October

Dr. J.A. Salthouse (University of Manchester), "Chemistry and Energy".

Tuesday 26th October

Dr. R.E. Richards (University of Oxford), "NMR Measurements on Intact Biological Tissue."

Tuesday 2nd November

Dr. B. Sutcliffe (University of York), "The Chemical Bond as a Figment of the Imagination."

Tuesday 16th November

Mr. R. Ficken (Rohm & Haas), "The Graduate in Industry."

.....

Tuesday 30th November

Dr. R.J. Donovan (University of Edinburgh) "The Chemistry of the Atmosphere."

Tuesday 18th January

Professor I. Fells (University of Newcastle), "Energy Storage: The Chemists' Contribution to the Problem."

Tuesday 8th February

Dr. M.J. Cleare (Johnson Matthey Research Centre), "Platinum Group Metal Compounds as Anti-Cancer Agents."

Tuesday 1st March

Professor J.A.S. Smith (Q.E. College, London), "Double Resonance."

Tuesday 8th March

Professor C. Eaborn (University of Sussex), "Structure and Reactivity."

1.2 1977 - 1978

a) University of Durham Chemistry Colloquia

Tuesday 27th September

Dr. T.J. Broxton (La Trobe University, Australia), "Interaction of Aryldiazonium Salts and Arylazoalkyl Ethers in Basic Alcoholic Solvents."

Wednesday 19th October

Dr. B. Heyn (University of Jena, DDR), " σ - Organo-Molybdenum Complexes as Alkene Polymerisation Catalysts."

Thursday 27th October

Professor R.A. Filler (Illinois Inst. of Technology, U.S.A.), "Reactions of Organic Compounds with Xenon Fluorides."

Wednesday 2nd November

Dr. N. Boden (University of Leeds), "NMR Spin-Echo Experiments for Studying Structure and Dynamical Properties of Materials Containing Interacting Spin- $\frac{1}{2}$ pairs."

.....

Wednesday 9th November

Dr. A.R. Butler (University of St. Andrews), "Why I lost Faith in Linear Free Energy Relationships."

Wednesday 7th December

Dr. P.A. Madden (University of Cambridge), "Raman Studies of Molecular Motions in Liquids."

Wednesday 14th December

Dr. R.O. Gould (University of Edinburgh), "Crystallography to the Rescue in Ruthenium Chemistry."

Wednesday 25th January

Dr. G. Richards, (University of Oxford), "Quantum Pharmacology."

Wednesday 1st February (2.30 pm)

Professor K.J. Ivin (Queens University, Belfast), "The olefin metathesis reaction: mechanism of ring-opening polymerisation of cycloalkenes."

Friday 3rd February

Dr. A. Hartog (Free University, Amsterdam, Holland), "Surprising recent Studies in Organo-magnesium Chemistry,"

Wednesday 22nd February

Professor J.D. Birchall (Mond Division, I.C.I. Ltd.), "Silicon in the Biosphere."

Wednesday 1st March

Dr. A. Williams (University of Kent), "Acyl Group Transfer Reactions."

Friday 3rd March

Dr. G. van Koten (University of Amsterdam, Holland), "Structure and Reactivity of Arylcopper Cluster Compounds."

.....

Wednesday 15th March

Professor G. Scott (University of Aston), "Fashioning Plastics to match the Environment."

Wednesday 22nd March

Professor H. Vahrenkamp (University of Freiburg, Germany), "Metal-Metal Bonds in Organometallic Complexes."

Wednesday 19th April

Dr. M. Barber (UMIST), "Secondary Ion Mass Spectra of Surfaces and Adsorbed Species."

Tuesday 16th May

Dr. P. Ferguson (C.N.R.S. Grenoble), "Surface Plasma Waves and Adsorbed Species on Metals."

Thursday 18th May

Professor M. Gordon (University of Essex), "Three Critical Points in Polymer Science."

Monday 22nd May

Professor D. Tuck (University of Windsor, Ontario), "Electrochemical Synthesis of Inorganic and Organometallic Compounds."

Wednesday - Thursday 24th/25th May

Professor P. Von R. Schleyer (University of Erlangen, Nurnberg.)

- 1 "Planar Tetra-co-ordinate Methanes, Perpendicular Ethylenes, and Planar Allenes."
- 2 "Aromaticity in Three Dimensions."
- 3 "non-classical Carbocations."

Wednesday 21st June

Dr. S.K. Tyrlik (Academy of Science, Warsaw), "Dimethylglyoxime-cobalt Complexes - Catalytic Black Boxes."

.....

Friday 23rd June

Professor W.B. Pearson (University of Florida), "Diode Laser Spectroscopy at 16 μm ."

Friday 30th June

Professor G. Mateescu (Cape Western Reserve University), "A Concerted Spectroscopy Approach to the Characterization of Ions and Ion Pairs: Facts, Plans, and Dreams."

b) Durham University Chemical Society

Thursday 13th October

Dr. J.C. Young, Mr. A.J.S. Williams (University of Aberystwyth), "Experiments and Considerations Touching Colour."

Thursday 20th October

Dr. R.L. Williams (Metropolitan Police Forensic Science Dept.) "Science and Crime."

Thursday 3rd November

Dr. G.W. Gray (University of Hull), "Liquid Crystals - Their Origins and Applications."

Thursday 24th November

Mr. G. Russell (Alcan), "Designing for Social Acceptability."

Thursday 1st December

Dr. B.F.G. Johnson (University of Cambridge), "Chemistry of Binary Metal Carbonyls."

Thursday 2nd February

Professor R.A. Raphael (University of Cambridge), "Bizarre Reactions of Acetylenic Compounds."

Thursday 16th February

Professor G.W.A. Fowles (University of Reading) "Home Wine-making".

.....

Thursday 2nd March

Professor M.W. Roberts (University of Bradford), "The Discovery of Molecular Events at Solid Surfaces."

Thursday 9th March

Professor H. Suschitzky (University of Salford), "Fruitful Fissions of Benzofuroxans,"

Thursday 4th May

Professor J. Chatt (University of Sussex), "Reactions of Co-ordinated Dinitrogen."

Tuesday 9th May

Professor G.A. Olah (Cape Western Reserve University, Cleveland, Ohio), "Electrophilic Reactions of Hydrocarbons."

