

NUCLEOPHILIC REACTIVITY  
TOWARDS ELECTRON-DEFICIENT NITROGEN

by

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ABSTRACT

A general survey of recent developments in the field of nucleophilic reactivity towards some familiar organic electron-deficient centres is presented and the chemistry of the three electron-deficient N-centres investigated is reviewed. A new scale of relative nucleophilicities of various substrates towards the electron-deficient N-centre of O-(2,4-dinitrophenyl)-hydroxylamine is given and explained in terms of Pearson's HSAB principle and the polarizability factor of Edwards and Pearson. The steric environment about the N-atom is found to be less congested than that of comparable carbon compounds. The relative nucleophilicities of substrates towards the hydroxylamine are compared with those towards peroxide oxygen, sulphenyl sulphur and  $I^+$  species.

The order of relative nucleophilicities of various substrates towards the nitroso group of alkyl nitrites is found to be similar to that for the nitrous acidium ion and is explained in terms of a dependence on both basicity and polarizability factors.

The facile reactions of 2,3,3-triethyl oxaziridine with selenocyanate is explained as a moderately soft N-centre in the light of the HSAB principle. The products of the acid hydrolysis of 2-benzyl-3,3-diethyloxaziridine are investigated. The formation of aniline by the acid-catalysed pathway and that of benzaldehyde by both the acid and the base-catalysed pathways is explained.

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PART 1

INTRODUCTION

## CHAPTER I

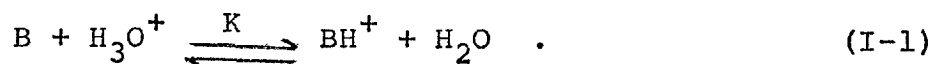
### General Introduction

The question of 'nucleophilic reactivity' towards various electron-deficient centres has long captured the interest of chemists and shall, no doubt, continue to do until an effective quantitative explanation is forthcoming.

Right from Lapworth's<sup>1</sup> so called 'cationoid' and 'anionoid' reagents and Ingold's<sup>2</sup> 'electrophiles' and 'nucleophiles' and recent attempts to correlate reactivity with various linear free-energy relationships, a considerable amount of data has accumulated, much of which has yet to be completely understood.

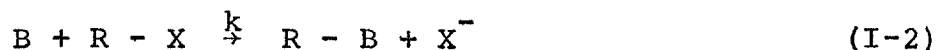
The chemical world transacts in terms of electrons and 'reagents which act by donating their electrons to, or sharing them with a foreign atomic nucleus' were termed nucleophiles by Ingold<sup>2</sup>. This definition has been modified subsequently as a reagent which supplies electrons to form a new bond between itself and another atom<sup>3</sup>. According to Hudson<sup>4</sup>, 'nucleophilic reactivity' (or nucleophilicity) represents the reactivity of an electron donor in an organic displacement reaction. Ingold<sup>2</sup> regarded basicity (that is, affinity for a hydrogen nucleus) as a special manifestation of nucleophilic character or 'nucleophilicity' and nowadays the term 'nucleophilic' usually refers to rate processes, whereas 'basicity' refers to equilibrium protonation<sup>5</sup>.

Thus,



The equilibrium constant K in eqn. (I-1) is a measure of the basicity of the species B, whereas the constant k, in

the displacement reaction, eqn. (I-2),



is a measure of the nucleophilic reactivity of B. The larger the value of k, the greater is the nucleophilic strength<sup>6</sup> of B.

The existence of a parallelism between basicity and nucleophilic reactivity seems logical.

#### Nucleophilicity Parallels Basicity

Smith<sup>7</sup> studied the nucleophilic reactivities of some 32 different anionic nucleophiles (all oxygen bases) towards chloroacetate ion and observed a correlation between basicity and rate. An excellent correlation between basicity and rate was also reported<sup>8</sup> by Ibne-Rasa and Edwards for the reaction of various p-substituted anilines with peracetic acid. Gold and Jefferson<sup>9</sup> found a fairly good correlation between basicity and rate for the pyridine base catalysed hydrolysis of acetic anhydride. Jencks and Carriuolo<sup>10</sup> also reported a reasonable correlation between basicity and rate for their studies of catalysed p-nitrophenylacetate hydrolysis. Bruice and Lapinski<sup>11</sup> also stressed the importance of basicity. Zook and Miller<sup>12</sup> observed that nucleophilicity increased with basicity in some enolate reactions.

Ciuffarin et al<sup>13</sup> studied the reactions of p-nitrophenyl-triphenylmethanesulphenate with a variety of amine nucleophiles in 45% dioxan-water and observed the large effect of basicity of the nucleophile on the reaction rate. Ueno<sup>14</sup> and his colleagues studied the reactions of 2-methylimino (IVa), 2-phenylimino-1, 3-dithiolane (IVb), S-S'-dimethyl-N-methyl (Va) and S-S'-dimethyl-N-phenyliminodithiocarbonate (Vb) and

found that the nucleophilic reactivities of iminodithiocarbonates decreased in the order IVa > IVb > Va > Vb and that this order was almost in agreement with that of the basicities of the imino groups.

Biggi and Pietra<sup>15</sup> in their studies of 2,4-dinitrochlorobenzene with various amines in 3:2 dioxan-water at 25.4°C reported the existence of a correlation between rate and basicity for nucleophiles of the same type.

These are some of the straightforward observations where nucleophilicity parallels basicity, however lots of contradictory and apparently puzzling observations also exist in the literature necessitating greater insight into the subject.

#### Nucleophilicity does not Parallel Basicity

Inorganic halides, for example, do not follow their basicity order in reactions in aqueous solutions. Smith<sup>7</sup> observed that the reactivity of sulphite ( $\text{SO}_3^{-2}$ ) and thiosulphate ( $\text{S}_2\text{O}_3^{-2}$ ) was far greater than their basicities would suggest. Swain and Scott<sup>5</sup> reported the striking reactivities of some feebly basic anions containing elements below the first row of the Periodic Table, such as  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{SCN}^-$ ,  $\text{S}_2\text{O}_3^{-2}$ ,  $\text{HPSO}_3^{-2}$  etc. Also, the anions of the nitroalkanes and carbanions of  $\beta$ -diketones are less reactive than their basicities would suggest<sup>3</sup>. Bartlett and Small<sup>16</sup> reported the lack of basicity order in the case of entering nucleophiles such as  $\text{OAc}^-$ ,  $\text{Cl}^-$ ,  $\text{Br}^-$ ,  $\text{I}^-$ ,  $\text{SCN}^-$ ,  $\text{S}_2\text{O}_3^{-2}$ ,  $\text{OH}^-$  toward  $\beta$ -propiolactone. Ritchie<sup>17</sup> also reported that towards the triaryl-methylation, azide and methoxide ions reacted faster than the cyanide ion, although the latter was more basic and more polarizable.

Aniline has been reported<sup>15</sup> to react much more rapidly in aromatic nucleophilic substitution than a primary aliphatic amine of similar pKa. Towards acetic anhydride, nitrite ion reacts some 93 times faster than acetate ion whereas both ions show nearly equal reactivity towards p-nitrophenylacetate. Similarly toward ethylchloroformate, nitrite ion is about 140 times more reactive than fluoride but surprisingly they show equal reactivity towards p-nitrophenylacetate<sup>18</sup>.

Laidler and Hinshelwood<sup>19</sup> found that triethylamine was about 26 times more nucleophilic than pyridine toward methyl iodide, but about 6 times less nucleophilic towards isopropyl iodide in benzene solution. Pearson<sup>20</sup> and his co-workers reported that thiourea was about twenty eight times more nucleophilic than pyridine toward alkyl bromides. Surprisingly the nucleophiles showed very similar reactivities toward mustard cation<sup>21</sup>.

Hydroxide ion seemed to be less reactive than chloride ion or even water towards ethylene oxide and also appeared to be unreactive in the Scotten-Baumann procedure for acylation<sup>5</sup>, but, toward  $\beta$ -chloroethylethylenesulphonium ion<sup>22</sup> and triphenylcarbonium ion<sup>23</sup> the hydroxide ion was found to be more reactive than water, chloride ion or aniline. Thiourea and iodide, though reported to be very reactive nucleophiles, showed little reactivity toward p-nitrophenylacetate<sup>10</sup>.

Zoltewicz and Jacobson<sup>24</sup> found that pyridazine and phthalazine showed 12 fold rate enhancement toward 2,4-dinitrophenylacetate whereas pyrimidine and pyrazine did not. Enhanced reactivities were also reported for hypochlorite ion ( $\text{ClO}^-$ ), perhydroxyl ion ( $\text{HO}_2^-$ ), hydroxylamine ( $\text{NH}_2\text{OH}$ ), azide ( $\text{N}_3^-$ ) and 4-aminopyridine-1-oxide<sup>10,25</sup> relative to their basicities.

Also hydroxylamine and hydrazine were reported to be more reactive by factors of 4000 and 316 respectively than alkylamines of the same basicity<sup>18</sup>.

A very great challenge was, therefore, presented to chemists to account for all these observations and to correlate the rates and reactivities of the various nucleophiles.

## I.1 Correlation of Nucleophilic Reactivity

### I.1.1 Swain and Scott Correlation

It was soon realised that basicities alone could not always predict the relative nucleophilicities of reagents and other empirical criteria have to be found. The first quantitative correlation of relative rates came from Swain and Scott<sup>5</sup>. They suggested that for S<sub>N</sub>2 reactions, the nucleophilicity towards a standard substrate (methylbromide) could be used to predict the relative nucleophilicity toward other substrates. The linear free-energy relationship they suggested was

$$\log \left( \frac{k}{k_0} \right) = sn + s'e \quad (\text{I-3})$$

where  $n$  is a measure of the nucleophilic reactivity of the reagent,  $e$  measures the electrophilic reactivity of the reagent and  $s$  and  $s'$  are the substrate constants measuring its discrimination towards electrophilic and nucleophilic reagents. They defined  $n = 0$ ,  $e = 0$  for water and, assuming  $s'e$  to be negligible compared to  $sn$ , eqn. (I-3) reduced to

$$\log \left( \frac{k}{k_0} \right) = sn \quad (\text{I-4})$$

They also suggested that when the nucleophile and the substrate were fixed, the eqn. (I-3) could be transformed easily to represent the Brønsted Catalysis Law<sup>26</sup> for acids and bases and the Grunwald-Winstein Correlation<sup>27</sup> for solvolysis rates. Swain et al defined  $\rho = 1$  for methylbromide, thereby reducing eqn. (I-4) to (I-5)

$$\log \left( \frac{k}{k_0} \right) = n \quad (I-5)$$

where  $k_0$  is the rate constant for reaction in water and  $k$  the corresponding rate constant for any specific nucleophile.  $\log \left( \frac{k}{k_0} \right)$ , therefore, represents quantitatively the nucleophilicity of the reagent. They determined the ratio  $\log \left( \frac{k}{k_0} \right)$  for  $N_3^-$ ,  $OH^-$ ,  $I^-$ ,  $S_2O_3^{2-}$  and aniline with methylbromide at 25°C in aqueous solutions and evaluated  $n$  values from eqn. (I-5). Further, they determined  $\log \left( \frac{k}{k_0} \right)$  values for other substrates which were used as secondary standards to evaluate  $n$  values for more nucleophiles. They were satisfied that their correlation held good for 47 reactions (11 new and 36 from the literature) of various nucleophiles with a variety of organic substrates.

Later, Ibne-Rasa<sup>6</sup> pointed out that, of the nine substrates studied, six (ethyltosylate, benzylchloride, epichlorohydrin, glycidol, mustard cation and methylbromide) had tetrahedral carbon as their electrophilic centres. Only one (benzoyl chloride) had a  $sp^2$  carbon as its electrophilic centre. In benzene sulphonyl chloride the electrophilic centre was sulphur and in  $\beta$ -propiolactone, nucleophilic attack could have taken place either on a  $sp^2$  or a  $sp^3$  carbon. Ibne-Rasa<sup>6</sup> criticized the fact that the substrates studied by Swain et al

lacked diversity and in the case of the sulphur substrate that the data were really insufficient for a logical conclusion.

Subsequently Koskikallio<sup>28</sup> found that it was not possible to obtain a single set of nucleophilicity constants which would give a good fit of the Swain-Scott eqn. to rates of reactions involving both non-basic and basic nucleophiles and proposed the following linear free energy relationship eqn. (I-6)

$$\log k = a pK_a + b + \Delta b \quad (\text{I-6})$$

where  $k$  is the second order rate constant for the nucleophile in water,  $K_a$  is the acid constant of the conjugate acid of the nucleophile and  $b = 0$  for basic anionic nucleophiles containing oxygen as the nucleophilic atom. The constant,  $a$ , measures the sensitivity of the reaction to the basicity of the nucleophile and  $\Delta b$  is the sensitivity of the reaction to a change from oxygen to some other nucleophilic atom such as nitrogen or sulphur.

#### I.1.2 Edwards Double Basicity Scale

In order to eliminate the limitations of the Swain-Scott correlation and to explain several discrepancies, Edwards<sup>21</sup> proposed his famous equation incorporating a relationship between electrode potential and nucleophilic character<sup>29</sup>.

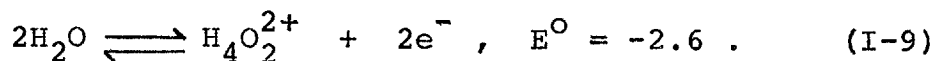
$$\log \left( \frac{K}{K_O} \right) = \alpha E_n + \beta H \quad (\text{I-7})$$

where  $K/K_O$  is a relative (to water) rate or equilibrium

constant ratio,  $E_n$  is a nucleophilic constant characteristic of the electron donor,  $H$  is the relative basicity of the donor towards a proton and  $\alpha$  and  $\beta$  are substrate constants which measure the sensitivity of the substrate to changes in  $E_n$  and  $H$  respectively. By definition,  $H = pK_a + 1.74$ , where  $K_a$  is the ionization constant of the conjugate acid of the nucleophile in water at 25°C and 1.74 is a correction term for the  $pK_a$  of  $H_3O^+$ . The term  $E_n$  is the standard electrode potential of the reagent  $X^-$  in the equilibrium reaction



relative to that of water in the similar equilibrium



$E_n$  is then defined by

$$E_n = E^0 + 2.6. \quad (I-10)$$

This eqn. (I-7), which encompasses two very important properties of the nucleophile, viz. the electron polarizability and basicity, appeared to be of general applicability.

The Edwards relationship or the 'oxi-base scale' has been widely applied. Very recently Baciocchi and Lillocci<sup>30</sup> showed it could be applied to the dehalogenation of 1-chloro-2-iodo-1,2-diphenylethane induced by a variety of nucleophiles. Behrman<sup>31</sup> and his colleagues also reported that the nucleophilic reactivity of some peroxyanions could be expressed in

terms of the Edwards equation.

One great advantage of the oxibase scale is that once the two substrate constants  $\alpha$  and  $\beta$  have been determined from the rate data, the rate of any number of nucleophiles, for which  $E_n$  and  $H$  are known, can be calculated. However, Edwards soon realised that, in several cases,  $\beta$  was negative which indicated that the  $E_n$  term included a significant contribution from basicity which, therefore, did not appear solely in the  $H$  term. He therefore modified<sup>32</sup> his equation by taking into account the fact that the tendency of a nucleophile to be oxidised was dependent on both its polarizability and basicity. He redefined  $E_n$  as

$$E_n = aP + bH \quad (I-11)$$

where  $a$  and  $b$  were constants having values 3.6 and 0.0624 respectively,  $P$  was a measure

$$P \equiv \log \left( \frac{R_\infty}{R_{H_2O}} \right) \quad (I-12)$$

of the polarizability of the nucleophile relative to that of water as in eqn. (I-12) and  $R$  represented the molar reactivity at infinite wavelength. Substitution of eqn. (I-11) in (I-7) resulted in

$$\log \left( \frac{K}{K_O} \right) = AP + BH \quad (I-13)$$

where  $A = \alpha a$  and  $B = \beta + \alpha b$ . The substrate basicity constant was  $B$ . The  $E_n$  values of some nucleophiles (e.g.  $F^-$ ,  $H_2O$ ,  $Cl^-$ ,  $Br^-$ ,  $I^-$ ,  $OH^-$  etc.) were calculated using the relation

(I-11) and found to be in good agreement with those based on electrode potential data and the B value became positive for most cases in contrast to the previous negative  $\beta$  values.

## I.2 Factors Determining Nucleophilic Reactivities

Edwards and Pearson<sup>33</sup> suggested three important factors determining nucleophilic reactivities. These are basicity, polarizability and the presence of unshared pair of electrons on the atom adjacent to the nucleophilic atom which they preferred to call the ' $\alpha$ -effect'. These factors are explained below.

### I.2.1 Basicity

Since bases are electron pair donors and the term basicity represents the ease of donation of that pair and displacement reactions are generalised acid-base reactions, it is understandable that basicity be an important factor. Indeed, in some reactions, it alone explains the reactivity order as already mentioned. According to Edwards and Pearson<sup>33</sup>, a high positive charge on the substrate in the transition state leads to a strong interaction with the high negative potential of basic nucleophiles. This lowers the energy of the activated complex and causes a high rate of reaction. The basicity should therefore be an increasingly important factor in the rate of substitution as the positive charge on the electrophilic atom in the substrate increases. The coefficient  $\beta$  in the Edwards eqn. increases with increasing charge on the substrate. They further suggested that for a substantial lowering of the energy to occur by electrostatic effects, it

was necessary that either the positive charge be situated in the region of negative potential or the negative charge be situated in the region of positive potential. However, in the case of the nucleophilic atom containing too many electrons, repulsion of electrons between the nucleophilic atom and the atom undergoing nucleophilic attack will raise the energy rapidly as the reactants approach, thus destroying the basicity effect of the nucleophile.

### I.2.2 Polarizability

In the case of elements of the second, third and subsequent rows of the Periodic Table, the nucleus of the atom concerned exerts little control on the electrons of the outermost orbital. As a result, these electrons become polarized toward electron deficient centres. Edwards and Pearson considered two factors to be important. The first was the polarization of the bonding electrons of the nucleophile towards the electrophilic centre of the substrate. The second was the polarization of the non-bonding electrons of the nucleophile away from the electrophilic atom of the substrate thus reducing the electrostatic repulsion between the centres involved. Generally, basicity and polarizability do not go together but in sulphide ion ( $S^{-2}$ ) for example, both these properties are present.

In the light of the above discussion, one can understand why polarizable molecules like thiourea, thiocyanate, iodide etc. should be strikingly reactive. In the case of iodide, for example, (in the bimolecular transition state) because of the polarizability, the electron density need not correspond to the location of the nucleus<sup>34</sup>, thereby reducing the Pauli

repulsion and enhancing reactivity. This is not possible in <sup>the</sup> case of non-polarizable species like hydroxyl and fluoride ions. Biggi and Pietra<sup>15</sup> regarded the high reactivity of thiophenoxide ion towards 2,4-dinitro chlorobenzene as a measure of polarizability.

### I.2.3 Alpha Effect

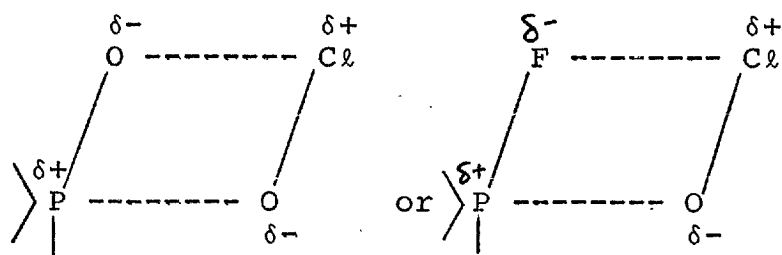
Edwards and Pearson defined the  $\alpha$ -effect as the effect of the presence of an unshared pair(s) of electrons on the atom  $\alpha$ - to the nucleophilic atom.

Since the discovery of this effect in the early sixties, many citations have appeared in the literature. For example, the  $\alpha$ -effect was observed by Zoltewicz et al<sup>24</sup> in the case of pyridazine and phthalazine towards 2,4-dinitrophenylacetate. Pearson and Edington<sup>35</sup> showed that perhydroxyl ion is about 34 times more reactive towards benzylbromide in 50% acetone-water at 25°C than the hydroxide ion. Fedor and Bruice<sup>36</sup> observed a large  $\alpha$ -effect in the methoxylamine catalysed hydrolysis of ethyl trifluorothiolacetate. Bell<sup>37</sup> observed a large  $\alpha$ -effect even in the general base catalysed dehydration of acetaldehydehydrate.

Epstein et al<sup>25</sup> reported a high reactivity of hypochlorite towards isopropylmethylphosphonofluoridate (sarin). Jencks and Carriuolo<sup>10</sup> also observed high reactivity for some  $\alpha$ -nucleophiles like  $\text{NH}_2\text{NH}_2$ ,  $\text{MeOO}^-$ ,  $\text{ClO}^-$ , N-hydroxyphthalimide. Ibne-Rasa and Edwards<sup>8</sup> observed a greater nucleophilic reactivity of N-phenyl hydroxylamine toward peroxy acetic acid. Jencks and Gilchrist<sup>38</sup> also observed high reactivity in the case of perhydroxylion toward four different substrates. McIsaac et al<sup>31</sup> studied the effect of the  $\alpha$ -nucleophile, perhydroxyl ion

towards  $\alpha$ -bromo-p-toluic acid and bromoacetic acid and found perhydroxyl ion to be about 13 times more reactive in each case than the hydroxide ion. In a series of phenylacetates, the  $\alpha$ -effect was greatest for p-nitrophenyl acetate and smallest for p-methoxy phenylacetate<sup>39</sup>. The high reactivity of the perhydroxyl ion towards benzonitrile in 50% acetone (hydroperoxide, over  $10^4$  times as fast as that of the hydroxide ion) was also reported by Wiberg<sup>40</sup>. Jencks<sup>41</sup> observed high reactivity of  $H_2O_2$  toward p-nitro phenyl acetate.

Several attempts were made to explain the high reactivity of the  $\alpha$ -nucleophiles. Long before the discovery of the  $\alpha$ -effect, Epstein<sup>25</sup> et al believed that the unusual reactivity of hypochlorite towards sarin was due to bifunctional catalytic attack, i.e. the oxygen of the hypochlorite attacking the phosphorus atom and the positive chlorine attacking the phosphoryl oxygen (or the fluorine) thereby inducing polarization and aiding in displacement. They depicted the transition state as in Scheme (I-1).

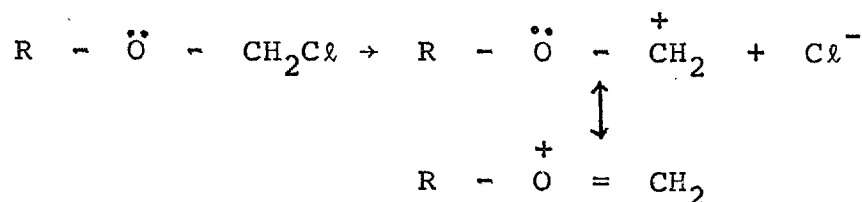


Scheme (I-1) Proposed transition state (bifunctional attack)  
in reaction between sarin and hypochlorite

From the effective Vander Waal's radii, the bond lengths of the participating groups and the spectral studies of the

various organic phosphorus compounds, their postulation seems to be reasonable.

Jencks<sup>10</sup> et al tried to explain the high reactivity of some hydroperoxides by assuming that the transition state was stabilized by hydrogen-bonding. Edwards and Pearson<sup>33</sup> attributed the high reactivity to the stabilization of the activated complex. According to them, in a displacement reaction, a pair of electrons tends to leave the nucleophilic atom in the activated complex. The presence of a pair of electrons on the adjacent atom then stabilizes the positive charge on the nucleophilic atom. The stabilization of the carbonium ion derived from an  $\alpha$ -halo ether would serve as an example (Scheme I-2).



Scheme (I-2) Stabilization of the carbonium ion derived from  $\alpha$ -haloether by the lone pair of electrons on the adjacent atom

Ibne-Rasa and Edwards<sup>8</sup> attributed the  $\alpha$ -effect to ground state destabilization. The electrostatic repulsion between the electrons on the nucleophilic atom and those on the  $\alpha$ -atom raise the energy of the ground state, while in the transition state, because of the denuded nature of the nucleophilic atom, this repulsion is considerably minimised.

Aubort and Hudson<sup>42</sup> put forward an explanation from the

M.O. point of view. They suggested that reactions involving an  $\alpha$ -nucleophile are accompanied by a decrease in  $p\pi - p\pi$  repulsion, since one of these orbitals forms a  $\sigma$ -bond, and  $p\pi - \sigma$  orbital interactions are generally of lower energy than  $p\pi - p\pi$  interactions. Also, the magnitude of the  $\alpha$ -effect is determined by the conformation of the nucleophilic species. They divided  $\alpha$ -nucleophiles into two types. In type one,  $p\pi - p\pi$  overlap is considerable in the ground state and, as a result, the  $\alpha$  nucleophiles, such as  $ROO^-$ ,  $ClO^-$ ,  $RSS^-$  would show enhanced reactivity. In type two, where the conformation of the  $\alpha$ -nucleophiles is such as to minimise the  $p\pi - p\pi$  (or  $sp^3 - sp^3$ ) repulsion in the ground state, there is no  $\alpha$ -effect due to electron repulsion. Therefore, the enhanced reactivity exhibited by  $NH_2OH$ ,  $NH_2NH_2$  etc. is due to some other factors such as intramolecular catalysis.

Klopman<sup>43</sup> et al, who preferred to call  $\alpha$ -nucleophiles 'supernucleophiles', assumed the enhanced reactivity to result from an orbital splitting that raised the energy of the highest filled orbital of the nucleophile and increased the 'frontier controlling effect'. They further suggested that for a reagent to be able to display its 'supernucleophilicity', it has to participate extensively in the rate determining step. Accordingly, substrates bearing a good leaving group (i.e. where formation of a new bond is energetically critical) should exhibit a large  $\alpha$ -effect. Otherwise, only small  $\alpha$ -effect should be exhibited.

Klopman<sup>43</sup> et al re-examined the application of the Edwards equation to the  $\alpha$ -nucleophiles and suggested that for a particular substrate to experience enhanced reactivity the ratio of the Edwards parameters,  $\alpha/\beta$ , must be large and  $\beta$  must be sizable.

McIsaac<sup>31</sup> et al observed that for different substrates,  $\log \frac{k_{\text{HO}_2^-}}{k_{\text{OH}^-}}$  vs.  $|\alpha\beta|$  was linear. Their data further showed an increase in the ratio  $\frac{k_{\text{HO}_2^-}}{k_{\text{OH}^-}}$  in the progression from  $\text{sp}^3$  to  $\text{sp}^2$  to  $\text{sp}$  carbon.

Dixon and Bruice<sup>44</sup> attempted to relate the Brønsted  $\beta$  value to the  $\alpha$ -effect. They suggested that a large amount of bond formation was essential for the stability of the transition state. They concluded that reactions exhibiting large Brønsted  $\beta$  value exhibit the  $\alpha$ -effect, whereas those showing small  $\beta$  values, in which the transition state resembles the reactants rather than the products, generally do not. Biggi and Pietra<sup>15</sup> have criticised this explanation and pointed out that, for a clear  $\alpha$ -effect to occur, a transition state structure such as that involved in nucleophilic displacement at a carbonyl carbon is required.

Dixon and Bruice<sup>45</sup>, by employing malachite green as the substrate, have reaffirmed the existence of a relation between the  $\alpha$ -effect and the Brønsted  $\beta$  value, but could not find any such correlation in the case of oxyanions and  $\text{HO}_2^-$ .

Klopman and Hudson<sup>46</sup> and recently Filippini and Hudson<sup>47</sup>, have tried to explain the  $\alpha$ -effect in terms of polyelectronic perturbation treatment and have deduced some semi-theoretical expressions.

### I.3 Hard and Soft Acids and Bases

Pearson<sup>48,49</sup> first proposed the useful principle of 'Hard and soft acids and bases' (HSAB). He defined a soft base as one in which the valence electrons were easily distorted (i.e. polarized or removed) such as  $\text{R}_2\text{S}$ ,  $\text{RSH}$ ,  $\text{RS}^-$ ,  $\text{I}^-$ ,  $\text{SCN}^-$ ,

$S_2O_3^{-2}$ ,  $R_3P$ ,  $R_3As$ ,  $(RO)_3P$ ,  $CN^-$ ,  $RNC$ ,  $SeCN^-$ ,  $H^-$ ,  $R^-$ . A hard base has the opposite properties and is illustrated by  $OH^-$ ,  $F^-$ ,  $CH_3CO_2^-$ ,  $PO_4^{-3}$ ,  $SO_4^{-2}$ ,  $Cl^-$ ,  $RNH_2$ ,  $N_2H_4$ . A hard acid was defined as one of small size with high positive charge and with no valence electrons that were easily distorted or removed, e.g.  $H^+$ ,  $Li^+$ ,  $Mg^{+2}$ ,  $Al^{+3}$ ,  $RSO_2^+$ ,  $SO_3$ ,  $RCO^+$ . A soft acid, on the other hand, is one in which the acceptor atom is of large size, small or zero positive charge or has several valence electrons which are easily distorted or removed, e.g.  $Cu^+$ ,  $Ag^+$ ,  $RS^+$ ,  $RSe^+$ ,  $I^+$ ,  $Br^+$ ,  $HO^+$ ,  $Cl$ ,  $Br$ ,  $I$ ,  $N$ ; bulk metals also were treated as soft acids.

According to Pearson, hard acids preferred to coordinate with hard bases and soft acids with soft bases. The underlying theories<sup>50</sup> and applications<sup>51</sup> of the principle have been discussed by Pearson. Hudson<sup>52,53</sup> applied the principle to many 'ambident',<sup>54</sup> nucleophiles in Organic and Organo-Phosphorus chemistry.

Pearson<sup>48</sup> further classified solvents in terms of their hardness or softness. He treated solvents viz  $HF$ ,  $H_2O$  and hydroxylic solvents as hard solvents and as such they should strongly solvate hard bases like  $F^-$ ,  $OH^-$  and other oxygenanions. A variety of dipolar aprotic solvents, such as dimethylsulphoxide, dimethylformamide, sulfolane, nitroparaffins and acetone, were regarded as soft acid solvents. These, he suggested, would have a mild preference for solvating large anions. Hard solvents will tend to level basicity while soft solvents will not. The HSAB principle seems to be very promising.

#### I.4 Reference Substrates

Pearson and co-workers<sup>55</sup> suggested the use of  $\text{Pt}(\square)$ , a very soft electrophilic centre and the tetrahedral carbon in methyl iodide, a moderately soft electrophilic centre as reference substrates. They studied the nucleophilic reactivities of a wide range of nucleophiles toward both trans  $\{\text{Pt}(\text{py})_2\text{Cl}_2\}$  and  $\text{MeI}$  in methanol at  $25^\circ\text{C}$  and defined the nucleophilic reactivity constants,  $n_{\text{pt}}$  and  $n_{\text{MeI}}$  as the logarithm of the ratio of the second order rate constant of the nucleophile and the second order rate constant for the solvolysis in methanol. Thus for a nucleophile, Nu,

$$n_{\text{pt}} = \log \left( \frac{k_{\text{Nu}}}{k_{\text{MeOH}}} \right) \quad (\text{I-14})$$

and

$$n_{\text{MeI}} = \log \left( \frac{k_{\text{Nu}}}{k_{\text{MeOH}}} \right) \quad (\text{I-15})$$

$n_{\text{pt}}$  and  $n_{\text{MeI}}$  were defined as in eqns. (I-14) and (I-15) respectively.

There existed no correlation between  $n_{\text{pt}}$  and  $n_{\text{MeI}}$  and no relation between the  $n_{\text{pt}}$  and the strength of the nucleophile as a proton base. However, there are indications that proton basicity has more effect on rates with methyl iodide than with the  $\text{Pt}(\square)$  complex. Belluco<sup>56</sup> et al also recommended the use of  $\text{Pt}(\square)$  as a reference substrate and their nucleophilic constants  $n_{\text{pt}}^{\circ}$  were in good agreement with those of Pearson<sup>55</sup> and his co-workers.

Another series of  $n_{\text{pt}}^{\circ}$  values was calculated by Gaylor and Senoff<sup>57</sup> and regarded as an overall relative measure of the nucleophilicity of organic sulphides of the type

$\text{XC}_6\text{H}_4\text{-S-C}_6\text{H}_4\text{X}$ , towards trans- $\{\text{Pt}(\text{py})_2\text{Cl}_2\}$  in methanol.

A correlation involving cation-nucleophile reactions by Ritchie<sup>17</sup> is available. The data have been obtained from the reactions of crystal violet, malachite green, a wide range of substituted aryl diazonium ions, tropylium ion, phenyltropylium ion, p-chlorophenyltropylium ion and p-dimethylaminophenyltropylium ions with nucleophiles. The nucleophilic constant  $N^+$  has been defined as

$$\log \left( \frac{k_N}{k_{\text{H}_2\text{O}}} \right) = N^+ \quad (\text{I-16})$$

where  $k_N$  is the rate constant for the reactions of a cation with a given nucleophilic system,  $k_{\text{H}_2\text{O}}$  is the rate constant for the reactions of the same cation with water in water, and  $N^+$  is a parameter characteristic of the nucleophilic system and independent of the cation.

### I.5 Influence of Solvent

Solvent has a great influence on the relative reactivities of nucleophiles. Ritchie<sup>17</sup> suggested that when reactions in different solvents were considered, the correlations of Swain-Scott and Edwards were bound to fail. Acid dissociation constants of a variety of acids in methanol, DMF, DMSO have been measured by Parker et al<sup>58</sup> and it was found that the acid-base equilibrium was strongly influenced by transfer from a dipolar aprotic to protic solvents. Parker<sup>59</sup> previously pointed out that small negative particles (e.g.  $\text{OH}^-$ ,  $\text{F}^-$  etc.) were strongly solvated by protic solvents (by ion-dipole interactions and by hydrogen bonding). A polar solvent reduces

the nucleophilic reactivity of a highly solvated ion more than that of a weakly solvated one. Hudson<sup>4</sup> suggested therefore that the nucleophilic order might change with change of solvent.

The data of Fuchs<sup>60</sup> et al showed the reactivity order of methyltosylate in methanol to be  $\text{N}_3^- > \text{I}^- > \text{SCN}^- > \text{Br}^- > \text{Cl}^-$ ; whereas that of propyltosylate in DMSO was  $\text{S}_2\text{O}_3^{2-} > \text{OH}^- \sim \text{MeO}^- \sim \text{F}^- > \text{PhO}^- > \text{N}_3^- > \text{Cl}^- > \text{Br}^- > \text{I}^- > \text{SCN}^-$ . A change of order in the case of halides and thiocyanate is noticeable.

Winstein<sup>61</sup> and co-workers also claimed the reactivity order  $\text{Cl}^- > \text{Br}^- > \text{I}^-$  for nucleophilic substitution in acetone.

Kice<sup>62</sup> et al reported a change in the order of nucleophilic reactivity towards sulphenyl sulphur when going from a protic to a dipolar aprotic solvent. The order of reactivity in 60% dioxan was shown to be  $\text{I}^- > \text{SCN}^- \gg \text{Br}^- \gg \text{Cl}^-$  whereas in acetone the observed order was almost reversed  $\text{Cl}^- > \text{Br}^- > \text{I}^- > \text{SCN}^-$ .

Miller and Parker<sup>63</sup> reported that rate constants for reactions in dipolar aprotic solvents were approximately  $10^5$  times greater than for reactions in protic solvents.

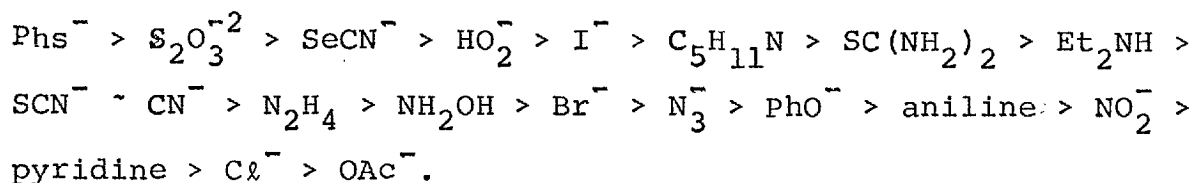
As far as reactivities towards soft electrophilic centres are concerned, Belluco et al<sup>56</sup> suggest that the relative nucleophilic reactivity remains unchanged regardless of the nature of the solvent.

## I.6 Orders of Nucleophilic Character

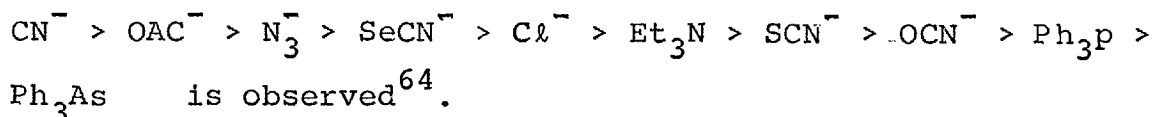
### I.6.1 Saturated Carbon

Saturated carbon centres have been the subject of intense studies and, as a result, much data are available. Pearson

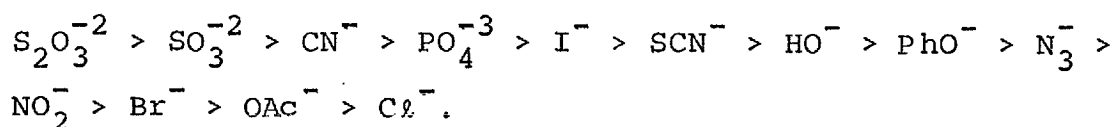
et al<sup>55</sup> consider methyl iodide as a moderately soft electrophilic centre and the relative order of nucleophilicities of various reagents is:-



A similar order is found for methyl bromide<sup>5</sup>. In MeCN solvent, however, a changed reactivity order:



Koskikallio<sup>28</sup> reported the following reactivity order towards methylperchlorate in water at 25°C.

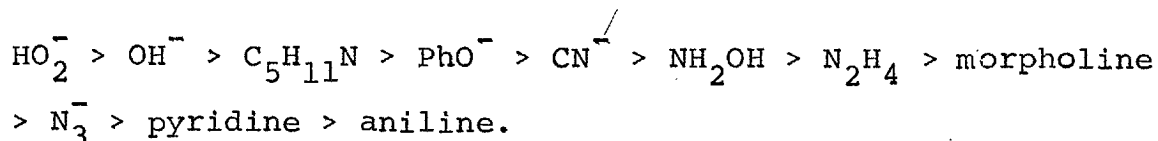


Other interesting reactivity orders (mostly pre-1963) can be found in the review of Bunnett<sup>3</sup>.

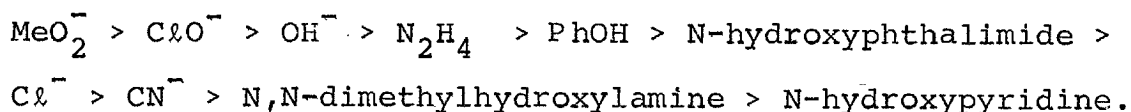
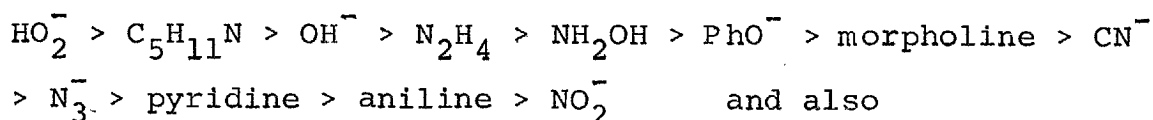
### I.6.2 Carbonyl Carbon

As a result of the polarization of the bond towards oxygen in carbonyl carbon, the electrophilic centre resembles the proton in having a high positive charge density and the basicity of the reagent is therefore of overriding importance. This is evident from several results. Thus Jencks and Gilchrist<sup>38</sup> observed the following reactivity order towards

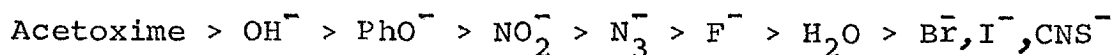
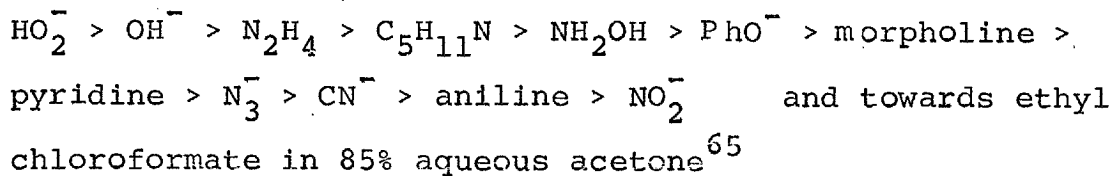
phenyl acetate in water at 25°C:-



Towards p-nitrophenyl acetate, however, the observed order changed slightly<sup>10,38</sup>, i.e.



Towards 1-acetoxy-4-methoxy-pyridinium perchlorate the observed order was<sup>38</sup>:-

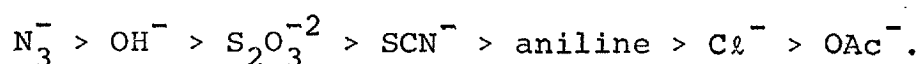


was observed. Thus nucleophilic reactivity primarily depends on basicity in the case of carbonyl carbon, although other factors (e.g. α-effect) play a part.

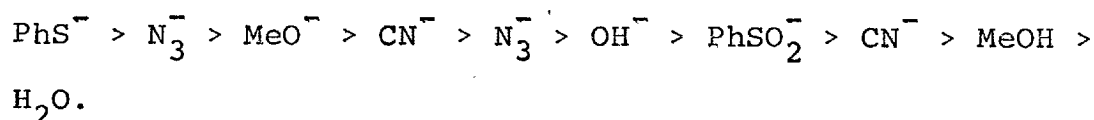
### I.6.3 Carbonium Carbon

In the case of free carbonium ions, basicity should be important as a result of the high positive charge density

but other factors, such as solvation, stability of the transition state and steric factors may also play a part. Swain, Scott and Lohmann<sup>66</sup> studied the reactivities of a variety of nucleophiles towards carbonium ions. They found that anionic nucleophiles were more reactive than water by factors of  $10^3$  to  $10^5$  towards the triphenyl methyl cation. The relative order was:-

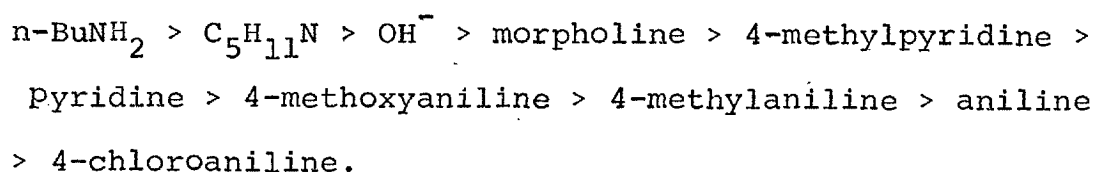


Other results have been obtained from studies with carbonium ions derived from malachite green or similar compounds<sup>17</sup>. In this case, the reactivity order was:-

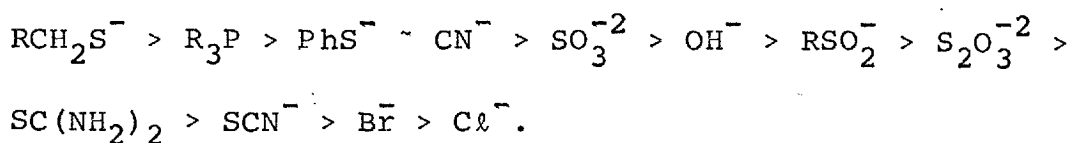


#### I.6.4 Sulphur

Ciuffarin<sup>13</sup> et al observed the following nucleophilic order toward p-nitrophenyltriphenylmethanesulphenate in 45% dioxan-water.



Also Parker and Kharasch<sup>67</sup> in their review of the breaking of the sulphur-sulphur bond suggest the order



Edwards and Pearson considered that nucleophilic attack on bivalent sulphur depended on both polarizability and basicity. Much information about sulphur electrophilic centres comes from the excellent work of Kice<sup>68,69</sup> et al, some of whose results are presented in Table (I-1) (I-2) and (I-3) below.

(TABLE I-1)<sup>68,69</sup>

Relative nucleophilicities ( $k_{\text{Nu}}/k_{\text{Cl}}$ ) of a variety of nucleophiles towards electrophilic sulphur compared with other electrophilic centres

| Nucleophile                       | Sulphenyl Sulphur<br>(-s-s-)<br>$\begin{array}{c} \parallel \\ \text{O} \end{array}$ | Sulphinyl Sulphur<br>$\begin{array}{c} \text{O} \\ \parallel \\ (-\text{s}-\text{s}-) \\ \parallel \parallel \\ \text{O} \text{ O} \end{array}$ | Peroxide<br>(HO <sub>2</sub> <sup>+</sup> H <sub>2</sub> ) | SP <sup>3</sup> Carbon<br>(MeBr) |
|-----------------------------------|--------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|----------------------------------|
| SC(NH <sub>2</sub> ) <sub>2</sub> | .....                                                                                | 2.9 x 10 <sup>2</sup>                                                                                                                           | too fast                                                   | 2.3 x 10 <sup>2</sup>            |
| I <sup>-</sup>                    | 1.4 x 10 <sup>4</sup>                                                                | 83                                                                                                                                              | 2.0 x 10 <sup>5</sup>                                      | 1 x 10 <sup>2</sup>              |
| SCN <sup>-</sup>                  | 5.4 x 10 <sup>3</sup>                                                                | 14                                                                                                                                              | 5.0 x 10 <sup>2</sup>                                      | 54                               |
| Br <sup>-</sup>                   | 35                                                                                   | 5.4                                                                                                                                             | 2.8 x 10 <sup>2</sup>                                      | 7                                |
| Cl <sup>-</sup>                   | (1.0)                                                                                | (1.0)                                                                                                                                           | (1.0)                                                      | (1.0)                            |
| OAc <sup>-</sup>                  | .....                                                                                | 0.75                                                                                                                                            | too slow                                                   | 0.48                             |
| F <sup>-</sup>                    | .....                                                                                | 0.37                                                                                                                                            | .....                                                      | 0.10                             |

Examination of the data [Table (I-1)] reveals that the order of nucleophilic reactivity toward sulphenyl sulphur, sulphinyl sulphur, peroxide oxygen and SP<sup>3</sup> carbon is the same, viz. I<sup>-</sup> > SCN<sup>-</sup> > Br<sup>-</sup> > Cl<sup>-</sup>, but the relative rates suggest that

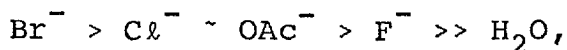
sulphenyl sulphur is much more reactive than sulphinyl sulphur and almost comparable to the peroxide oxygen. However, the reactivity of sulphinyl sulphur is comparable to that of  $SP^3$  carbon. Kice<sup>68</sup> et al, therefore, concluded that sulphenyl sulphur was a softer electrophilic centre than sulphinyl sulphur and comparable in softness with peroxide oxygen.

TABLE (I-2)<sup>70</sup>

Relative nucleophilicities toward sulphinyl vs. sulphonyl sulphur

| Nucleophiles         | Sulphinyl Sulphur<br>$\begin{array}{c} \text{O} \\    \\ (-\text{S}-\text{S}-) \\    \quad    \\ \text{O} \quad \text{O} \end{array}$ | Sulphonyl Sulphur<br>$\begin{array}{c} \text{O} \quad \text{O} \\    \quad    \\ (-\text{S}-\text{S}-) \\    \quad    \\ \text{O} \quad \text{O} \end{array}$ |
|----------------------|---------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| $\text{Br}^-$        | 7.2                                                                                                                                   | 0.0009                                                                                                                                                        |
| $\text{Cl}^-$        | 1.3                                                                                                                                   | 0.0016                                                                                                                                                        |
| $\text{OAc}^-$       | (1.0)                                                                                                                                 | (1.0)                                                                                                                                                         |
| $\text{F}^-$         | 0.49                                                                                                                                  | 59                                                                                                                                                            |
| $\text{H}_2\text{O}$ | $1.1 \times 10^{-5}$                                                                                                                  | $3.0 \times 10^{-5}$                                                                                                                                          |

It is seen from Table (I-2) that toward sulphinyl sulphur the reactivity order is:-



whereas toward sulphonyl sulphur the order is quite different i.e.  $\text{F}^- \gg \text{OAc}^- \gg \text{Cl}^- > \text{Br}^- > \text{H}_2\text{O}$ .

This is in good agreement with the HSAB principle<sup>48,49</sup> which suggests that sulphonyl sulphur is a much harder~~er~~ electrophilic centre than sulphinyl sulphur. Kice<sup>70</sup> et al further compared sulphonyl compounds with carbonyl carbon and their data are reproduced in Table (I-3).

TABLE (I-3)<sup>70</sup>

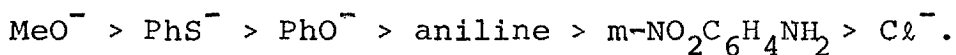
Relative nucleophilicities toward sulphonyl sulphur vs. carbonyl carbon

| Nucleophiles                 | Sulphonyl Sulphur<br>$\begin{array}{c} \text{O} \quad \text{O} \\    \quad    \\ (-\text{S}-\text{S}-) \\    \quad    \\ \text{O} \quad \text{O} \end{array}$ | Carbonyl Carbon<br>$(\text{CH}_3-\text{C}-) \\    \\ \text{O}$ |
|------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------|
| n-BuNH <sub>2</sub>          | 5.9 x 10 <sup>3</sup>                                                                                                                                         | 3.1 x 10 <sup>3</sup>                                          |
| N <sub>3</sub> <sup>-</sup>  | 3.3 x 10 <sup>2</sup>                                                                                                                                         | 3.5 x 10 <sup>2</sup>                                          |
| F <sup>-</sup>               | 59                                                                                                                                                            | 3.3                                                            |
| NO <sub>2</sub> <sup>-</sup> | 10                                                                                                                                                            | 7.7                                                            |
| OAc <sup>-</sup>             | (1.0)                                                                                                                                                         | (1.0)                                                          |
| H <sub>2</sub> O             | 3 x 10 <sup>-5</sup>                                                                                                                                          | 2 x 10 <sup>-4</sup>                                           |

Examination reveals that sulphonyl sulphur is harder than carbonyl carbon, thus lending further weight to the HSAB principle<sup>48,49</sup>.

### I.6.5 Aromatic Carbon

Edwards and Pearson<sup>33</sup> suggest that both polarizability and basicity should be important here too. Bevan and Hirst<sup>71</sup> observed the following order of reactivity towards p-fluoronitrobenzene in MeOH at 25°C:-

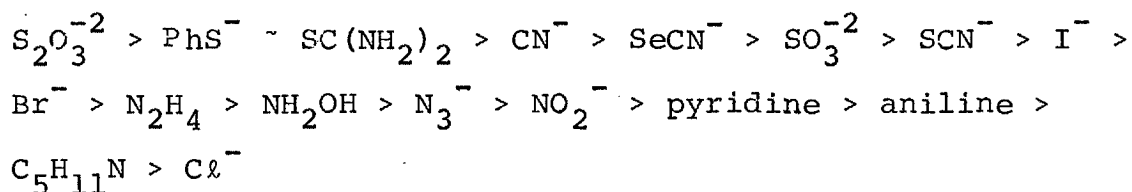


Burnett and Davis<sup>72</sup> reported the order of nucleophilic reactivity towards 2,4-dinitrofluorobenzene in 60% dioxan-water as



### I.6.6 Platinum II

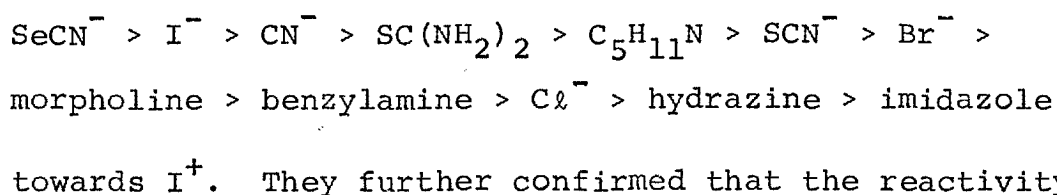
Platinum (II) compounds are very soft electrophilic centres<sup>55</sup> and the HSAB principle suggests that soft nucleophiles should be very reactive. The order of reactivity given by Pearson *et al*<sup>55</sup> and Belluco<sup>73</sup> *et al*



confirms this. As pointed out earlier<sup>56</sup>, the reactivity order in the case of soft electrophilic centres seems to be unaffected by a change of solvent.

### I.6.7 Towards I<sup>+</sup>

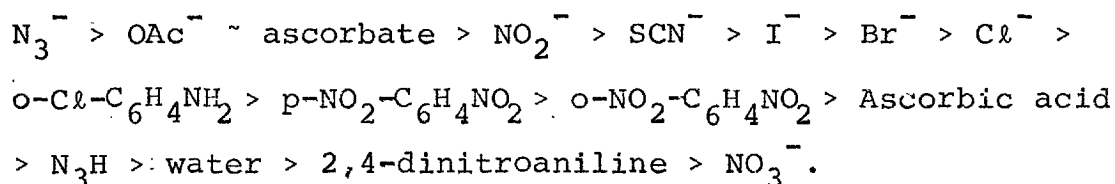
Iodine in erythro-1-chloro-2-iododiphenylethane is a soft electrophilic centre and the HSAB principle holds well. Baciocchi<sup>30</sup> *et al* have reported the following order



order ( $I^- > Br^- > Cl^-$ ) is the same in both methanol and DMF in agreement with the previous claim<sup>56</sup>.

#### I.6.8 Trivalent Nitrogen

Very little data is available about the reactivity of the nitrogen electrophilic centre. Nitrogen in the nitrous acidium ion ( $H_2ONO^+$ ) is expected to be as hard as carbonyl carbon and the basicity, rather than the polarizability of the entering nucleophile ought to be important. Ridd<sup>74</sup> gave the following reactivity sequence towards nitrous acidium ion:-



It is expected that compounds of the type ( $-N\begin{smallmatrix} H \\ \diagup \diagdown \\ H \end{smallmatrix}$ ), in which N is moderately soft, should show a stronger dependence on polarizability factors.

## CHAPTER II

### O-Hydroxylamine Derivatives

Although the N-alkyl and the O-alkyl hydroxylamines have been known for many years, the O-arylhydroxylamines have been prepared only very recently. The synthesis of O-mesitoyl-hydroxylamine by Carpino<sup>75</sup> is about 13 years old.

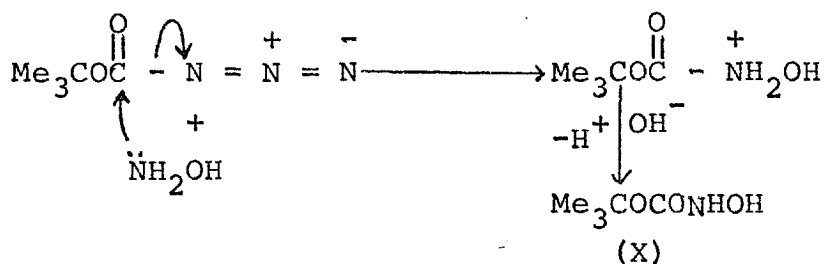
Bumgardner and Lilly<sup>76</sup> claimed the first known synthesis of O-phenylhydroxylamine, by aminating potassium phenoxide with hydroxylamine-O-sulphonic acid. A few months later, Nicholson and Peak<sup>77</sup> modified the synthesis.

The first known synthesis of an N-alkyl-O-arylhydroxylamine was achieved by Sheradsky<sup>78</sup> et al only very recently.

#### II.1 Preparation of O-(2,4-dinitrophenyl)-hydroxylamine

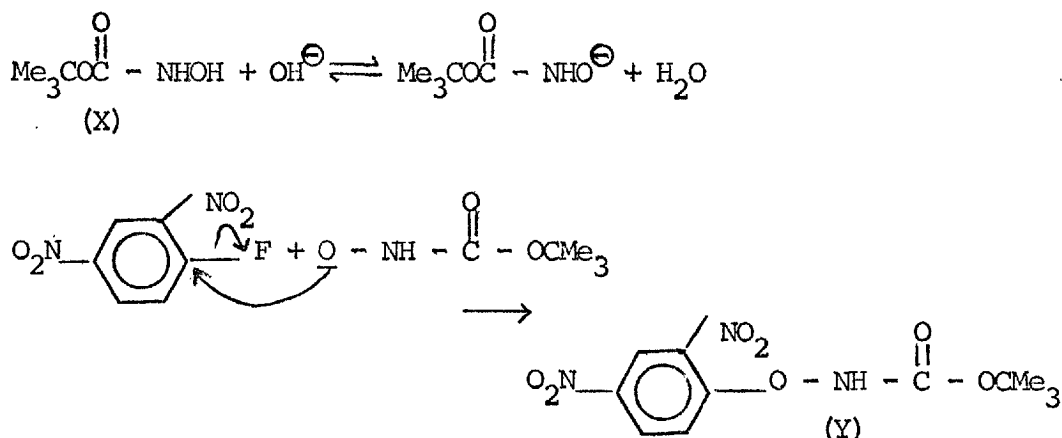
Only an outline of the synthesis is given here. Sheradsky and his colleagues<sup>78</sup> carried out the synthesis by the hydrolytic cleavage of the N-C bond of the corresponding N-aryl-oxy carbamate, by a brief treatment with trifluoroacetic acid.

Conversion of the hydroxylamine to t-butyl-N-hydroxy carbamate (X) was effected by treating hydroxylamine hydrochloride in alkaline solution with t-butyloxy carbonyl azide. This step probably involved nucleophilic attack by the free hydroxylamine on the carbonyl carbon of the azide followed by the loss of a proton as shown in Scheme (II-1).



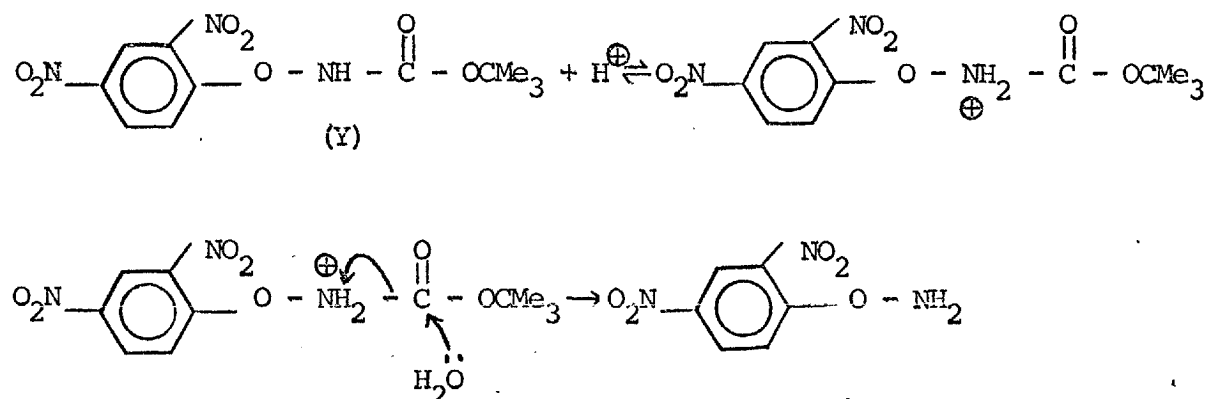
Scheme (II-1) Formation of the t-butyl-N-hydroxy carbamate (X)

Conversion of (X) to the O-(2,4-dinitrophenoxy)-carbamate (Y) was achieved by treatment with 2,4-dinitrofluorobenzene (Scheme II-2).



Scheme (II-2) Preparation of the (nitroaryloxy) carbamate

The final stage was cleavage of the N-C bond; probably via the protonated form (Scheme II-3).



Scheme (II-3) Hydrolytic cleavage of the C-N bond in (Y)

## II.2 Properties of the Hydroxylamine Derivatives

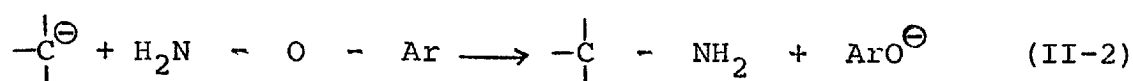
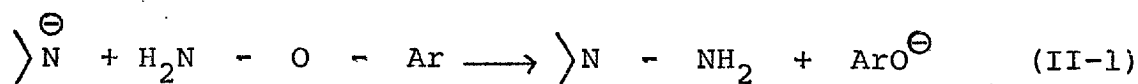
The lower alkylhydroxylamines are volatile substances, liquids or low-melting solids. O-substituted hydroxylamines generally boil at lower temperatures than the N-substituted

derivatives, probably due to the loss of the hydrogen-bonded structure.

The alkyl hydroxylamines and monoaryl hydroxylamines are sufficiently basic to form salts with mineral acids. The O-substituted compounds are weaker bases in comparison with N-substituted isomers<sup>79</sup>.

Most hydroxylamine derivatives are not very stable as free bases, but the O-(nitroaryl)hydroxylamines, which are yellow or orange yellow crystalline solids, are fairly stable.

O-(nitroaryl)-hydroxylamines, particularly O-(2,4-dinitrophenyl)hydroxylamine undergo ready nucleophilic substitution with anionic nitrogen and carbanions in various solvents to form the corresponding hydrazines or amines, respectively, as in eqns. (II-1) and (II-2).



Some typical examples<sup>78,80</sup> are given in Table (II-1). The products formed suggest that nucleophilic attack occurs at the electron-deficient nitrogen of the O-(2,4-dinitrophenyl)-hydroxylamine.

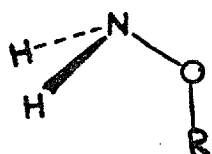
TABLE (II-1)<sup>78,80</sup>

| Nucleophile (anion)                    | Product                                            | Yield % |
|----------------------------------------|----------------------------------------------------|---------|
| Phthalimide                            | N-aminophthalimide                                 | 88      |
| N-tosylbenzylamine                     | 1-benzyl-1-tosyl-hydrazine                         | 93      |
| 2,4-dimethyl-3,5-di-carbethoxy pyrrole | 1-amino-2,4-dimethyl-3,5-di-carbethoxy pyrrole     | 95      |
| 9-carbomethoxy fluorene                | 9-amino-9-carbomethoxy fluorene                    | 50      |
| Diethylphenylmalonate                  | Diethyl- $\alpha$ -amino- $\alpha$ -phenylmalonate | 53      |
| Thiophenol                             | S-phenylsulphenamide                               | -       |

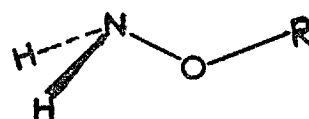
The chemistry of the organic hydroxylamine derivatives has attracted a great deal of attention and Zeeh and Metzger<sup>81</sup> have recently reviewed the chemistry of the N- and O- hydroxylamine derivatives in detail.

### II.3 Structural Features

Hydroxylamine itself is believed<sup>82</sup> to exist in cis and trans isomeric forms. Davies and Spiers<sup>83</sup> made an extensive study of the infrared spectra of O-methyl hydroxylamines which indicated that the nitrogen valencies were pyramidally inclined with a preferred skew or trans conformation about the N-O axis. This supported the cis-trans structures.



cis



trans

Scheme (II-4) Cis-trans isomerism in O-substituted hydroxylamines

Probably O-(2,4-dinitrophenyl)hydroxylamine exists also in the isomeric forms.

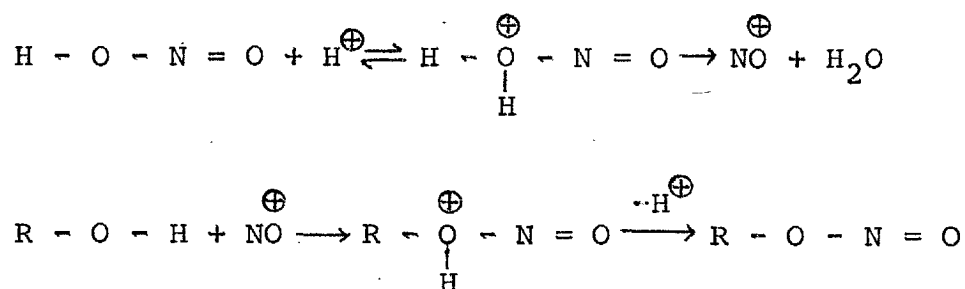
### CHAPTER III

#### Alkyl nitrites

In this chapter, a brief description of the preparation, properties and reactions of alkyl nitrites is given.

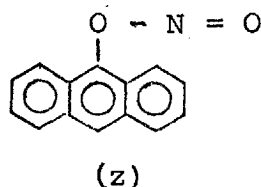
#### III.1 Preparation of Alkyl nitrites

Alkyl nitrites have been prepared<sup>84,85</sup> in aqueous solution by nitrosation of the corresponding alcohol with a suitable nitrosating agent at 0°C (Scheme III-1).

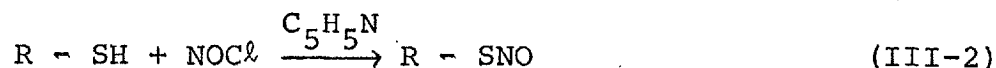
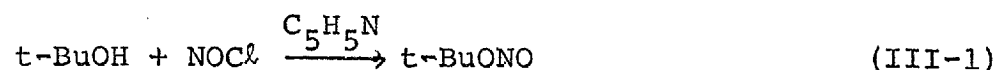


Scheme (III-1) Preparation of an alkyl nitrite by nitrosation of the corresponding alcohol

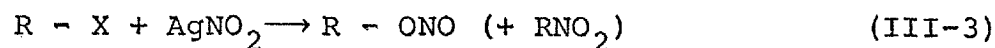
The usual nitrosating agents, such as nitrosyl chloride or sodium nitrite and sulphuric acid, are quite satisfactory. Electrophilic attack of the nitrosonium ion on the electron-rich oxygen of the alcohol appears to take place; thus, aromatic alcohols have been nitrosated to the nitrite, but phenols have not yet been O-nitrosated to the stable nitrite. However, Rindone and Scolastico<sup>86</sup> have claimed the synthesis of 9-anthrylnitrite (z) by (Cerium ammonium nitrate) oxidation



of anthracene in anhydrous acetonitrile solution. Nitrosyl chloride in pyridine has been used to nitrosate t-butylalcohol and some thiols to the corresponding nitrites<sup>87</sup> as in eqns. (III-1) and (III-2) respectively.



Kornblum<sup>54</sup> et al prepared alkyl nitrites by the action of silver nitrite on suitable alkyl halides.



### III.2 Properties of Alkyl nitrites

Alkyl nitrites are sweet-smelling yellowish substances. Methyl nitrite is a gas and ethyl nitrite a low boiling liquid. Higher alkyl nitrites are usually liquids. Alkyl nitrites decompose slowly at room temperature and are light sensitive, but have been stored in the 'fridge for weeks with little decomposition. Alkyl nitrites are insoluble in water but dissolve in all common organic solvents.

Alkyl nitrites are physiologically active materials and have found therapeutic applications in small doses<sup>87</sup>. They cause a marked fall in blood pressure by dilation of the peripheral arteries. In large amounts, they produce 'methemoglobinemia' resulting in cyanosis and asphyxia<sup>88</sup>.

### III.3 Structure of Alkyl nitrites

Electron-diffraction studies of methyl nitrite reveal that<sup>87</sup>

the C-O distance is 1.44 Å, the O-N distance is 1.37 Å and the double bond N=O distance to be 1.22 Å (the value is 1.24 Å in the case of the nitrite ion itself<sup>89</sup>). The C-O-N angle has been estimated to be 109.5°, which is essentially the same as the O-N-O angle (115° in the case of the nitrite ion<sup>89</sup>).

The existence of rotational isomerism in alkylnitrites resulting in a planar cis form (possibly stabilized by hydrogen bonding) and a planar trans form has been well established by spectral studies<sup>90,91,92</sup>. Fig. (III-1) depicts the structures of cis and trans methylnitrite, showing bond lengths and bond angles<sup>93</sup>.

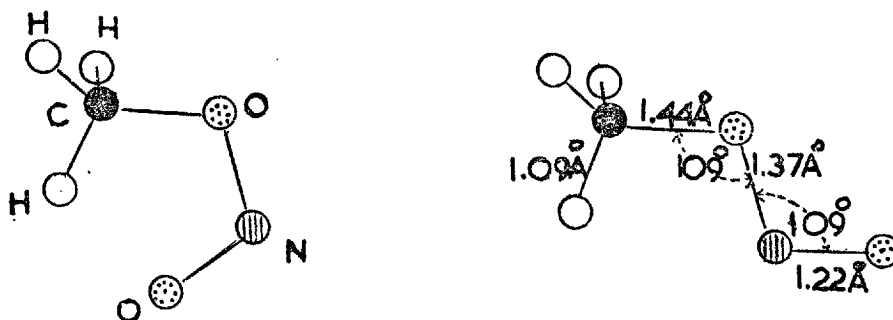


Fig. (III-1) Cis and trans methylnitrite

#### III.4 U.V. Spectra

Alkylnitrites absorb in the U.V. region with a high extinction maximum near  $\lambda = 220$  nm and with a low extinction maximum at  $\lambda = 358$  nm. The spectrum shows multiple structure in the  $\lambda = 310$  to 400 nm region and resembles that of a nitrosamine. However, nitrosamine maxima are solvent dependent

whereas those of alkyl nitrite (RONO) are virtually independent of R (in RONO) and solvent<sup>94</sup>. Haszeldine and Mattinson<sup>90</sup> reported that the U.V. spectra of n-BuONO in the vapour or liquid state and in solutions in  $\text{CCl}_4$ ,  $\text{CHCl}_3$  and light petroleum are identical, not only with regard to the positions of the maxima, but also to their relative heights (see Fig. III-2). The peak C remains smaller than peak B, when B and

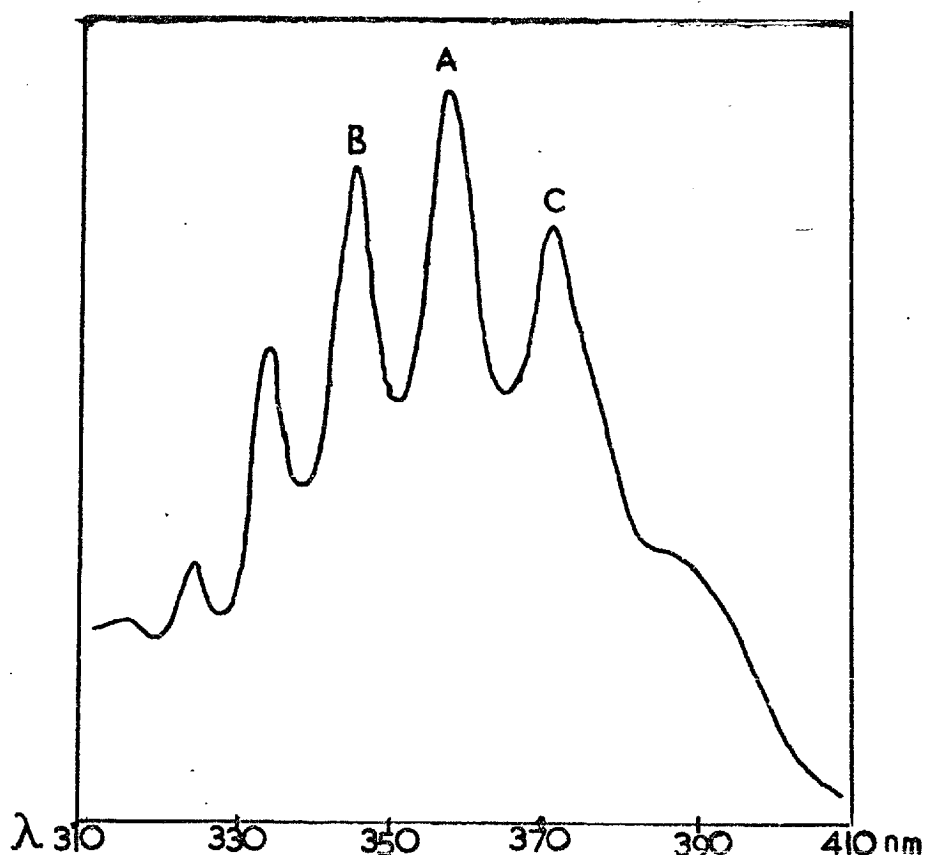


Fig. (III-2) U.V. Spectrum of n-butyl nitrite in n-hexane

C flank the main peak A. Changing the solvent to acetonitrile or dimethylformamide causes negligible changes in the wavelength of the peaks, but the relative heights of B and C change, i.e. C becomes higher than B. Haszeldine *et al*<sup>90,94</sup> explained this in terms of a change in the cis:trans ratio. The extinction coefficient ( $\epsilon$ ) of alkyl nitrites is independent of solvent as exemplified by Table (III-1).

TABLE (III-1)

Extinction Coefficients of n-BuONO in different solvents

| Solvent                | (90)<br>$\lambda$ max (nm) | $\epsilon$ |
|------------------------|----------------------------|------------|
| CHCl <sub>3</sub>      | 357                        | 80         |
| Light Petroleum        | 357                        | 92         |
| CCl <sub>4</sub>       | 357                        | 89         |
| CH <sub>3</sub> CN     | 357                        | 70         |
| n-BuOH                 | 357                        | 79         |
| DMF                    | 357.5                      | 75         |
| n-Hexane <sup>a)</sup> | 358                        | 90         |

a) determined experimentally

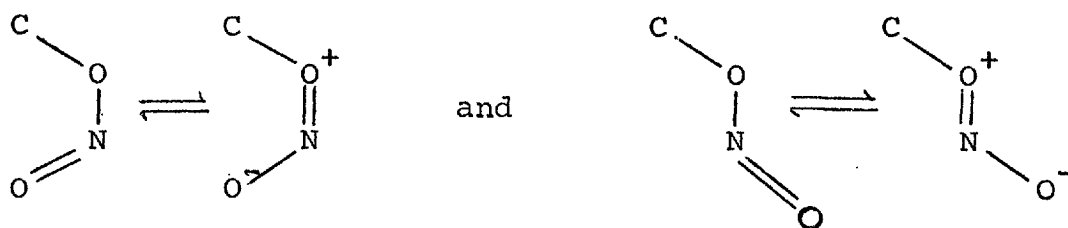
III.5 N.M.R. Spectra

In order to confirm the existence of the rotational isomerism in alkylnitrites, Plette et al<sup>92</sup> studied the p.m.r. spectra of methyl, ethyl and n-propyl nitrite at about -60°C, when rotational isomerism doubling of the methyl peak in MeONO, and of the methylene peaks in ethyl and n-propylnitrites was observed. The separation of the doubling was  $32 \pm 2$  cycles in all three cases. They assumed that the trans form predominated in MeONO but the cis form in the ethyl and n-propyl nitrites.

III.6 Action of Heat

There is considerable rigidity about the O-N bond in an alkylnitrite probably due to the resonance of the following

(Scheme III-2) type.<sup>95</sup>



Scheme (III-2) Resonance structures in an alkyl nitrite

The O-N bond distance is 1.37 Å which has about 15% double bond character<sup>96</sup> and supports the view. The potential barrier about the N=O bond is 33.5 K joules mole<sup>-1</sup>, and is considerably higher than that in ethane (~ 12.5 K joules<sup>97</sup> mole<sup>-1</sup>) but not sufficiently high to prohibit thermal interconversion<sup>93</sup>.

Neogi and Chowdhuri<sup>98</sup> reported the conversion of alkyl nitrite to the isomeric nitroalkane by heat at ~ 100°. Levy<sup>99</sup> and many other chemists took an active interest in the thermal reactions of alkyl nitrites and various mechanisms have been proposed to explain the products of thermal decomposition.

### III.7 Action of Light

Alkyl nitrites undergo various light induced reactions; the overall pattern being very similar to that of pyrolysis. Coe and Doumani<sup>100</sup> identified acetone and nitrosomethane as the photochemical reaction products of *t*-butyl nitrite. Gray and Style<sup>101</sup> examined the photolysis of methyl nitrite over a wide range of temperature, and explained their results in terms of primary rupture of the CH<sub>3</sub>O - NO bond. Nussbaum and Robinson<sup>102</sup> have reviewed the development of the preparative

photolysis of organic nitrites in detail.

### III.8 Alkylnitrite as a Nitrosating Agent

Alkylnitrites have long been known as diazotising and nitrosating agents. Griess<sup>103</sup>, as early as 1865, pointed out that 'pure nitrite of ethyl as well as nitrite of amyl' could be used as a diazotising agent. The poor solubility of  $\text{NaNO}_2$  in organic solvents is a disadvantage which has been overcome by the use of alkylnitrites.

An alkylnitrite and hydrogen chloride is the most widely used reagent combination and has the advantage of yielding a reaction mixture which, by vacuum distillation, can be freed of reagents and at least one by-product, the alcohol, formed from the nitrite.

n-Butylnitrite in 85% sulphuric acid has also been used as a convenient nitrosating agent.

It has been claimed<sup>104</sup> that an alkylnitrite in dimethylformamide can replace the amino group of an amine by hydrogen via the diazo compound, even in the absence of an acid. The use of alkylnitrite in the production of diazonium salts from the protonated amines is well known. Cadogan<sup>105</sup> used pentyl nitrite as a diazotising agent in preparing biphenyl from aniline, 3-phenyl pyridine from 3-amino pyridine, 4-methoxy biphenyl from p-anisidine and 3-phenyl quinoline from 3-amino quinoline. A selection of aromatic amines was also found to react<sup>106</sup> with pentylnitrite in the presence of bromoform to form the corresponding aryl bromide in acceptable yield in a Sandmeyer type of reaction.

### III.9 Hydrolysis and Solvolysis

Hydrolysis of alkyl nitrites is markedly catalysed by acids but little by bases. Allen<sup>107</sup> has studied the kinetics of the acid-catalysed hydrolysis of *n*-propyl, *t*-butyl and diphenylmethylnitrites in aqueous dioxan solutions. With perchloric acid, the observed first-order rate coefficients were found to be proportional to the hydrogenion concentration as shown in the rate expression:

$$-\frac{d}{dt} [\text{RONO}] = k_1 [\text{RONO}] = k_2 [\text{H}^+] [\text{RONO}] \quad (\text{III-4})$$

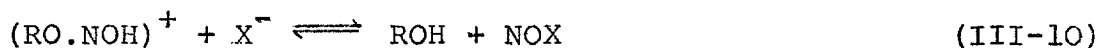
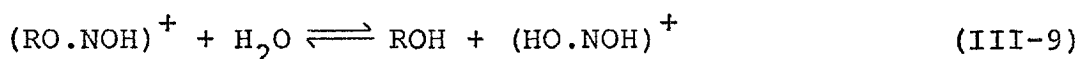
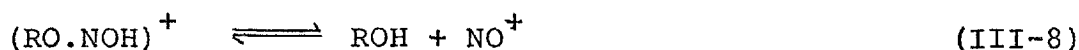
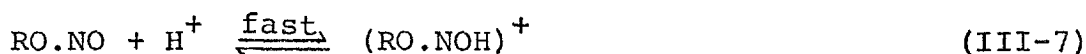
However, in the presence of hydrochloric acid, he observed a faster rate of hydrolysis, which was no longer directly proportional to the acid concentration, and suggested the following rate expression:

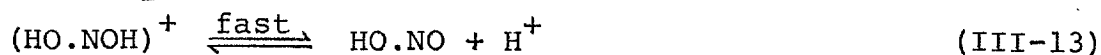
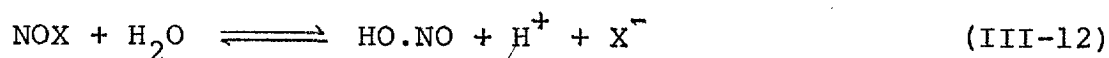
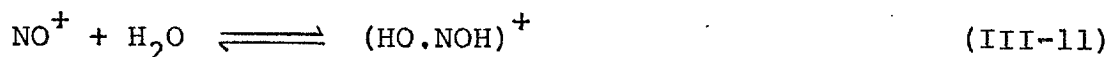
$$-\frac{d}{dt} [\text{RONO}] = k_2 [\text{HCl}] [\text{RONO}] + k_3 [\text{HCl}]^2 [\text{RONO}] \quad (\text{III-5})$$

The eqn. (III-5) could also be written in the form

$$-\frac{d}{dt} [\text{RONO}] = k_2 [\text{H}^+] [\text{RONO}] + k_3 [\text{H}^+] [\text{Cl}^-] [\text{RONO}] \quad (\text{III-6})$$

Allen<sup>107</sup> suggested the following mechanism for the acid catalysed hydrolysis of alkyl nitrites.

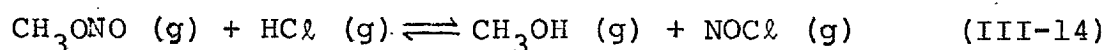




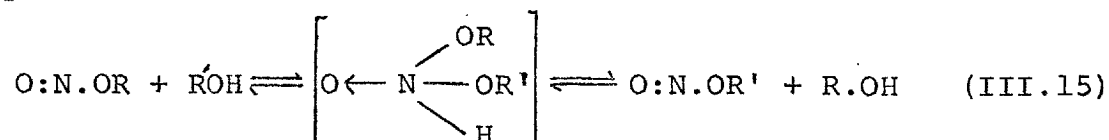
He assumed that the eqns. (III-7) and (III-13) were very rapid and maintained throughout the reaction, and that eqn. (III-9) was the rate determining step. However, in the presence of halide ions, eqns. (III-9) and (III-10) probably take place simultaneously giving rise to the observed rate expression (III-6). Allen<sup>107</sup> also studied the alkaline hydrolysis of n-propyl and t-butylnitrites in aqueous dioxane solutions containing varying concentrations of sodium hydroxide. He observed that t-butyl nitrite reacted about 50 times slower than the n-propyl derivative.

Allen<sup>107</sup> concluded that the nitrosyl-oxygen bond cleaved during hydrolysis. This view arose from the observed retention of configuration during the hydrolysis of optically active 1-methylheptyl nitrite, by the alcoholysis products of n-propyl and t-butyl nitrites, and, for the t-butylester in acid solution, by the absence of olefin formation and by experiments with isotopically enriched (<sup>18</sup>O) water.

The gas phase reaction of methylnitrite with hydrogen chloride resulted in the following equilibrium<sup>108</sup>:



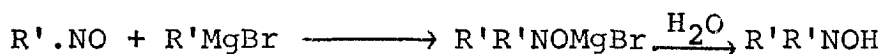
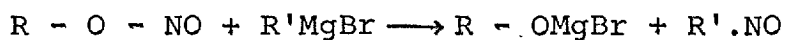
Solvolytic reactions via complex formation<sup>109</sup> according to eqn. (III-15)



in which the alkyl group of the nitrite is exchanged for that of an alcohol (in which it is dissolved) have been postulated, but do not seem to have been proved.

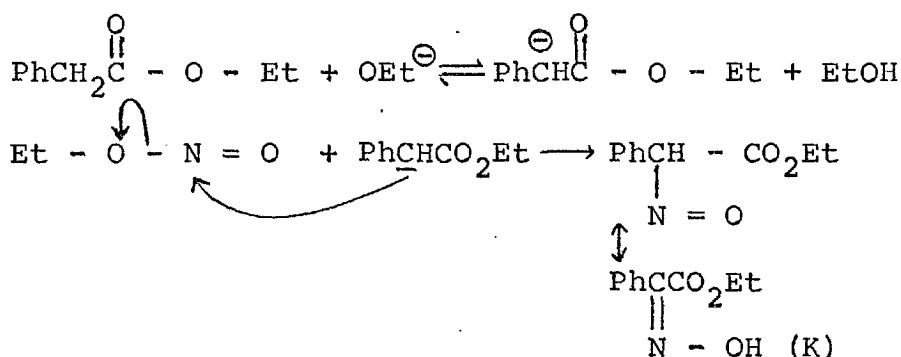
### III.10 Reaction with Grignard Reagents

Alkyl nitrites also react with Grignard reagents. The first product seems to be a nitroso compound, which reacts further with excess of the reagent to furnish N-disubstituted<sup>95</sup> hydroxylamine, Scheme (III-3).



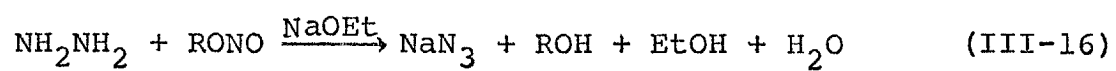
Scheme (III-3) Reactions of alkyl nitrite with Grignard reagent

Alkyl nitrites condense with compounds containing reactive methylene groups in the presence of a base (NaOEt or KOEt). Thus, ethyl nitrite reacts with ethyl phenyl acetate and potassium ethoxide in ethanol to give the potassium salt of the oxime of ethyl phenyl glyoxinate<sup>95</sup>. The reaction probably involves nucleophilic attack of the carbanion of ethyl phenyl acetate on the electron-deficient nitrogen (Scheme III-4).



Scheme (III-4) Nucleophilic attack of the carbanion on the nitrogen

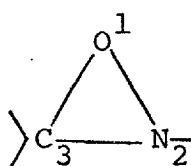
The following reaction<sup>87</sup> with hydrazine in the presence of NaOEt is of interest. /



## CHAPTER IV

### Oxaziridines

Oxaziridines are three membered ring compounds with carbon, nitrogen and oxygen atoms constituting the ring. The possibility of alkyl and aryl substitution either at carbon or nitrogen or at both has produced an interesting class of organic compounds.



Oxaziridine Ring

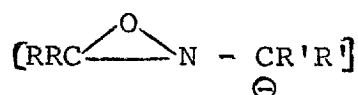
For details reference to an excellent study by Lobo<sup>110</sup> is available.

The oxaziridine ring is under strain and studies<sup>110</sup> have revealed the conditions for the opening of the ring. Hydrolyses of various oxaziridines have been studied under acidic and basic conditions and it is assumed that acid-hydrolysis proceeds with a rapid pre-equilibrium protonation, followed by breakdown of the conjugate acid. Both N-protonation and O-protonation are possible, but the N-protonated form is supposed to be stable and it is the O-conjugate acid which successfully leads to reaction by N-O cleavage. Simultaneous  $\alpha$ -proton abstraction by a water molecule acting as a base in the case of the primary 2-alkyl oxazirides, or by extensive migration of a group  $\alpha$  to the electron-deficient nitrogen of the ring, in the case of secondary 2-alkyl oxaziridines and tertiary 2-alkyl oxaziridines has been suggested.

In the case of an aryl group in position 3 of the O-conjugate acid, C-O bond cleavage has been assumed to take place.

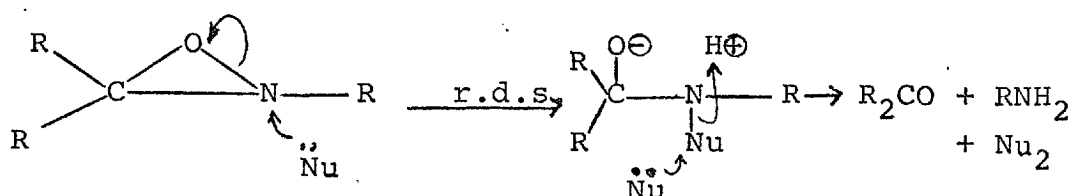
Hydrolysis under basic conditions has been shown to be a heterolytic bimolecular process involving the rate-determining abstraction of the proton  $\alpha$  to the nitrogen atom of the ring of the neutral oxaziridine.

Differences in the rates arising from structural differences in the oxaziridine have been explained in terms of the stability of the incipient carbanion



formed by  $\alpha$ -proton abstraction.

Lobo<sup>110</sup> attempted to study nucleophilic reactivity towards 2,3,3-triethyloxaziridine, and suggested that the N atom of the oxaziridine was the target of the nucleophilic attack. The steric congestion around the nitrogen which results when a t-butyl group is introduced on to it and the observed slower rate of release of iodine seem to favour the conclusion. The following mechanism has been put forward by Lobo<sup>110</sup> for the nucleophilic attack (Scheme IV-1).



Scheme (IV-1) Nucleophilic attack on the oxaziridine ring

Some of the results<sup>110</sup> are tabulated below (Table IV-1).

TABLE (IV-1)<sup>110</sup>

Nucleophilic ring opening of 2,3,3-triethyl oxaziridine

Temp = 25° ± .1°C

| Catalysts               | $10^3 k_2$<br>mole <sup>-1</sup> . l . sec <sup>-1</sup> |
|-------------------------|----------------------------------------------------------|
| OH <sup>-</sup>         | 7.17                                                     |
| PhO <sup>-</sup>        | 6.17                                                     |
| Me <sub>2</sub> NH      | 7.17                                                     |
| piperidine              | 5.0                                                      |
| 2,6-Dimethyl piperidine | 1.3                                                      |
| Cyanide                 | 0.93                                                     |
| Iodide                  | 1.67                                                     |
| Thiocyanate             | 3.0                                                      |
| Water                   | 0.00165                                                  |

Lobo<sup>110</sup> further claimed that a satisfactory correlation existed with the Edwards equation (see Chapter I) and  $\alpha$  and  $\beta$  values were reported to be 0.78 and 0.095 respectively. The Brønsted  $\beta$  value was 0.03.

Lobo<sup>110</sup> concluded that the important factor for nucleophilic reactivity towards the electron-deficient N in an oxaziridine was not the basicity, and the low Edwards  $\beta$  value seems to justify this view.

/

PART 2

DISCUSSION OF THE EXPERIMENTAL RESULTS

## CHAPTER V

### Basic and Nucleophilic Bond Cleavage of O-(Nitroaryl)- hydroxylamines

The O-(nitroaryl)-hydroxylamines in question are mostly O-(2,4-dinitrophenyl)-hydroxylamine and its N-methyl derivative. Sheradsky et al<sup>78</sup> pointed out that because the nitroaryloxy group, a good leaving group, it would be easily displaced by nucleophiles, which would therefore be aminated. In this chapter, the results of nucleophilic displacement of the nitro-aryloxy group are reported and discussed. Most of the kinetic experiments were carried out at  $25^{\circ} \pm 0.1^{\circ}\text{C}$  and the rates usually followed eqn. (V-1)

$$\text{Rate} = k_o [\text{substrate}] \quad (\text{V-1})$$

where  $k_o$  is the rate constant observed for the displacement of the nitroaryloxy group and  $[\text{substrate}]$  refers to the stoichiometric concentration of the hydroxylamine derivative in question. Good first order plots were obtained for most reactions studied up to 87-90% reaction. Evidence of this is given in fig. (V-1) in which  $\log \frac{\text{O.D.}_{\infty} - \text{O.D.}_o}{\text{O.D.}_{\infty} - \text{O.D.}_t}$  has been plotted against time for the sodium thiocyanate catalysed hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine in water at  $25^{\circ}\text{C}$  ( $\mu = 1.0$ ) and remains linear for more than 93% of reaction. In some cases, however, particularly  $\text{HO}^{\ominus}$  and  $\text{HO}_2^{\ominus}$ , first order behaviour was observed only over the first 50-60% of reaction. This matter is discussed further below. Most of the reactions were carried out in water in the presence

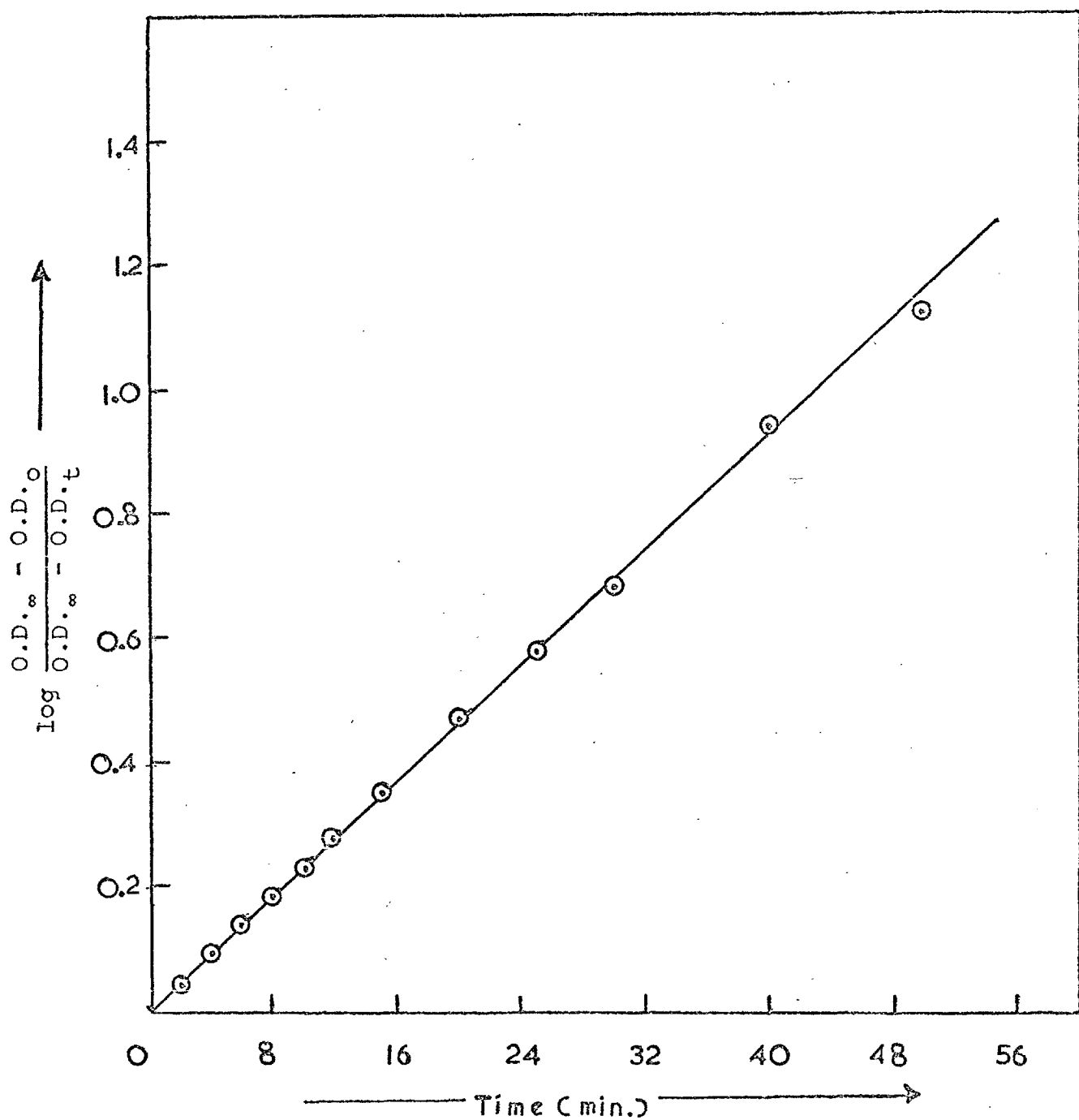


Fig. (V-1) Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by 0.05 M NaSCN at 25°C in water ( $\mu = 1.0$ ).

of a very small concentration of sodium hydroxide ( $1 \times 10^{-3}$  M) to ensure complete formation of the nitrophenoxide ion product. Only negligible catalysis occurred with sodium hydroxide at that concentration. The concentration of the nucleophile was maintained at least 10 times higher than the substrate concentration to ensure pseudo first order kinetics eqn. (V-1). The ionic strength,  $\mu$ , was kept constant by addition of  $\text{NaClO}_4$  where necessary. The second order rate coefficient,  $k_{bi}$ , for each nucleophile

$$\text{Rate} = k_{bi} [\text{substrate}] [\text{Nu}] \quad (\text{V-2})$$

was obtained from individual runs under identical conditions by dividing the observed rate ( $k_o$ ) by the molarity of the nucleophile concerned. The rate with ( $1 \times 10^{-3}$  M) NaOH was taken into consideration before computing the  $k_{bi}$  coefficients.

## V.1 Kinetic Results

### V.1.1 Catalysis by thiocyanate ion

Thiocyanate ion proved to be a good nucleophile. Reactions were carried out involving a tenfold change in thiocyanate ion concentration and the observed first order rate constants were dependent on thiocyanate ion concentration as illustrated by Table (V-1).

TABLE (V-1)

Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by sodiumthiocyanate at 25°C

(ionic strength = 1.0, maintained by NaClO<sub>4</sub>)

[NaOH] =  $1 \times 10^{-3}$  M; Initial [substrate] =  $(1-1.5) \times 10^{-4}$  m/l

| Expt. | $10^2 \cdot [\text{SCN}^-]$<br>M | $10^4 k_o$<br>sec <sup>-1</sup> |
|-------|----------------------------------|---------------------------------|
| 389   | 10                               | 19.2                            |
| 409   | 8                                | 14.2                            |
| 410   | 5                                | 8.8                             |
| 411   | 1                                | 2.1                             |

V.1.2 Catalysis by piperidine

Reactions were carried out with different concentrations of piperidine and  $k_{bi}$  coefficients agreed within 4% which also indicated the first order dependence on the concentration of the amine involved {Table (V-2)}.

TABLE (V-2)

Piperidine catalysed hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine ( $\mu = 1.0$ , temp = 25°C)

Initial [substrate] =  $(1-1.5) \times 10^{-4}$  m/l

| Expt. | [OH <sup>-</sup> ]<br>M | [Piperidine]<br>M | $10^4 k_o$ sec <sup>-1</sup> | $10^4 k_{bi}$<br>l mole <sup>-1</sup> sec <sup>-1</sup> |
|-------|-------------------------|-------------------|------------------------------|---------------------------------------------------------|
| 399   | 0.001                   | 0.10              | 81                           | 810                                                     |
| 470   | 0.01                    | 0.045             | 35                           | 778                                                     |

### V.1.3 Catalysis by hydroxide ion

Good first order kinetics could not be obtained for reactions carried out with dilute sodium hydroxide solutions. A typical plot is shown in fig. (V-2) in which after about 55-60% reaction, gradual slowing down can be seen. However, first order rates calculated from the initial slope of the plot of  $\log \left( \frac{O.D._{\infty} - O.D._0}{O.D._{\infty} - O.D._t} \right)$  versus time showed first order dependence on the hydroxide ion concentration. In order to minimise error, very low concentrations of hydroxide ion were used which gave reasonably good first order kinetics. This showed dependence on the hydroxide ion concentration. Fig. (V-3) illustrates the point; other data similarly obtained may be found in Table (V-3).

TABLE (V-3)

Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine under basic condition at 25°C

| Expt. | [OH <sup>-</sup> ]<br>M | $\mu$ | initial<br>[substrate]<br>10 <sup>4</sup> M | 10 <sup>4</sup> k <sub>o</sub> sec <sup>-1</sup> | 10 <sup>4</sup> k <sub>bi</sub><br>l mole <sup>-1</sup> sec <sup>-1</sup> |
|-------|-------------------------|-------|---------------------------------------------|--------------------------------------------------|---------------------------------------------------------------------------|
| 479   | 0.123                   | -     | ~ 1                                         | 1.92                                             | 15.58                                                                     |
| 478   | 0.4                     | -     | ~ 1                                         | 5.98                                             | 14.95                                                                     |
| 477   | 0.4                     | -     | ~ 9                                         | 5.75                                             | 14.37                                                                     |
| 475   | 0.98                    | -     | ~ 1                                         | 14.7                                             | 14.94                                                                     |
| 387   | 0.01                    | -     | ~ 1                                         | 0.095                                            | 9.5                                                                       |
| 487   | 0.01                    | 1.0   | ~ 1                                         | 0.067                                            | 6.67                                                                      |
| 486   | 0.02                    | 1.0   | ~ 1                                         | 0.13                                             | 6.67                                                                      |
| 488   | 0.04                    | 1.0   | ~ 1                                         | 0.275                                            | 6.87                                                                      |

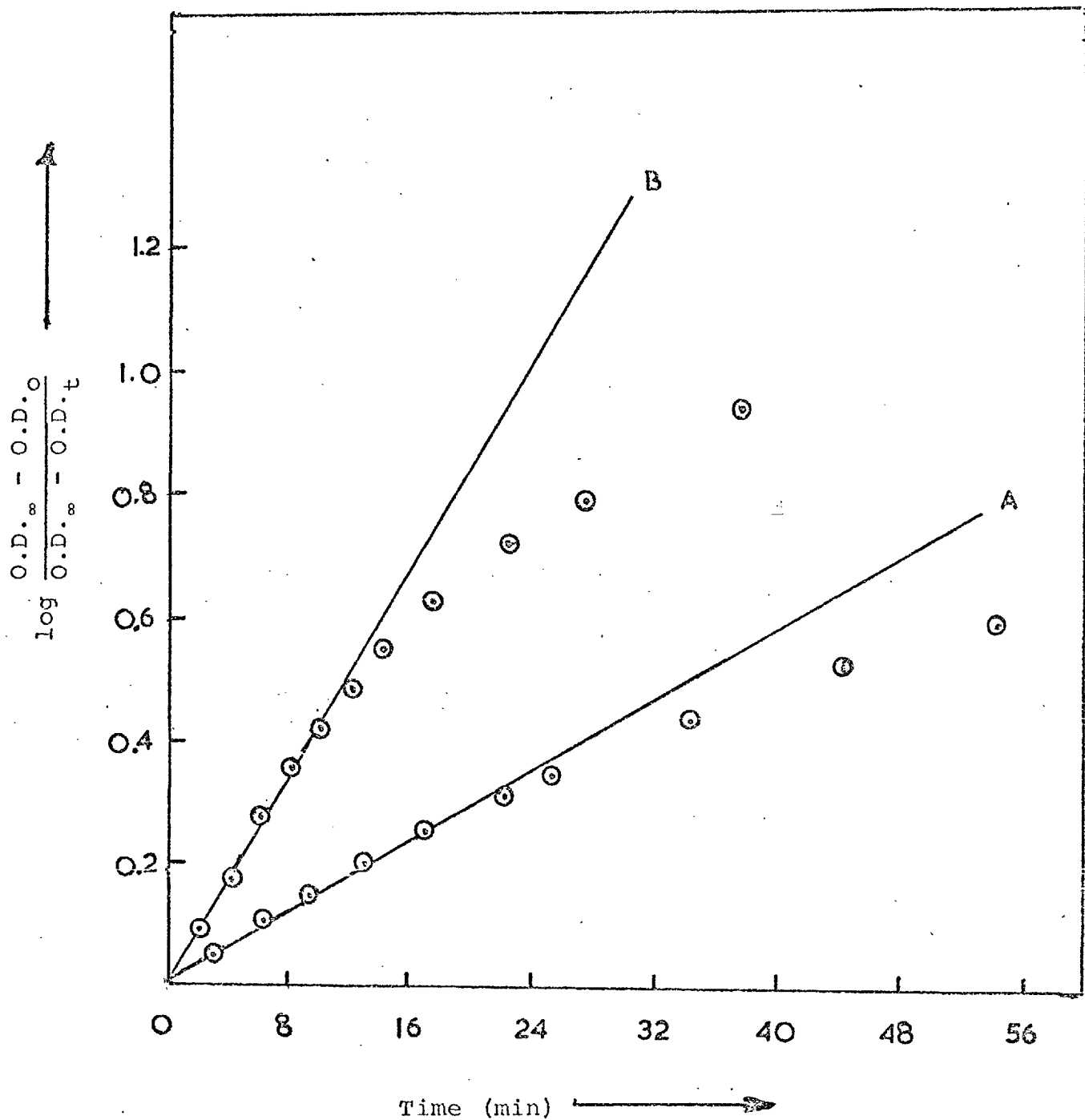


Fig. (V-2) Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by (25°C)

A) hydroxide ion ( $\mu$  not adjusted)

B) perhydroxyl ion ( $\mu = 1.0$ )

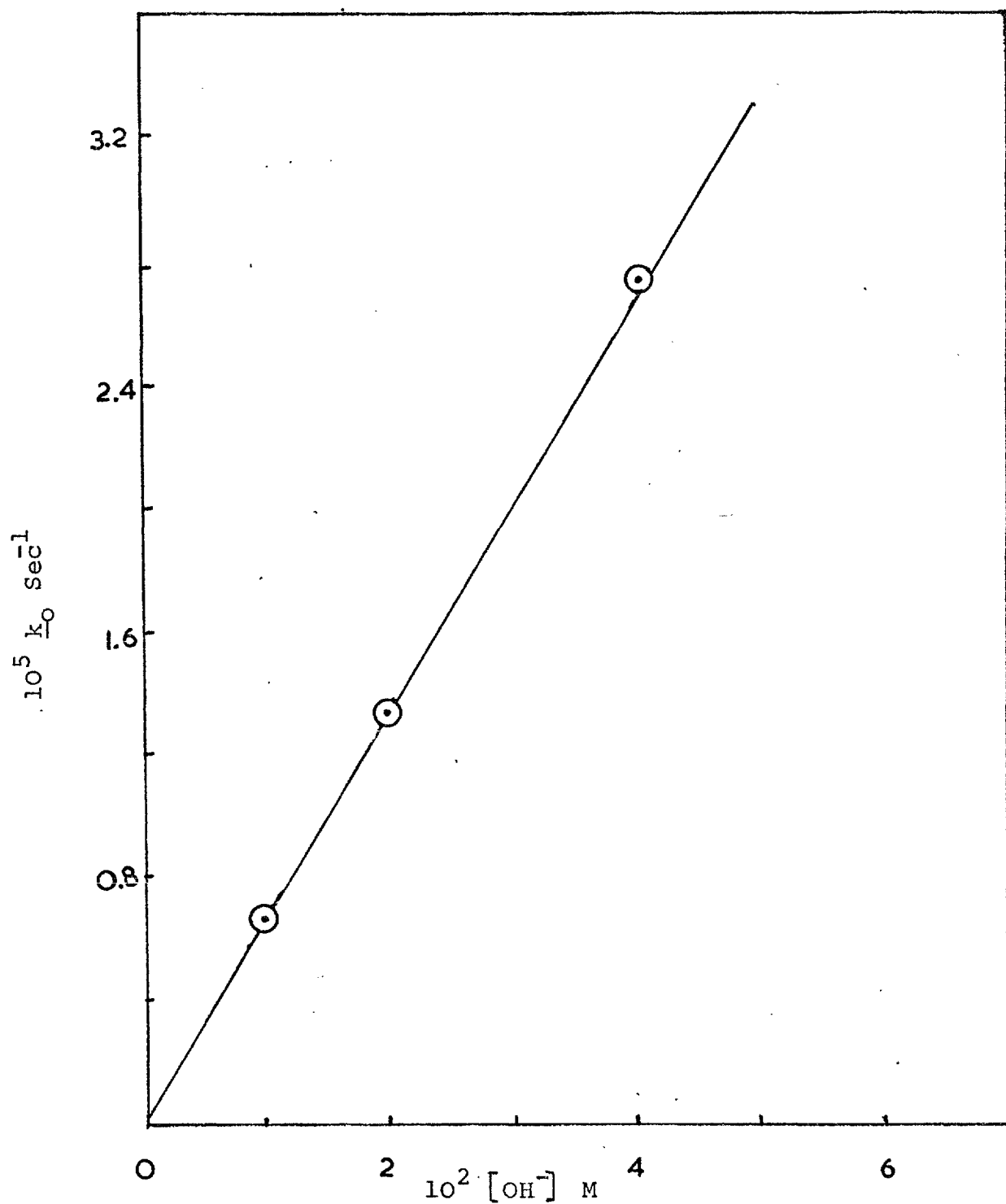


Fig. (V-3) First order dependence on the concentration of hydroxide ion.

#### V.1.4 Catalysis by perhydroxyl ion ( $\text{HOO}^\ominus$ )

The same difficulty mentioned in the case of hydroxide (section V.1.3.) was experienced here also. A typical plot at  $25^\circ\text{C}$  of  $\log \left\{ \frac{\text{O.D.}_\infty - \text{O.D.}_0}{\text{O.D.}_\infty - \text{O.D.}_t} \right\}$  versus time is shown in fig. (V-2). However, rates calculated from the initial slope showed first order dependence on the perhydroxyl ion concentration when reactions were carried out at lower temperatures as exemplified by Table (V-4) and fig. (V-4).

TABLE (V-4)

Perhydroxyl ion catalysed hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine at  $4^\circ\text{C}$

$$\mu = 1.0$$

$$\text{Initial [substrate]} \approx (1-1.5) \times 10^{-4} \text{ m/l}$$

| Expt. | Total<br>[NaOH]<br>M | Total<br>[H <sub>2</sub> O <sub>2</sub> ]<br>M | $10^4 k_o \text{ sec}^{-1}$ |
|-------|----------------------|------------------------------------------------|-----------------------------|
| 426   | 0.08                 | 0.08                                           | 6.63                        |
| 428   | 0.04                 | 0.04                                           | 3.28                        |
| 427   | 0.02                 | 0.02                                           | 1.35                        |

Other data obtained at  $25^\circ\text{C}$  are tabulated below, Table (V-5).

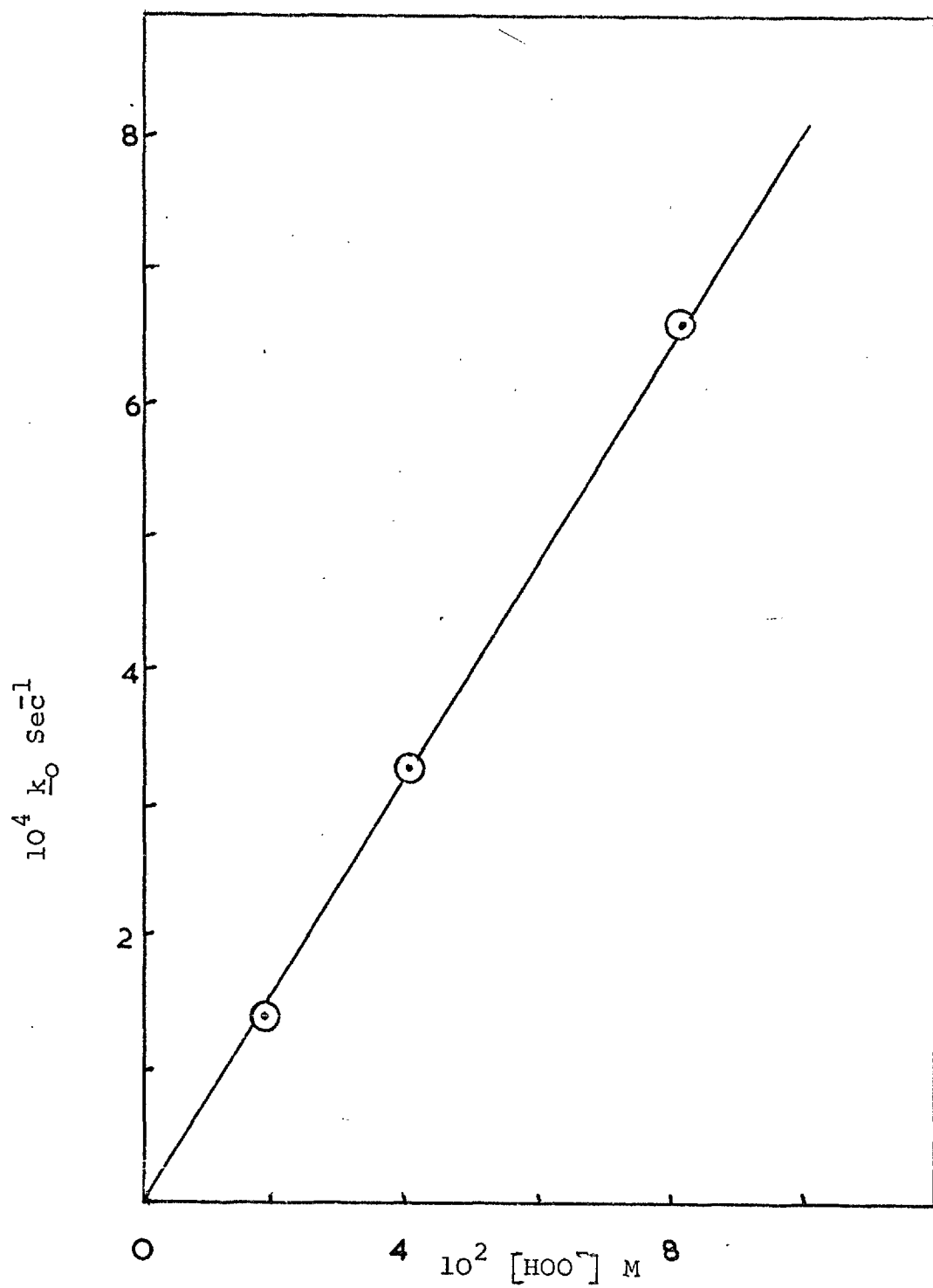


Fig. (V-4) First order dependence on the concentration of perhydroxyl ion ( $HOO^-$ ).

TABLE (V-5)

Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by perhydroxyl ion at 25°C

$$\mu = 1.0$$

$$\text{Initial [substrate]} \approx (1-1.5) \times 10^{-4} \text{ m/l}$$

| Expt. | Total<br>[NaOH]<br>M | Total<br>[H <sub>2</sub> O <sub>2</sub> ]<br>M | p <sup>H</sup> | Effective <sup>a)</sup><br>[HOO <sup>⊖</sup> ] M | 10 <sup>4</sup> k <sub>o</sub> sec <sup>-1</sup> | 10 <sup>4</sup> k <sub>bi</sub><br>l mol <sup>-1</sup> sec <sup>-1</sup> | Mean<br>10 <sup>4</sup> k <sub>bi</sub>   |
|-------|----------------------|------------------------------------------------|----------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------------------------------|-------------------------------------------|
| 421   | 0.021                | 0.02                                           | 11.8           | 0.0133                                           | 10.73                                            | 807                                                                      |                                           |
| 422   | 0.1                  | 0.02                                           | -              | ~ 0.02                                           | 16.78                                            | 839                                                                      | 851                                       |
| 473   | 0.03                 | 0.02                                           | 11.6           | 0.011                                            | 10.0                                             | 909                                                                      | l mole <sup>-1</sup><br>sec <sup>-1</sup> |

a) calculated from the Henderson equation.

The difficulties experienced with HO<sup>⊖</sup> and HO<sub>2</sub><sup>⊖</sup> will be discussed in due course.

#### V.1.5 Catalysis by other nucleophiles

A wide range of other nucleophiles differing in structure and reactivity were studied but in less detail than SCN<sup>⊖</sup>. The first order rate constants (k<sub>o</sub>) at 25°C are reported in Table (V-6). Since all these reactions were carried out in the presence of (1 x 10<sup>-3</sup> M) NaOH, it was necessary to deduct a small correction, estimated to be 0.008 x 10<sup>-4</sup> sec<sup>-1</sup> {by extrapolating the straightline to 1 x 10<sup>-3</sup> M NaOH in fig. (V-3)}, for the rate due to hydroxide from the observed rate in each case. The second order rate constants (k<sub>bi</sub>) are to be found in the last column of Table (V-6). The ionic strength (μ) was maintained at 1.0 by the addition of NaClO<sub>4</sub> where necessary, except in the case of pyridine, 2,6-lutidine and phenoxide ion nucleophiles where no NaClO<sub>4</sub> was added.

TABLE (V-6)

Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by various nucleophiles at  $25^{\circ} \pm 0.1^{\circ}\text{C}$

Initial [substrate]  $\approx (1-1.5) \times 10^{-4}$  m/l

[NaOH] =  $1 \times 10^{-3}$   $\mu$  = 1.0 (for exception see sec. V.1.5)

| Expt.                     | [Nu] M             | Nu                                                                 | $10^4 k_o \text{ sec}^{-1} \text{ a)}$ | $10^4 k_{bi} \text{ l mole}^{-1} \text{ sec}^{-1}$ |
|---------------------------|--------------------|--------------------------------------------------------------------|----------------------------------------|----------------------------------------------------|
| 381                       | 1.0                | NaCl                                                               | 0.032                                  | 0.032                                              |
| 382                       | 1.0                | NaBr                                                               | 2.67                                   | 2.67                                               |
| 383                       | 1.0                | NaN <sub>3</sub>                                                   | 3.26                                   | 3.26                                               |
| 386                       | 1.0                | NaOAc                                                              | 0.029                                  | 0.029                                              |
| 389                       | 0.1                | NaSCN                                                              | 19.16                                  | 191.6                                              |
| 391                       | 0.1                | NaCN                                                               | 21.16                                  | 211.6                                              |
| 393                       | 0.01               | Na <sub>2</sub> S <sub>2</sub> O <sub>3</sub>                      | 99.0                                   | 9900.0                                             |
| 395                       | 1.05               | Pyridine                                                           | 2.62                                   | 2.495                                              |
| 396                       | 0.01               | Thiourea                                                           | 46.44                                  | 4644.0                                             |
| 399                       | 0.1                | Piperidine                                                         | 81.0                                   | 810.0                                              |
| 400                       | 0.1                | Benzylamine                                                        | 6.79                                   | 67.9                                               |
| 401                       | 0.1                | n-Butylamine                                                       | 8.66                                   | 86.6                                               |
| 402                       | 0.1                | Morpholine                                                         | 17.37                                  | 173.7                                              |
| 403                       | 0.1                | Et <sub>2</sub> NH                                                 | 24.82                                  | 248.2                                              |
| 404                       | 1.0                | NaNO <sub>2</sub>                                                  | 1.16                                   | 1.16                                               |
| 405                       | 1.0                | NH <sub>2</sub> OH                                                 | 69.72                                  | 69.72                                              |
| 406                       | 0.01               | KI                                                                 | 28.12                                  | 2812.0                                             |
| 408                       | 1.0                | N <sub>2</sub> H <sub>4</sub>                                      | 62.36                                  | 62.36                                              |
| 412                       | 0.01               | KSecN                                                              | 91.57                                  | 9157.0                                             |
| 413                       | 0.1                | PhO <sup>-</sup> Na <sup>+</sup>                                   | 0.05                                   | 0.5                                                |
| 424                       | 1.05               | 2,6-Lutidine                                                       | 0.872                                  | 0.83                                               |
| 437                       | $8 \times 10^{-4}$ | Sec(NH <sub>2</sub> ) <sub>2</sub>                                 | 146.0                                  | 182500.0                                           |
| 465                       | 0.01               | p-Me-C <sub>6</sub> H <sub>4</sub> SO <sub>2</sub> Na <sup>+</sup> | 3.22                                   | 322.0                                              |
| 472                       | 0.26               | Aniline                                                            | 2.0                                    | 7.69                                               |
| 488                       | 0.04               | Hydroxide                                                          | 0.275                                  | 6.87                                               |
| 421, )<br>422, )<br>473 ) | -                  | HOO <sup>-</sup>                                                   | see Table (V-5)                        | 851.0                                              |

a) rate due to  $1 \times 10^{-3}$  M NaOH has been deducted.

#### V.1.6 Relative Nucleophilicity

The term 'relative nucleophilicity' has been defined as in eqn. (V-3).

$$\log \left( \frac{k_{bi}}{k_{H_2O}} \right) = \text{relative nucleophilicity} \quad (V-3)$$

where  $k_{bi}$  has the same significance as defined previously and  $k_{H_2O}$  is the second order rate constant when water is the nucleophile. The value of  $k_{H_2O}$  has been estimated to be  $0.036 \times 10^{-7} \text{ l mole}^{-1} \text{ sec}^{-1}$  by extrapolating the straight-line to zero hydroxide ion concentration {see fig. (V-3)} and assuming the concentration of water to be 55.5 m/l.

The nucleophiles have been arranged in order of their relative nucleophilicities in Table (V-7).

TABLE (V-7)

Relative nucleophilicities towards O-(2,4-dinitrophenyl)-  
hydroxylamine

| Nucleophile                                 | $k_{bi}/k_{H_2O}$  | $\log \left( \frac{k_{bi}}{k_{H_2O}} \right)$ |
|---------------------------------------------|--------------------|-----------------------------------------------|
| SeC(NH <sub>2</sub> ) <sub>2</sub>          | $5.07 \times 10^9$ | 9.705                                         |
| S <sub>2</sub> O <sub>3</sub> <sup>-2</sup> | $2.75 \times 10^8$ | 8.439                                         |
| SeCN <sup>-</sup>                           | $2.54 \times 10^8$ | 8.405                                         |
| SC(NH <sub>2</sub> ) <sub>2</sub>           | $1.29 \times 10^8$ | 8.11                                          |
| I <sup>-</sup>                              | $7.81 \times 10^7$ | 7.893                                         |
| HOO <sup>-</sup>                            | $2.36 \times 10^7$ | 7.373                                         |
| Piperidine                                  | $2.25 \times 10^7$ | 7.352                                         |
| p-Toluenesulphinate                         | $8.94 \times 10^6$ | 6.951                                         |
| Et <sub>2</sub> NH                          | $6.89 \times 10^6$ | 6.838                                         |
| CN <sup>-</sup>                             | $5.88 \times 10^6$ | 6.769                                         |
| SCN <sup>-</sup>                            | $5.32 \times 10^6$ | 6.726                                         |
| Morpholine                                  | $4.82 \times 10^6$ | 6.683                                         |
| n-Butylamine                                | $2.40 \times 10^6$ | 6.38                                          |
| NH <sub>2</sub> OH                          | $1.94 \times 10^6$ | 6.288                                         |
| Benzylamine                                 | $1.88 \times 10^6$ | 6.274                                         |
| N <sub>2</sub> H <sub>4</sub>               | $1.73 \times 10^6$ | 6.238                                         |
| Aniline                                     | $2.14 \times 10^5$ | 5.329                                         |
| HO <sup>-</sup>                             | $1.91 \times 10^5$ | 5.281                                         |
| N <sub>3</sub> <sup>-</sup>                 | $9.0 \times 10^4$  | 4.954                                         |
| Br <sup>-</sup>                             | $7.42 \times 10^4$ | 4.87                                          |
| Pyridine                                    | $6.93 \times 10^4$ | 4.84                                          |
| NO <sub>2</sub> <sup>-</sup>                | $3.22 \times 10^4$ | 4.508                                         |
| 2,6-Lutidine                                | $2.3 \times 10^4$  | 4.362                                         |
| PhO <sup>-</sup>                            | $1.39 \times 10^4$ | 4.143                                         |
| Cl <sup>-</sup>                             | $8.9 \times 10^2$  | 2.949                                         |
| OAc <sup>-</sup>                            | $8.05 \times 10^2$ | 2.906                                         |

### V.1.7 Effect of polarity of solvent

Reaction rates were also investigated in various dioxan-water (v/v) mixtures at 25°C for O-(2,4-dinitrophenyl)-hydroxylamine. In all these runs, the initial concentration of sodium thiocyanate was maintained constant (0.051 M). The experimental data are presented in Table (V-8) and the relationship is shown in fig. (V-5).

TABLE (V-8)

Hydrolysis O-(2,4-dinitrophenyl)-hydroxylamine catalysed by NaSCN at 25°C in various dioxan-water mixtures

| Expt.             | % water (v/v) | $10^2 k_o \text{ sec}^{-1}$ |
|-------------------|---------------|-----------------------------|
| 432               | 10            | 1.28                        |
| 435               | 25            | 1.21                        |
| 438               | 50            | 0.55                        |
| 434               | 75            | 0.25                        |
| 410 <sup>a)</sup> | 100           | 0.088                       |

a) taken from previous expt.;  $[\text{SCN}^-] = 0.05 \text{ m/l}$

Some reactions with hydroxide ion were also carried out in mixed solvents and data are given in Table (V-8.1), the usual substrate concentration was maintained;  $\mu$  was not adjusted.

TABLE (V-8.1)

Hydroxide catalysed reactions of O-(2,4-dinitrophenyl)-hydroxylamine in mixed solvents at 25°C

| Expt. | Solvent<br>(v/v)         | $[\text{NaOH}]$<br>M | $10^4 k_o \text{ sec}^{-1}$ | $10^4 k_{bi}$<br>$\text{l mole}^{-1} \text{ sec}^{-1}$ |
|-------|--------------------------|----------------------|-----------------------------|--------------------------------------------------------|
| 436   | 80:20 dioxan-water       | 0.01                 | 0.58                        | 58                                                     |
| 439   | 80:20 acetonitrile-water | 0.02                 | 0.62                        | 31                                                     |

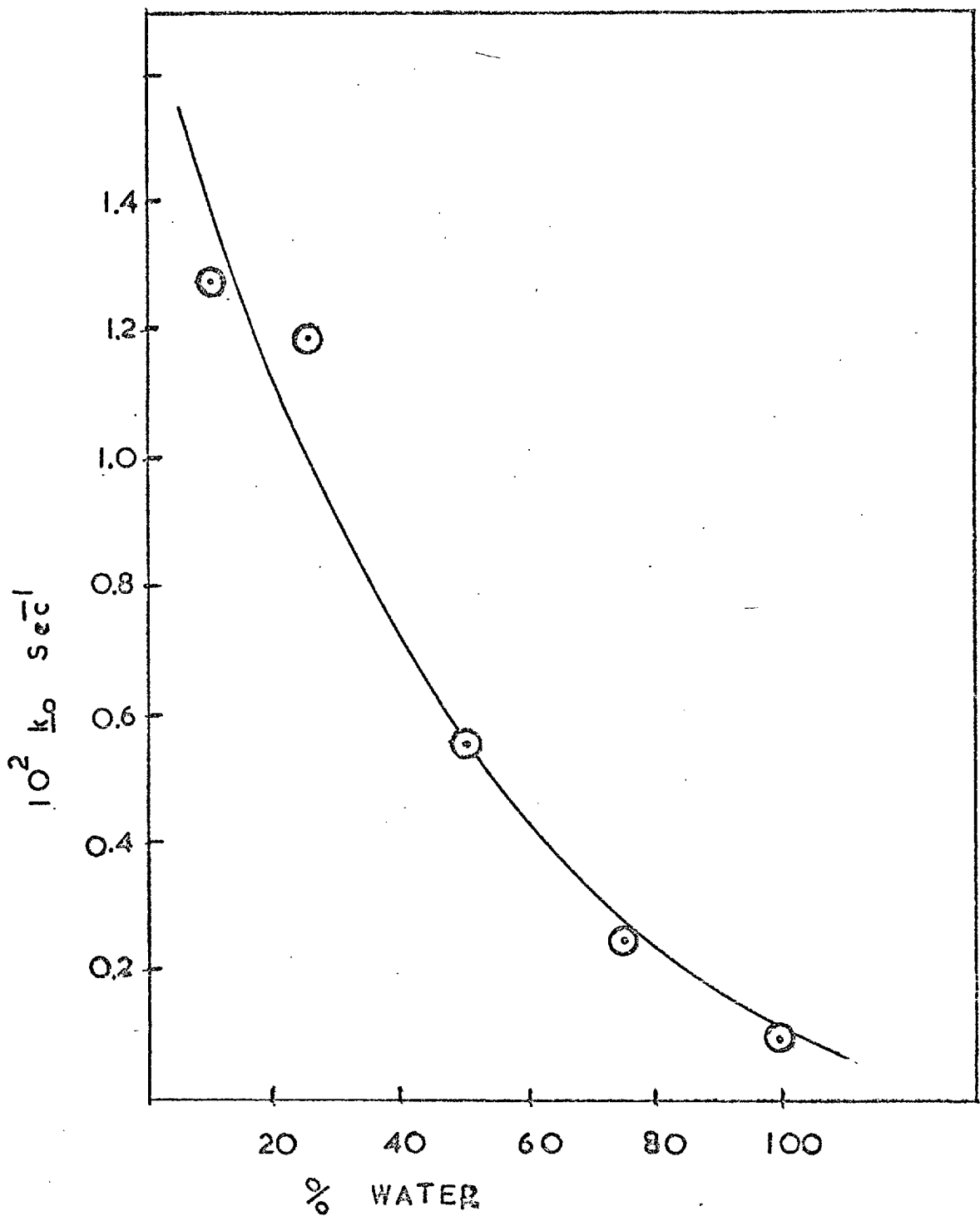


Fig. (V-5) Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by 0.051 M NaSCN in various dioxan-water mixtures at 25°C.

Hydroxide ion was found to react about 6 times faster in dioxan-water and about 3 times faster in acetonitrile-water than in water alone.

#### V.1.8 Thermodynamic parameters

The hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine in water catalysed by thiocyanate was examined at various temperatures. The data are presented in Table (V-9).

TABLE (V-9)

Experimental data for calculating 'Energy of Activation'

$[\text{NaOH}] = 1 \times 10^{-3} \text{ M}$ ;  $\mu = 1.0$ ; initial [substrate]  $\approx (1-1.5) \times 10^{-4} \text{ m/l}$

| Expt. | $t^{\circ}\text{C}$ | $T^{\circ}\text{K}$ | $10^3/T$ | $[\text{SCN}^-]$<br>M | $10^4 k_o$<br>$\text{sec}^{-1}$ | $10^4 k_{bi}$<br>$\text{l mole}^{-1} \text{sec}^{-1}$ |
|-------|---------------------|---------------------|----------|-----------------------|---------------------------------|-------------------------------------------------------|
| 418   | 4                   | 277.15              | 3.608    | 0.2                   | 8.33                            | 41.67                                                 |
| 417   | 15.4                | 288.55              | 3.465    | 0.2                   | 23.0                            | 115.0                                                 |
| 419   | 34.5                | 307.65              | 3.25     | 0.02                  | 9.33                            | 466.67                                                |
| 420   | 39                  | 312.15              | 3.203    | 0.019                 | 12.33                           | 632.3                                                 |
| 389   | 25                  | 298.15              | 3.354    | 0.1                   | 19.167                          | 191.67                                                |

Logarithms of the bimolecular rate constants ( $k_{bi}$ ) were plotted against  $\frac{1}{T}$ , and from the slope  $\left[ = \frac{E_a^\ddagger}{2.303R} \right]$  of the best straightline, the energy of activation ( $E_a^\ddagger$ ) was calculated to be  $59 \text{ k J. mole}^{-1}$  {fig. (V-6)}.

The entropy of activation was then calculated from eqn. (V-4)

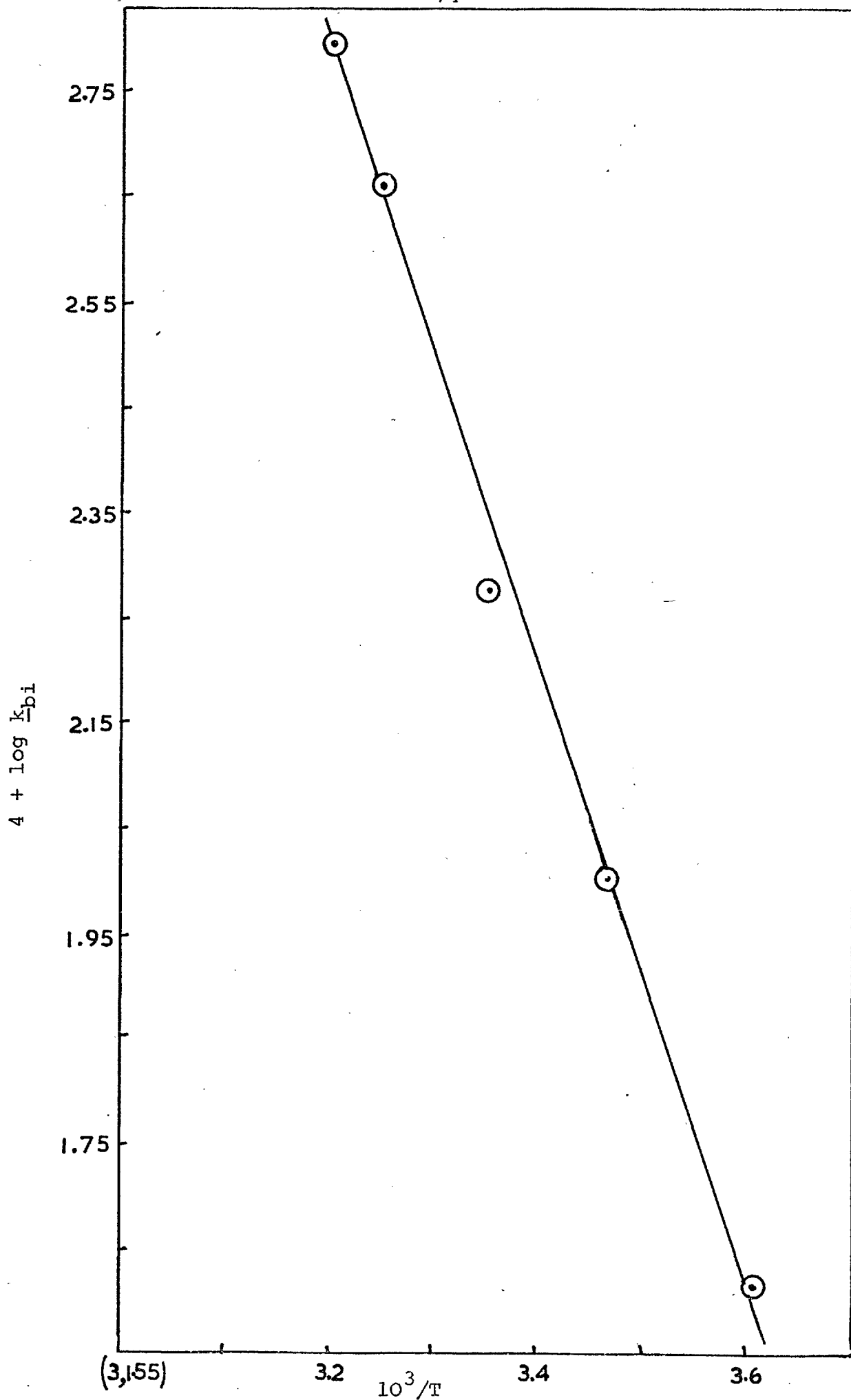


Fig. (V-6) Variation of  $k_{bi}$  (for  $SCN^-$ ) with temperature.

$$\log k_{bi} = \log \frac{k'T}{h} + \frac{\Delta S^\ddagger}{2.303R} - \frac{E_a^\ddagger}{2.303RT} \quad (V-4)$$

(neglecting the transmission coefficient which is usually unity)

where,  $k_{bi}$  has the same meaning as before,  $k'$  is the Boltzmann constant,  $h$  is Planck's constant,  $\Delta S^\ddagger$  is the entropy of activation,  $R$  is the molar gas constant and  $T$  is the temperature on the absolute scale. The entropy of activation ( $\Delta S^\ddagger$ ) was calculated to be  $-79 \text{ J.K}^{-1} \text{ mole}^{-1}$ .

Calculation of the thermodynamic parameters  $\Delta H^\ddagger$  (enthalpy) and  $\Delta F^\ddagger$  (free energy of activation) were made from eqns. (V-5) and (V-6) respectively.

$$\Delta H^\ddagger = E_a^\ddagger - RT \quad (V-5)$$

$$\Delta F^\ddagger = \Delta H^\ddagger - T\Delta S^\ddagger \quad (V-6)$$

The values calculated were

$$\Delta H^\ddagger = 56.5 \text{ k J. mole}^{-1}$$

$$\Delta F^\ddagger = 98 \text{ k J. mole}^{-1}$$

#### V.1.9 Hydrolysis of O-(2,4-dinitrophenyl)-N-methyl-hydroxylamine

Some nucleophilic displacement reactions on the above substrate were also investigated in water and are reported in Table (V-10). All the results reported were obtained at  $40^\circ\text{C}$ . No allowance has been made for the water rate in these runs and no sodium hydroxide has been added.

TABLE (V-10)

Hydrolysis of O-(2,4-dinitrophenyl)-N-methylhydroxylamine catalysed by nucleophiles at 40°C in water

| Expt. | Nu            | [Nu]<br>M | $10^4 k_o \text{ sec}^{-1}$ | $10^4 k_{bi}$<br>$\ell \text{ mole}^{-1} \text{ sec}^{-1}$ |
|-------|---------------|-----------|-----------------------------|------------------------------------------------------------|
| 444   | $\text{Cl}^-$ | 3.1       | 0.62                        | 0.199                                                      |
| 447   | $\text{Br}^-$ | 1.98      | 1.78                        | 0.9                                                        |
| 448   | $\text{I}^-$  | 0.7       | 2.27                        | 3.24                                                       |
| 453   | Pyridine      | 1.05      | 0.415                       | 0.395                                                      |
| 455   | 2,6-Lutidine  | 0.614     | 0.095                       | 0.15                                                       |

V.1.10 Reactions in dimethylsulphoxide

Some reactions were also carried out in the dipolar aprotic solvent (DMSO). The results are presented in Table (V-11). To counteract the spontaneous rate in this solvent, the reactions were followed by the differential U.V. method as described in Chapter IX.

TABLE (V-11)

Nucleophilic displacement reactions of O-(2,4-dinitrophenyl)-N-methyl-hydroxylamine in DMSO at 40°C

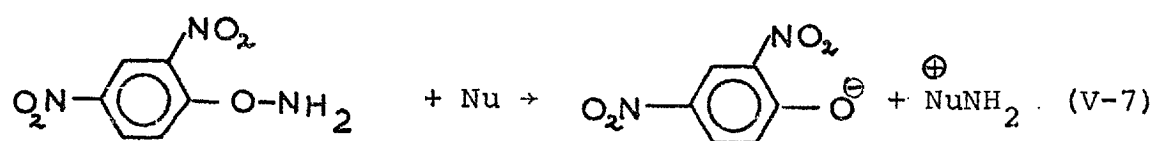
initial [substrate]  $\approx (10^{-7} - 10^{-8}) \text{ m}/\ell$

| Expt. | [Nu]  | Nu            | $10^4 k_o \text{ sec}^{-1}$ | $10^4 k_{bi}$<br>$\ell \text{ mole}^{-1} \text{ sec}^{-1}$ |
|-------|-------|---------------|-----------------------------|------------------------------------------------------------|
| 458   | 0.118 | $\text{Cl}^-$ | 0.068                       | 0.58                                                       |
| 459   | 0.059 | $\text{Br}^-$ | 0.104                       | 1.77                                                       |
| 460   | 0.038 | $\text{I}^-$  | 2.21                        | 58.0                                                       |

## V.2 Discussion

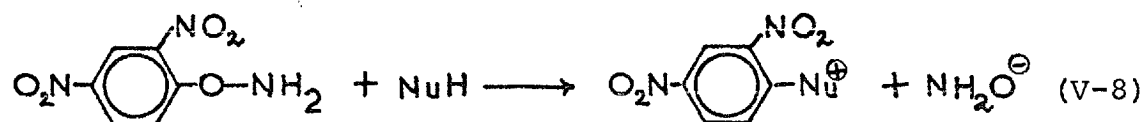
### V.2.1 Site of Nucleophilic Attack

Sheradsky<sup>78</sup> and his colleagues have already reported the amination of many substances (Table II-1) by O-(2,4-dinitrophenyl)-hydroxylamine which suggests that nucleophilic attack occurs on the nitrogen. Recently, Ross<sup>80</sup> has identified S-phenyl sulphenamide as the reaction product of O-(2,4-dinitrophenyl)-hydroxylamine with thiophenoxide. The products of reaction were investigated further in the present study. With one exception ( $\text{OH}^\ominus$  as mentioned previously), 2,4-dinitrophenoxide ion was formed in quantitative yield, as measured by U.V. assay of the reaction solutions at infinity {eqn. (V-7)}.

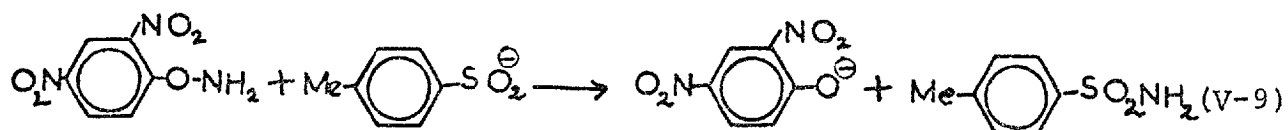


This suggests that for all the reactions investigated, cleavage of the O-N bond preferentially occurred. {eqn. (V-7)}.

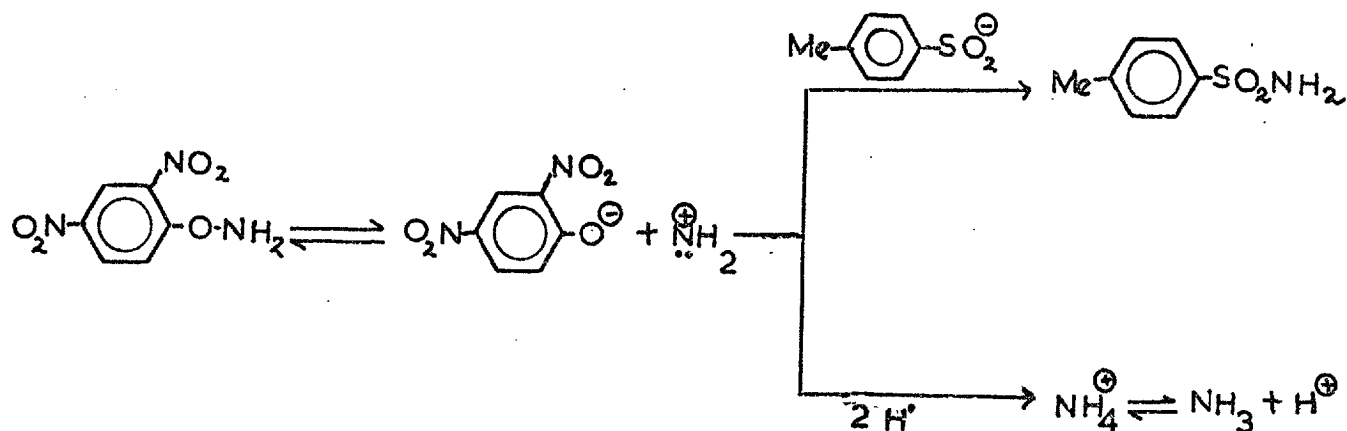
Had attack at the aromatic ring occurred {eqn. (V-8)}, then the yield of phenoxide ion would have been less than quantitative.



In one case, the reaction of p-toluene sulphinic acid anion with O-(2,4-dinitrophenyl)-hydroxylamine {eqn. (V-9)}, the yield of aminated product (p-toluenesulphonamide) obtained under conditions similar to those for the kinetic experiments was found



to be 87%. This further confirms that nucleophilic attack occurs predominantly at the N-atom. It also suggests that little reaction occurs via free nitrenium ions {Scheme (V-1)}, as reported for O-acylhydroxylamines<sup>111</sup>.



Scheme (V-1) Probable nitrenium ion intermediate

In this case, substantial amounts of ammonia would be expected at the expense of p-toluenesulphonamide.

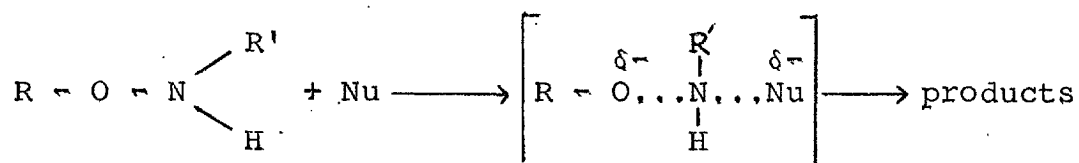
The possibility of an  $S_N1$  reaction, as implied by Scheme (V-1) is discussed further below.

#### V.2.2 Mechanism of Nucleophilic Substitution

The reactions of O-(2,4-dinitrophenyl)hydroxylamine in water catalysed by various nucleophiles are quite clean as shown by the beautiful isosbestic point(s) observed in most cases {fig.(IX-1)}.

Given as deduced above that substitution occurs predominantly at the N-atom, the question of whether this occurs by an  $S_N1$  or an  $S_N2$  pathway remains. As noted above, the isolation

of 87% of p-toluenesulphonamide from reaction with p-toluene-sulphinate ion clearly excludes significant  $S_N1$  reaction via a nitrenium ion. Most of the other evidence strongly supports an  $S_N2$  pathway as per Scheme (V-2).



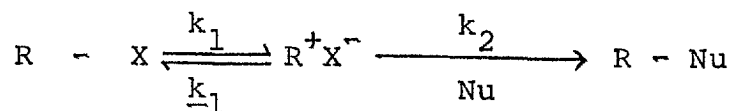
Scheme (V-2)  $S_N2$  transition state in reaction between O-(nitro-aryl)-hydroxylamine and nucleophile

Thus good second order kinetics are observed for the reaction of both  $SCN^\ominus$  and piperidine. Also, the rate of reaction closely depends on the structure of the nucleophile which shows that ionization of the O-(2,4-dinitrophenyl)-hydroxylamine is not rate-limiting.

For  $SCN^\ominus$ , the energy of activation ( $E_a^\ddagger$ ) and free energy of activation ( $\Delta F^\ddagger$ ), 59 and 98 kJ. mole<sup>-1</sup> respectively are low, in agreement with the facile reaction observed. The entropy of activation is of more interest as far as the mechanism is concerned. Its value of -79 J.K.<sup>-1</sup> mole<sup>-1</sup> (-19 e.u.) is in line with that expected for an  $S_N2$  mechanism<sup>112,113</sup> where loss of translational freedom occurs forming the transition state.

The 'contact ion-pair mechanism' suggested by Sneed and Larsen<sup>114</sup> as an alternative explanation for  $S_N2$  reactions and later supported by Scott<sup>115</sup> and Koskikallio<sup>116</sup>, which involves ionization of the substrate to a contact ion-pair, and subsequent reaction of the nucleophile with the carbonium ion of the contact ion-pair apparently occurring by a two step

process as per Scheme (V-3) does not seem to be applicable



Scheme (V-3) Contact ion-pair mechanism (involving two steps)

in the present case. The reaction of  $SCN^{\ominus}$  with O-(2,4-dinitro-phenyl)hydroxylamine was examined in various dioxan-water mixtures (Table V-8) with a wide variation in dielectric constant of the medium. The dependence of rate on solvent composition is shown in fig. (V-5). The curvature observed may be due to the preferential solvation of the activated complex by the component having the higher dielectric constant<sup>117</sup>. This dependence would have been observed more clearly if mole-fractions were available for the solvent composition. However, the highest rate is observed at lowest water concentration (and consequently lower dielectric constant of the medium). This cannot support the idea of significant charge development (and therefore ion formation) in the transition state and hence lends weight to the traditional  $S_N2$  mechanism. The effect of solvent on the reaction rate for  $SCN^{\ominus}$  clearly excludes an  $S_N1$  mechanism.

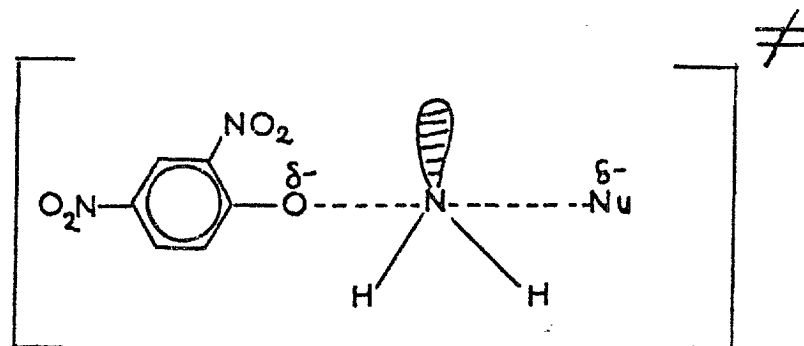
The  $SCN^{\ominus}$  is strongly solvated in water by hydrogen bonding; decrease of water concentration thereby increases the nucleophilicity of this ion. This effect probably accounts for the increased rate of reaction with increasing dioxan concentration in the mixed solvent.

### V.2.2.1 Steric Inhibition

$S_N2$  reactions at a tetrahedral carbon are subject to steric inhibition<sup>113</sup>, but the question of whether such steric hindrance would be expected for substitution at trivalent nitrogen has not previously been considered. The essential difference between a tetravalent carbon and a trivalent nitrogen is that in the latter, one of the four  $sp^3$  orbitals contains a non-bonding lone-pair of electrons only.

Moreover, for trivalent nitrogen compounds of the type  $Nabc$ , the energy barrier to inversion about the nitrogen is relatively small. In the case of ammonia, for example, the molecule inverts configuration passing through a planar form with an energy of about  $25 \text{ kJ. mole}^{-1}$  higher than the pyramidal form and the frequency of inversion is therefore high even at low temperatures<sup>118</sup>. This is why sundry attempts to resolve simple tertiary amines have failed. Therefore, the question of steric inhibition in the case of substitution of trivalent nitrogen compounds may not be clear cut.

In the first instance, however, it seems likely that charge repulsion between the incoming nucleophile and the nitrogen lone-pair of electrons will ensure that the latter exist in an  $sp^3$  hybridised orbital, and that the transition state for  $S_N2$  substitution is therefore similar to that for reactions of carbon compounds (z).



(z)

In this event, steric effects for substitution at nitrogen should be less than those observed for carbon.

In the case of nucleophilic attack on O-(2,4-dinitrophenyl)-hydroxylamine, the second order rate constant for pyridine is only about 3 times greater than that for 2,6-lutidine {Table (V-6)}. In the case of O-(2,4-dinitrophenyl)-N-methylhydroxylamine also almost the same order of steric inhibition is observed {Table (V-10)}. Thus, the small steric inhibition that is observed, refers mainly to the incoming group which is consistent with the prediction that the steric environment about N is more free than that found for substitution of comparable carbon compounds.

An important observation is that the reaction rates of the N-methylhydroxylamine are about 8 times slower than those for the unsubstituted compound. This stems probably from the inductive effect of the methyl group reducing the electron-deficient character of the N-atom rather than from a substantial steric effect.

Thus the above results clearly point to an  $S_N2$  pathway for the nucleophilic substitution investigated, at least for reagents more nucleophilic than 2,6-lutidine. There is a remote possibility that reactions of the weakest nucleophiles involve an  $S_N1$  component, but no direct evidence to this effect was obtained.

### V.2.3 Order of Nucleophilic Reactivity

The order of nucleophilic reactivity towards the N-atom, in O-(2,4-dinitrophenyl)hydroxylamine has been summarised in Table (V-7). This order is:

$\text{SeC}(\text{NH}_2)_2 > \text{S}_2\text{O}_3^{2-} > \text{SeCN}^- > \text{SC}(\text{NH}_2)_2 > \text{I}^- > \text{HOO}^- > \text{piperidine}$   
 $> \text{p-toluenesulphonate} > \text{Et}_2\text{NH} > \text{CN}^- > \text{SCN}^- > \text{morpholine} >$   
 $\text{n-butylamine} > \text{NH}_2\text{OH} > \text{benzylamine} > \text{N}_2\text{H}_4 > \text{aniline} > \text{OH}^- >$   
 $\text{N}_3^- > \text{Br}^- > \text{pyridine} > \text{NO}_2^- > \text{2,6-lutidine} > \text{PhO}^- > \text{Cl}^- > \text{OAc}^-.$

The high reactivity of selenium and sulphur bases is clearly evident suggesting that polarizability of the nucleophile is important. Likewise the reactivity of the iodide ion is also due to its high polarizability. The highly reactive nucleophiles {Table (V-7)} are also soft bases and their reactivity can be explained qualitatively in terms of the HSAB principle (Chapter I). Acetate, phenoxide and chloride ions, all of which are hard bases, show the lowest reactivity.

#### V.2.4 Alpha-effect

The results also show evidence of a small  $\alpha$ -effect (see Chapter I) for suitable nucleophiles. This is evident, for example, from the datum for perhydroxylion ( $\text{HO}_2^\ominus$ ) which is about 120 times more reactive than the hydroxide ion. The enhancement is small compared with those reported for other reactions, but is similar to that for nucleophilic displacement on benzyl bromide<sup>35</sup>. The implication is that substitution at electron-deficient nitrogen is similar to that at carbon.

Neither  $\text{NH}_2\text{OH}$  nor  $\text{N}_2\text{H}_4$  show significant rate enhancement in comparison with other amine bases. This is evident from the plot of  $\log k_{\text{bi}}$  {eqn. (V-2)} versus  $\text{pK}_{\text{Nu}}$  for various nitrogen bases shown in fig. (V-7). The data for  $\text{NH}_2\text{OH}$ ,  $\text{N}_3^\ominus$  and  $\text{N}_2\text{H}_4$  do not lie significantly off the best line drawn through various points. Again this suggests that  $\alpha$ -effects are small for the reaction.

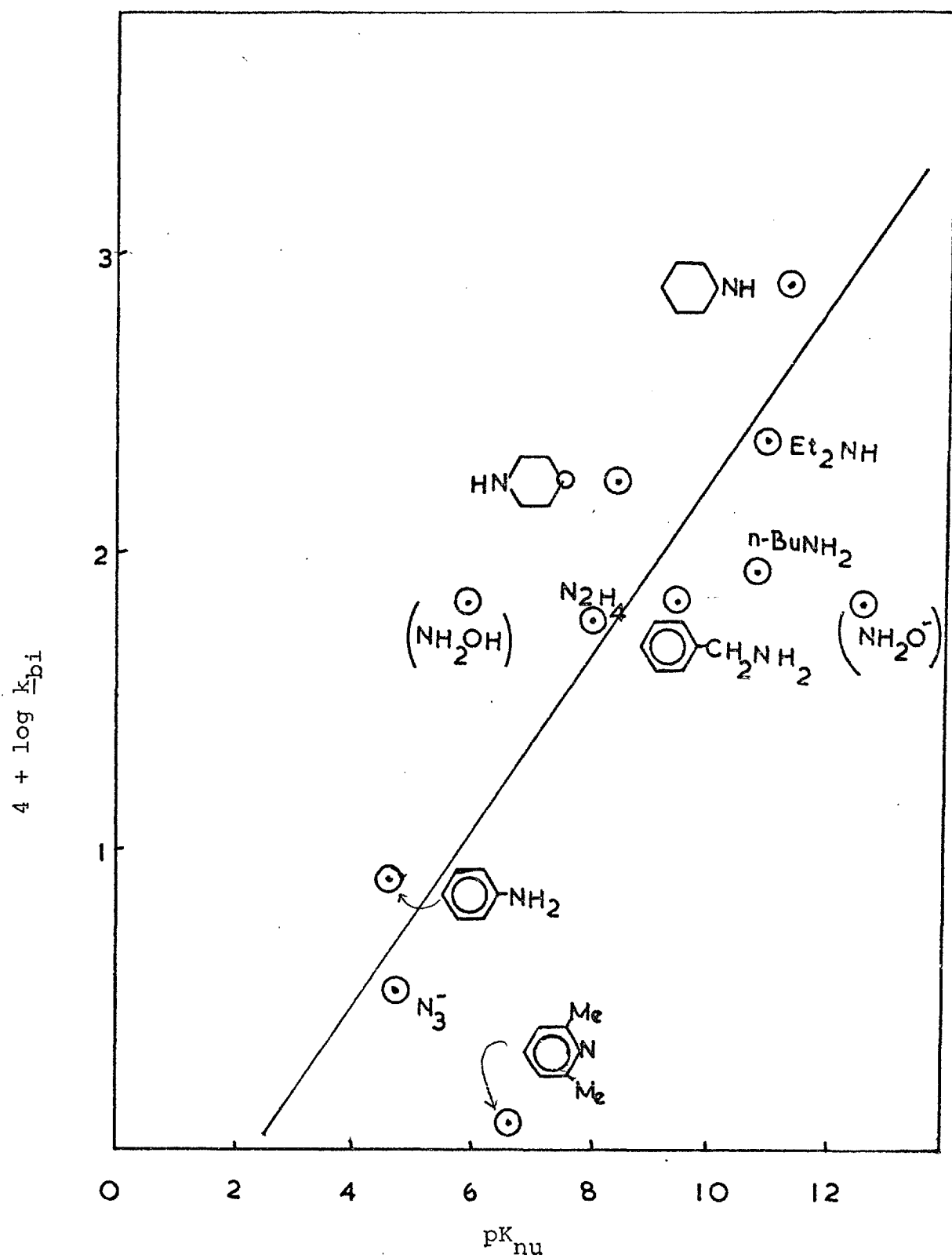


Fig. (V-7)  $\log K_{bi}$  against  $pK_{nu}$  of some  $\alpha$ -nucleophiles and nitrogen bases.

## V.2.5 Correlation of Reactivity

### V.2.5.1 Polarizability

Because of the importance of the polarizability factor, it is worthwhile to see how well the relative rates correlate with electrode potential which is a measure of electron polarizability. The relationship where  $\log \left[ \frac{k_{bi}}{k_{H_2O}} \right]$  is plotted against  $E_N$  is shown in fig.(V-8). The term  $E_N$  refers to Edwards<sup>21,32</sup> polarizability factor, which is the difference between the standard electrode potential ( $E_n^O$ ) for nucleophile (n) and that for  $H_2O$  {eqn.(V-10)}.

$$E_n = E_n^O - E_{H_2O}^O = E_n^O + 2.6 \quad (V-10)$$

The bimolecular rate coefficients ( $k_{bi}$ ) have been normalised similarly by subtraction of the coefficient for the  $H_2O$  nucleophile. Except for the cyanide ion and perhydroxyl ion, the latter having approximate  $E_N$  values, the other nucleophiles reasonably reflect the importance of the electron polarizability. The best straightline through these data has a slope of 3.3. This corresponds to the  $\alpha$  of the Edwards<sup>21,32</sup> equation.

### V.2.5.2 Brönsted Relation

A convenient Brönsted plot for the same data, however, shows wide scattering {fig.(V-9)} and the best straight line if any, has a very small slope (Edwards  $\beta$  parameter) suggesting the relative unimportance of the basicity factor.

### V.2.5.3 Edwards Correlation

Although it is evident from fig.(V-8) and fig.(V-9) that

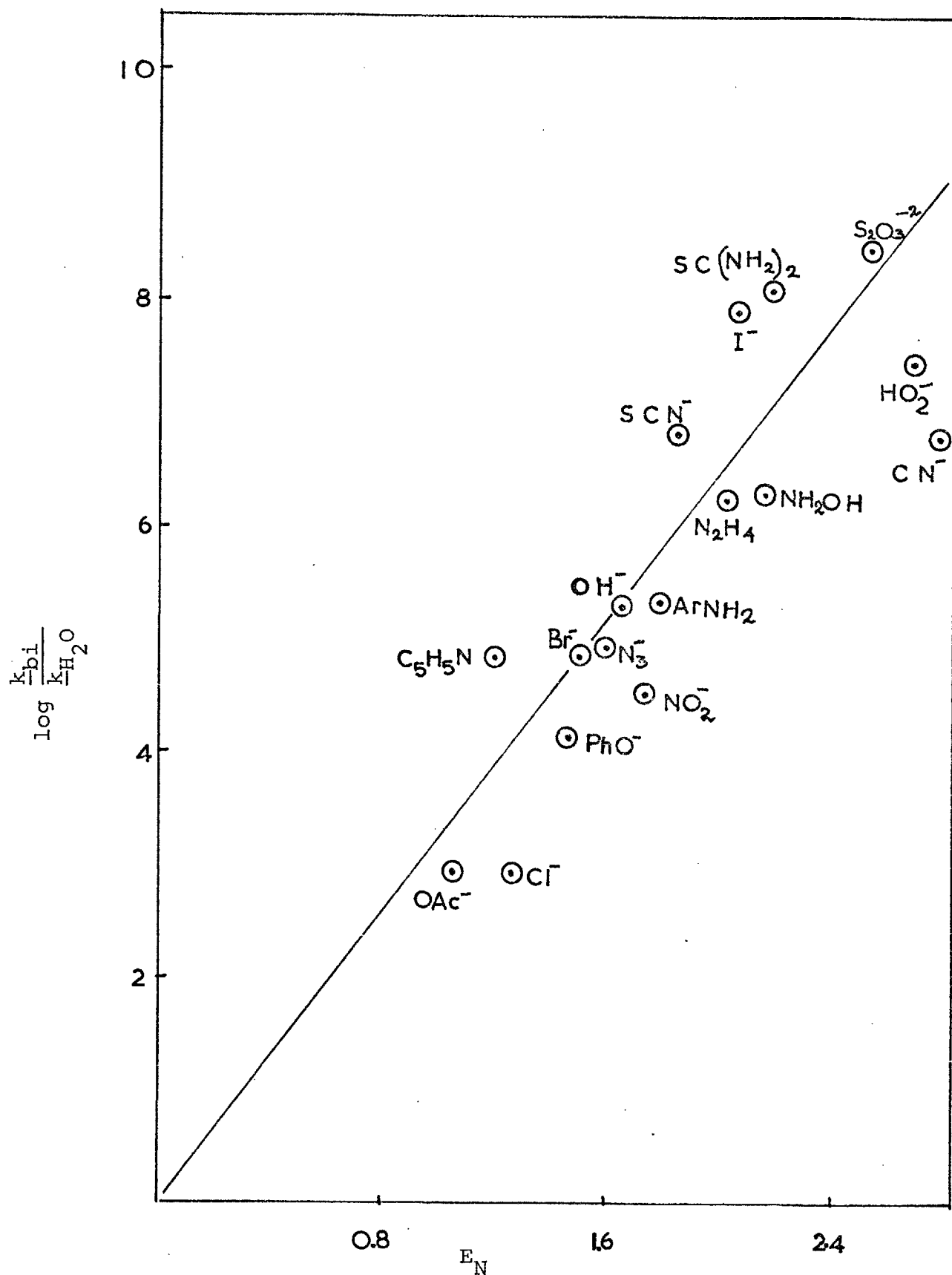


Fig. (V-8) Dependence of the relative rates on the polarizability of nucleophiles.

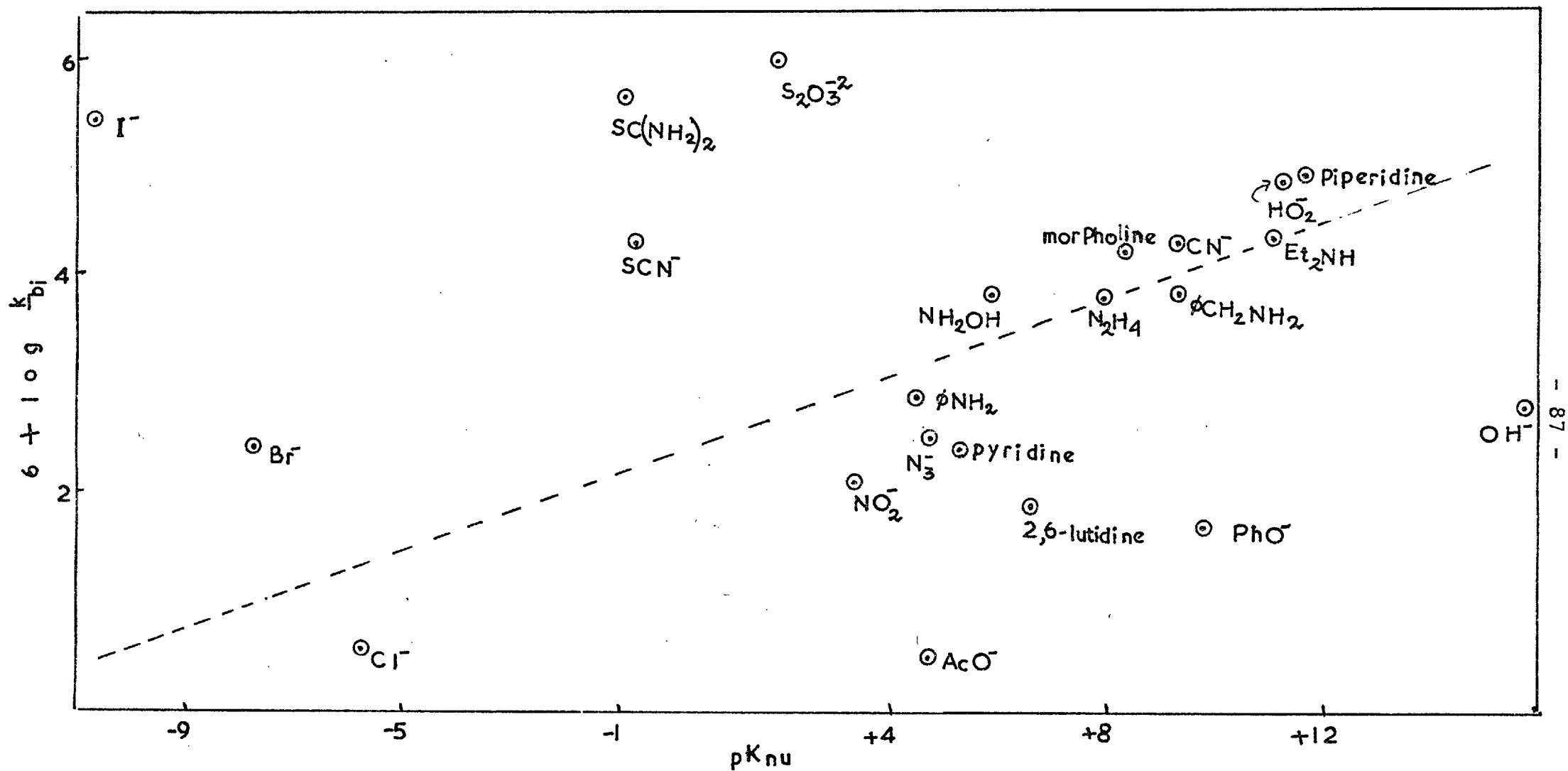


Fig.(V-9) Brønsted plot for the hydrolysis of O-(2,4-dinitrophenyl)hydroxylamine (25°C).

polarizability of the nucleophile is of prime importance in determining its reactivity, it is interesting to see how well the data are correlated by the Edwards equation (see Chapter I) which treats reactivity as a linear combination of polarizability and basicity. The necessary data are presented in Table (V-12) and fig.(V-10) shows the correlation.

TABLE (V-12)

Necessary data<sup>21,43,119</sup> for Edwards Correlation

| Nu                                          | $\frac{1}{E_N}$ | $\frac{1}{E_N} \log \left( \frac{k_{bi}}{k_{H_2O}} \right)$ | $H/E_N$ |
|---------------------------------------------|-----------------|-------------------------------------------------------------|---------|
| Br <sup>-</sup>                             | 0.66            | 3.214                                                       | -3.97   |
| N <sub>3</sub> <sup>-</sup>                 | 0.63            | 3.121                                                       | +4.08   |
| SCN <sup>-</sup>                            | 0.54            | 3.632                                                       | +0.55   |
| CN <sup>-</sup>                             | 0.35            | 2.369                                                       | +3.9    |
| S <sub>2</sub> O <sub>3</sub> <sup>-2</sup> | 0.39            | 3.291                                                       | +1.43   |
| C <sub>5</sub> H <sub>5</sub> N             | 0.83            | 4.017                                                       | +5.87   |
| SC(NH <sub>2</sub> ) <sub>2</sub>           | 0.45            | 3.649                                                       | +0.37   |
| NO <sub>2</sub> <sup>-</sup>                | 0.57            | 2.569                                                       | +2.94   |
| Cl <sup>-</sup>                             | 0.80            | 2.359                                                       | -2.42   |
| OAc <sup>-</sup>                            | 1.05            | 3.05                                                        | +6.8    |
| I <sup>-</sup>                              | 0.485           | 3.828                                                       | -4.37   |
| NH <sub>2</sub> OH                          | 0.465           | 2.917                                                       | +3.63   |
| N <sub>2</sub> H <sub>4</sub>               | 0.495           | 3.087                                                       | +4.78   |
| PhO <sup>-</sup>                            | 0.685           | 2.837                                                       | +8.04   |
| Aniline                                     | 0.562           | 2.994                                                       | +3.53   |
| HOO <sup>-</sup>                            | 0.374           | 2.76                                                        | +4.94   |
| HO <sup>-</sup>                             | 0.606           | 3.2                                                         | +10.6   |

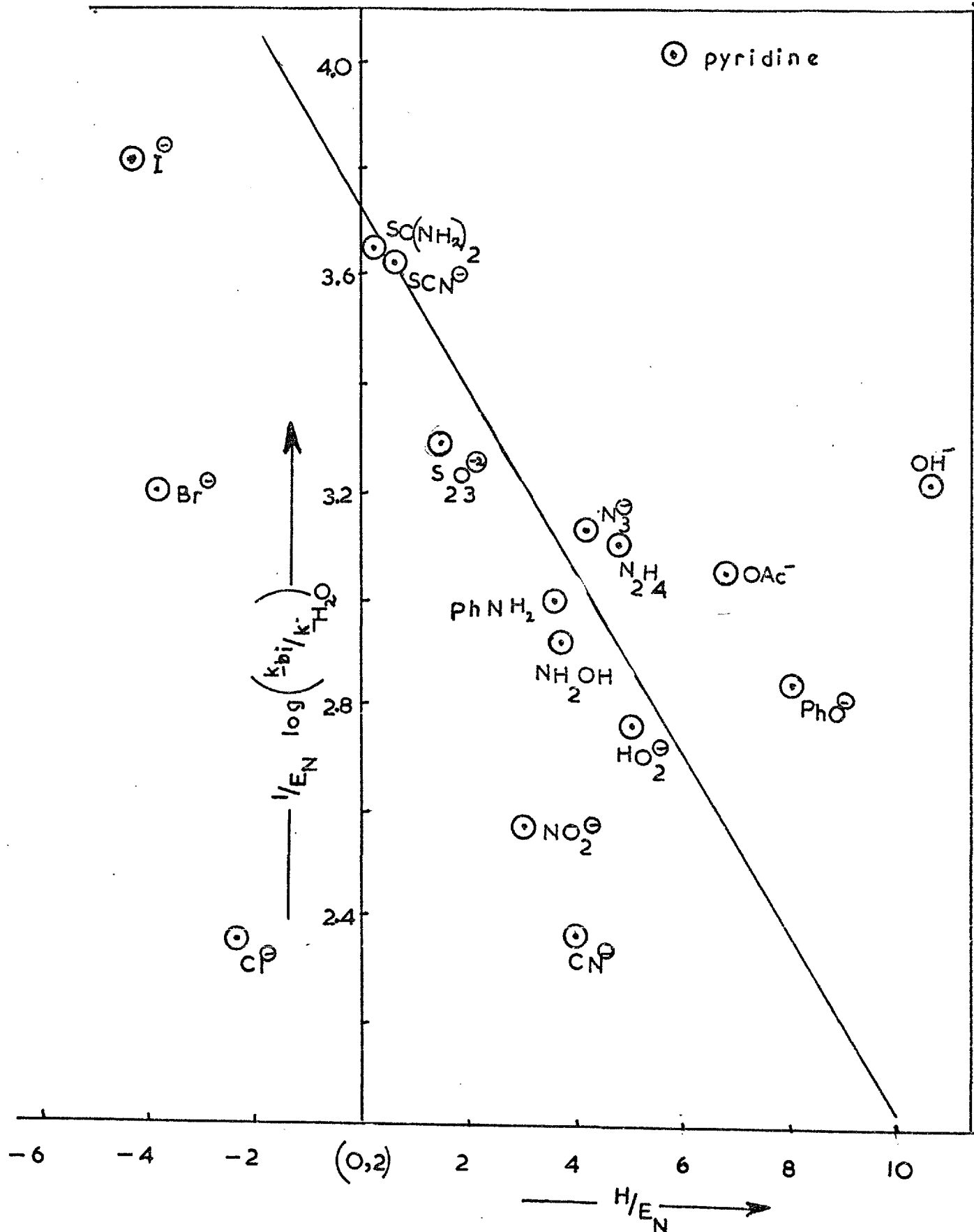


Fig. (V-10) A plot of Edwards linear free energy eqn. for reactions of O-(2,4-dinitrophenyl)hydroxylamine with various nucleophiles in water at 25°C.

It can be seen that the relationship is not very satisfactory and the plot of  $\frac{1}{E_N} \log \left[ \frac{k_{bi}}{k_{H_2O}} \right]$  vs.  $^H/E_N$  {see fig.(V-10)} is not better than that obtained from considering the polarizability factor alone (fig.V-8). In particular, the points for  $Cl^-$ ,  $Br^-$  and  $I^-$  lie well off the line, presumably because these nucleophiles have highly negative  $pK_A$  values. The points for pyridine and  $HO^\ominus$  lie off the line in the other direction and for  $HO^\ominus$  this is clearly linked to its highly positive  $pK_A$ . The implication is that the Edwards equation overweights the contribution from the basicity of the nucleophile. The best straightline drawn has an intercept ( $= \alpha$ ) of 3.7 and a slope ( $= \beta$ ) of -0.17 which again points to the importance of the polarizability factor. Comparison with polarizability constants ( $\alpha$ ) for displacement reactions on carbon shows that the present value is very similar to those reported<sup>21</sup> for benzyl chloride ( $\alpha = 3.53$ ) and benzoyl chloride ( $\alpha = 3.56$ ). This emphasizes that nucleophilic substitution at electron-deficient nitrogen is similar to that at carbon.

#### V.2.6 Comparison with other substrates

It is quite appropriate at this stage to compare the nucleophilic reactivity observed towards O-(2,4-dinitrophenyl)-hydroxylamine with that observed towards other electrophilic centres. This approach will provide practical knowledge about the 'softness' or 'hardness' of the nitrogen electrophile. Table (V-13) summarises some of the relative rates for purposes of comparison along with some important properties of the nucleophiles.

TABLE (V-13)

Relative Rates and some important properties of nucleophiles

| Nu            | 21<br>$E_N$   | 33,55<br>$pK_{Nu}$ | 116<br>$n_{CH_3Cl}$<br>(Water) | 5<br>$n_{CH_3Br}$<br>(Water) | 116<br>$n_{CH_3I}$<br>(Water) | 55<br>$n_{CH_3I}$<br>(MeOH) | 55<br>$n_{P_t(II)}$<br>(MeOH) | 116<br>$n_{PhSO_3Me}$<br>(Water) |
|---------------|---------------|--------------------|--------------------------------|------------------------------|-------------------------------|-----------------------------|-------------------------------|----------------------------------|
| $S_2O_3^{2-}$ | 2.52          | 1.9                | 6.35                           | 6.36                         | 7.44                          | 8.95                        | 7.34                          | 5.165                            |
| $SeCN^-$      |               |                    |                                |                              |                               | 7.85                        | 7.11                          |                                  |
| $SC(NH_2)_2$  | 2.18          | -0.96              |                                | 4.1                          |                               | 7.27                        | 7.17                          |                                  |
| $I^-$         | 2.06<br>(119) | -10.7              | 4.61                           | 5.04                         | 5.63                          | 7.42                        | 5.46                          | 3.383                            |
| $HOO^-$       | 2.676         | 11.5               |                                |                              |                               | (7.8)                       |                               |                                  |
| Piperidine    |               | 11.21              |                                |                              |                               | 7.3                         | 3.13                          |                                  |
| $Et_2NH$      |               | 11.0               |                                |                              |                               | ~7.0                        |                               |                                  |
| $CN^-$        | 2.79          | 9.3                | (5.2)                          |                              | 5.65                          | 6.7                         | 7.14                          | 4.3                              |
| $SCN^-$       | 1.83          | -0.7               | (4.65)                         | 4.77                         | 5.42                          | 6.7                         | 5.75                          | 3.5                              |
| Morpholine    |               | 8.33               |                                |                              |                               |                             |                               |                                  |
| $n-BuNH_2$    |               | 10.78              |                                |                              |                               |                             |                               |                                  |
| $NH_2OH$      | (43)<br>2.14  | 5.82 <sup>a)</sup> |                                |                              |                               | 6.6                         | 3.85                          |                                  |
| Benzylamine   |               | 9.33               |                                |                              |                               |                             |                               |                                  |
| $NH_2NH_2$    | (43)<br>2.02  | 7.93               |                                |                              |                               | 6.61                        | 3.86                          |                                  |
| Aniline       | 1.78          | 4.58               |                                | 4.49                         |                               | 5.7                         | 3.16                          |                                  |
| $OH^-$        | 1.65          | 15.74              | 4.14                           | 4.2                          | 4.69                          |                             |                               | 3.63                             |
| $N_3^-$       | 1.58          | 4.74               |                                | 4.0                          |                               | 5.78                        | 3.58                          | 3.345                            |
| $Br^-$        | 1.51          | -7.7               | 3.09                           | 3.89                         | 4.48                          | 5.79                        | 4.18                          | 2.563                            |
| $C_5H_5N$     | 1.2           | 5.23               |                                | 3.6                          |                               | 5.23                        | 3.19                          |                                  |
| $NO_2^-$      | 1.73          | 3.37               |                                |                              |                               | 5.35                        | 3.22                          | 3.271                            |
| $PhO^-$       | 1.46          | 9.89               |                                |                              |                               | 5.75                        |                               | 3.616                            |
| $Cl^-$        | 1.24          | -5.7               | (2.69)                         | 3.04                         | 3.36                          | 4.37                        | 3.04                          | 2.009                            |
| $OAc^-$       | 0.95          | 4.75               |                                | 2.72                         |                               | 4.3                         | <2.0                          | 2.327                            |

a) approximate  $pK_a$  for  $NH_2OH \rightleftharpoons NH_2O^- + H^+$  is ~ 12-13<sup>(120)</sup>

To effect this comparison, the ratio  $\log_{10} \frac{k_{bi}}{k_{H_2O}}$  is generally taken as a measure of the reactivity of any particular nucleophile towards O-(2,4-dinitrophenyl)-hydroxylamine. This means that the nucleophilic reactivity of  $H_2O$  is assumed to be unity, a procedure that has been widely adopted in the literature. The  $\log_{10} \frac{k_{bi}}{k_{H_2O}}$  ratio refers, of course, to reaction in  $H_2O$  at  $25^\circ C$ .

Various empirical indices are available for nucleophilic reactivity towards carbon centres. The relevant plots for  $MeCl$ ,  $MeBr$  and  $MeI$  are shown in fig. (V-11) → (V-13) respectively.

All the data for the methyl halides refers to studies in water solvent at  $25^\circ C$ , so these results are directly comparable with the present data. An interesting point is that the slope of each of these plots is close to unity ( $MeCl \approx 1.33$ ,  $MeBr \approx 1.31$  and  $MeI \approx 1.1$ ), which indicates that the reactivity towards electron-deficient nitrogen is similar to that for carbon compounds. Thus, bromide ion is about 60 times, 10 times and 3 times more reactive towards O-(2,4-dinitrophenyl)hydroxylamine than towards  $MeCl$ ,  $MeBr$  and  $MeI$  respectively. This indicates that the nitrogen electrophilic centre in question is similar to  $MeI$ .

This last deduction suggests that comparison with the extensive data obtained by Pearson<sup>55</sup> and his colleagues for substitution of  $MeI$  should be instructive. One disadvantage, however, is that Pearson's data refer to  $MeOH$  as solvent which is also taken as the reference nucleophile (i.e.  $k_{CH_3OH} = 1$ ). The relevant plot is shown in fig. (V-14). The line drawn through these data {Table (V-13)} has a slope close to unity ( $= 1.11$ ) and fits reasonably well, although deviations are

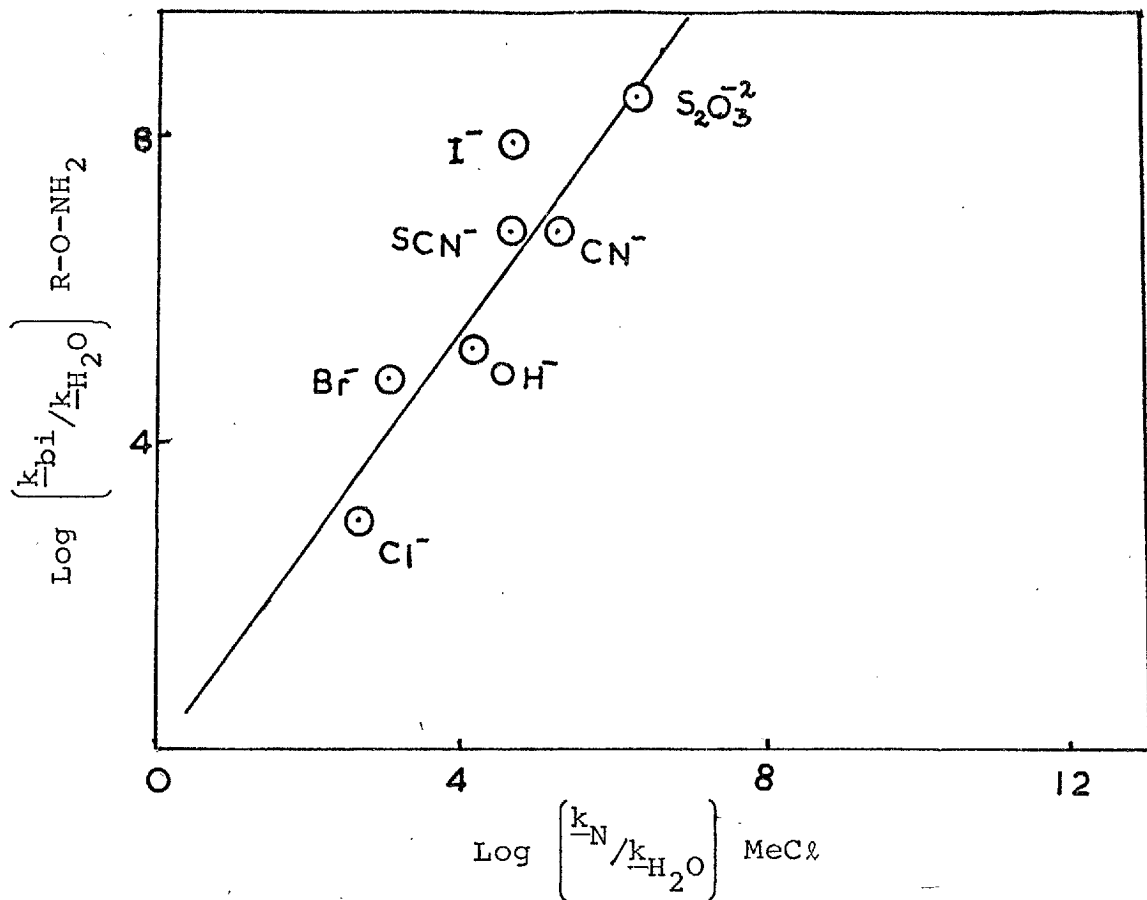


Fig. (V-11)

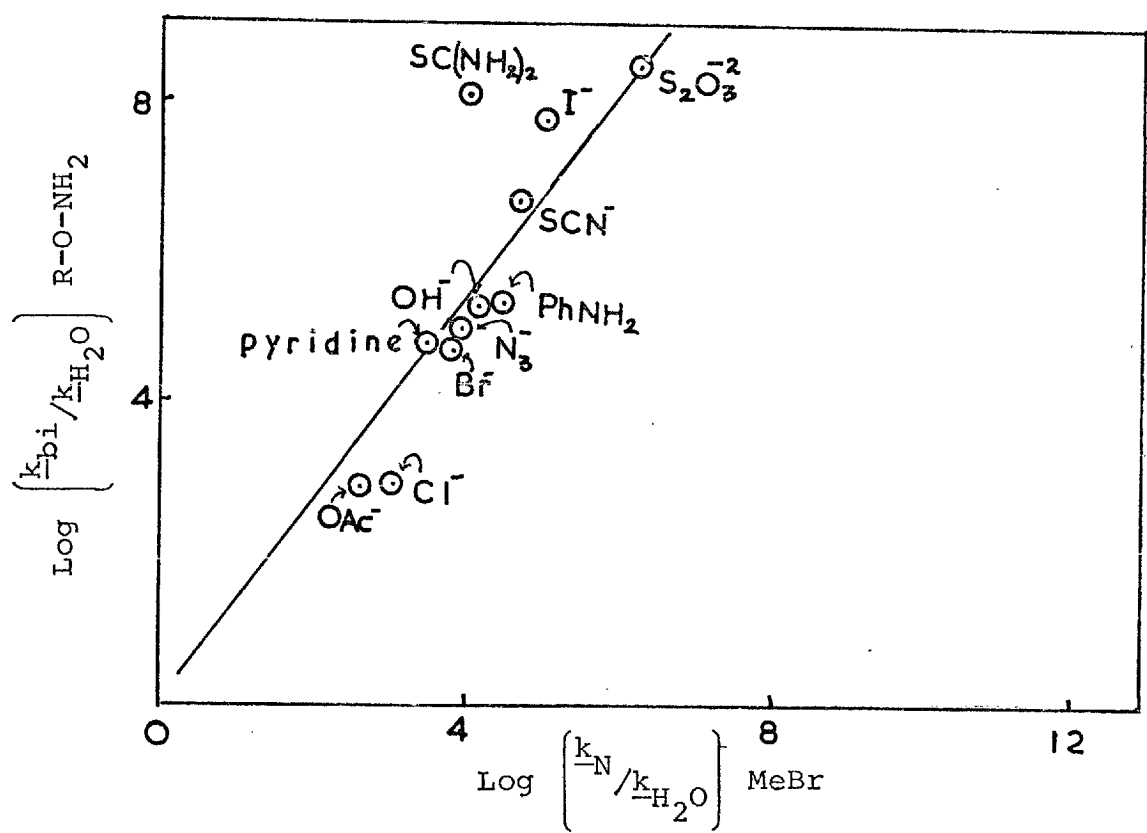


Fig. (V-12)

Comparison of relative reactivities of various nucleophiles towards O-(2,4-dinitrophenyl)hydroxylamine with those towards

- a) MeCl [fig. (V-11)]
- and
- b) MeBr [fig. (V-12)]

in water at 25°C.

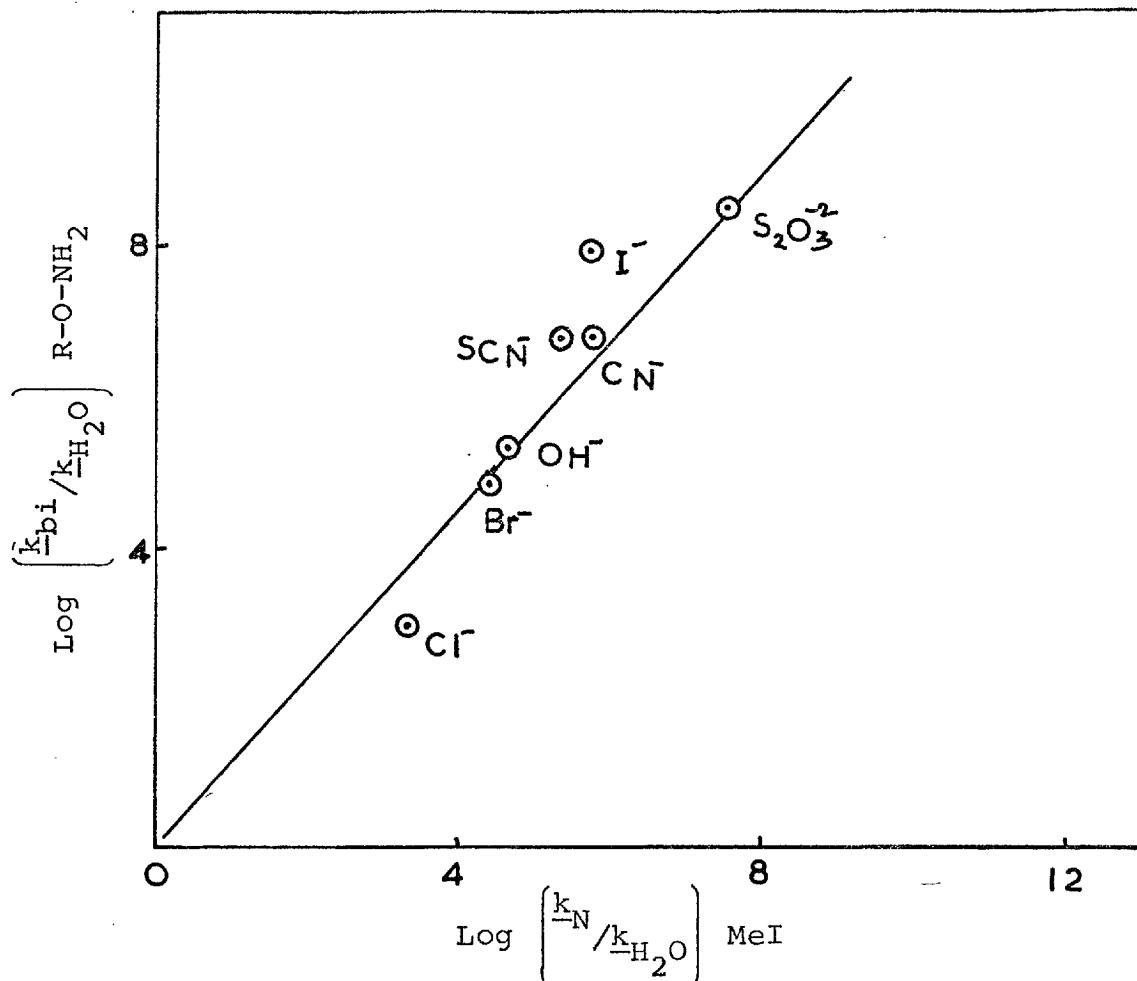


Fig. (V-13)

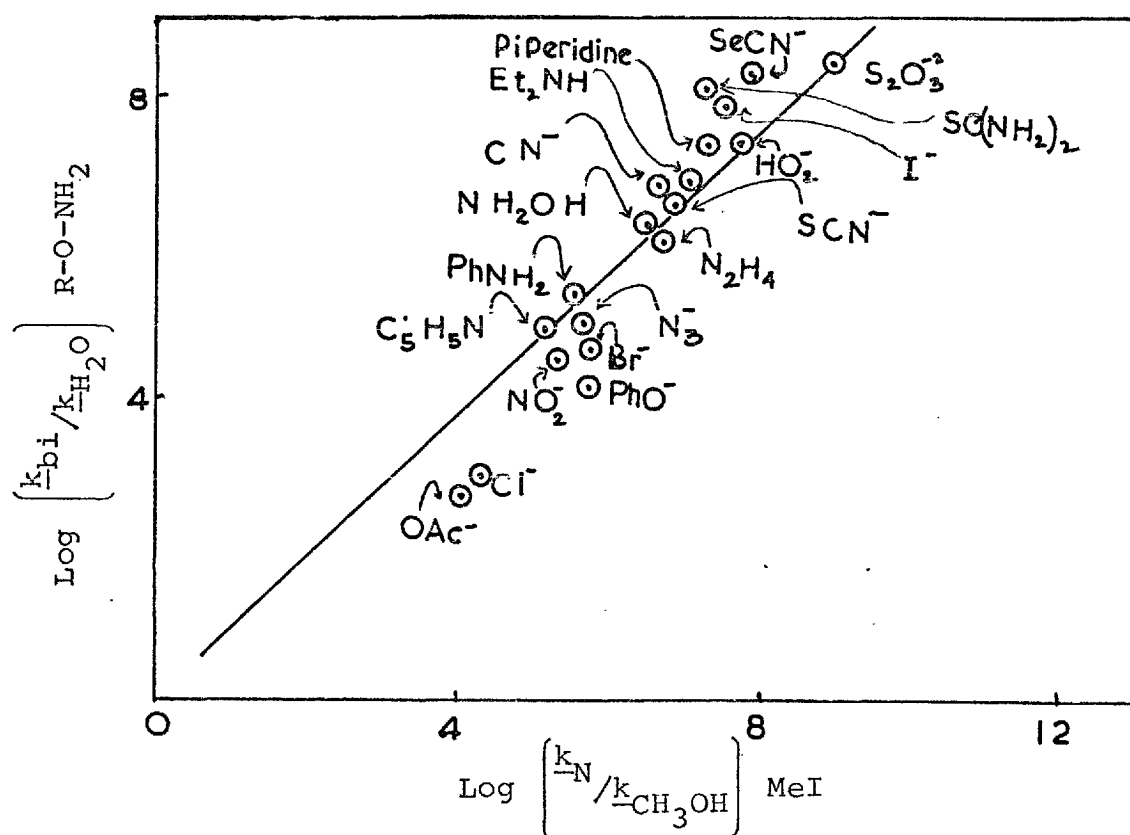


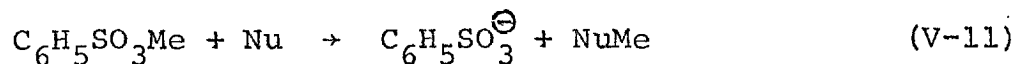
Fig. (V-14)

Comparison of relative nucleophilicities of various nucleophiles towards O-(2,4-dinitrophenyl)hydroxylamine in water with those towards

|        |     |             |                      |
|--------|-----|-------------|----------------------|
| a)     | MeI | in water    | fig. (V-13)          |
| and b) | MeI | in methanol | fig. (V-14) at 25°C. |

apparent for some nucleophiles. This lends further weight to the suggestion above that methyl iodide is a relatively good model for the hydroxylamine substrate, although the latter appears to be softer than the former.

Comparison with data {Table (V-13)} reported recently for substitution of methyl benzene sulphonate<sup>116</sup> (eqn. V-11)



is plotted in fig.(V-15). The points show considerable scatter and the straight line drawn has an approximate slope of 1.9. Comparison with bromide nucleophile reveals that it is about 200 times more reactive towards O-(2,4-dinitrophenyl)hydroxylamine than towards  $\text{PhSO}_3\text{Me}$ .

Although most of the previous studies have concerned substitution at carbon, some comparative data is available for other electrophilic centres. A Platinum (II) complex is regarded<sup>55</sup> as a very soft electrophilic centre. Some nucleophilicity constants involving Pt(II) have been reproduced in Table (V-13). The corresponding plot is shown in fig.(V-16). The poor correlation suggests that a transition metal is a poor model for the hydroxylamine substrate in question.

Nucleophilic reactivity towards other non-carbon centres has been reported, but here the data is less complete. Usually, the value for substitution by  $\text{H}_2\text{O}$  is not available. To effect a comparison in these cases, chloride ion has been taken as the reference nucleophile, and  $\log \left[ \frac{k_2}{k_{\text{Cl}}} \right]$  ratios from the literature are given in Table (V-14) for substitution at sulphenyl sulphur<sup>69,70</sup> {eqn.(V-12)}, peroxide oxygen<sup>121</sup> {eqn. (V-13)} and iodonium ion<sup>30</sup> {eqn. (V-14)} together with those

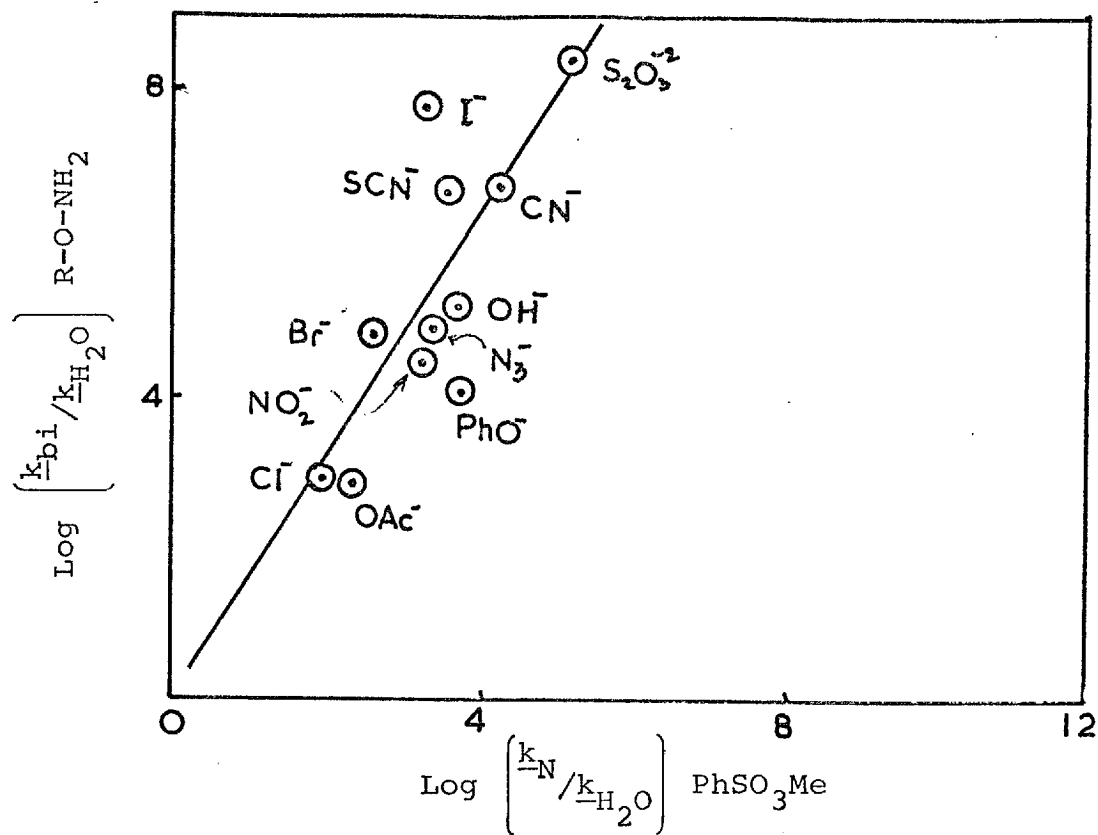


Fig. (V-15)

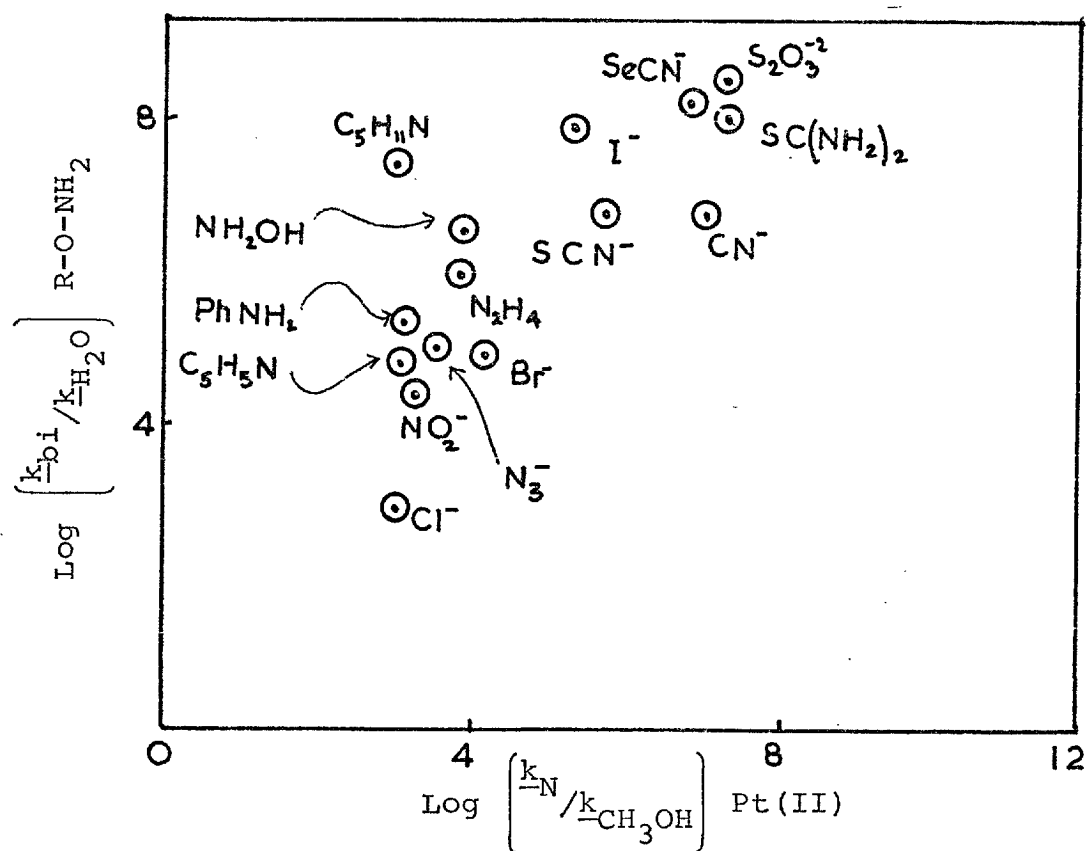


Fig. (V-16)

Comparison of relative reactivities of various nucleophiles towards O-(2,4-dinitrophenyl)hydroxylamine in water with those towards

a)  $\text{PhSO}_3\text{Me}$  in water, fig. (V-15)

and b)  $\text{Pt(II)}$  complex in  $\text{MeOH}$ , fig. (V-16)

at  $25^\circ\text{C}$ .

for O-(2,4-dinitrophenyl)hydroxylamine.

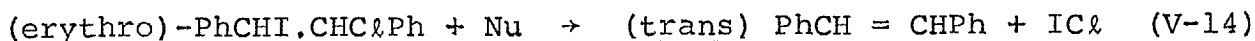
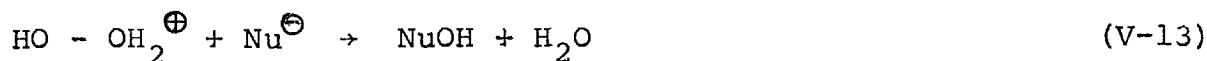
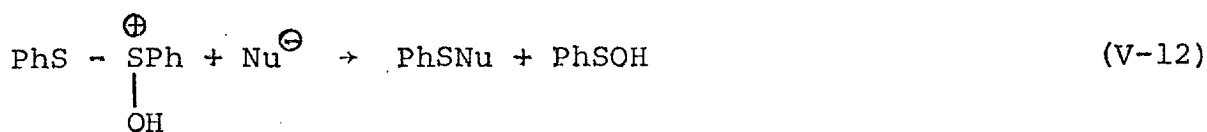


TABLE (V-14)

Comparison of Relative Rates towards non-carbon electrophilic centres

| Nu                         | $\log \left[ \frac{k_{bi}}{k_{Cl^-}} \right]_{N^+}$ | $\log \left[ \frac{k_2}{k_{Cl^-}} \right]_{I^+}$ | $\log \left[ \frac{k_2}{k_{Cl^-}} \right]_{S^+}$ | $\log \left[ \frac{k_2}{k_{Cl^-}} \right]_{O^+}$ |
|----------------------------|-----------------------------------------------------|--------------------------------------------------|--------------------------------------------------|--------------------------------------------------|
| $\text{SeCN}^-$            | 5.456                                               | 2.607                                            |                                                  |                                                  |
| $\text{I}^-$               | 4.944                                               | 2.378                                            | 4.146                                            | 5.3                                              |
| $\text{CN}^-$              | 3.82                                                | 2.045                                            |                                                  |                                                  |
| $\text{SC}(\text{NH}_2)_2$ | 5.161                                               | 1.95                                             |                                                  |                                                  |
| Piperidine                 | 4.403                                               | 1.229                                            |                                                  |                                                  |
| $\text{SCN}^-$             | 3.78                                                | 1.134                                            | 3.73                                             | 2.699                                            |
| $\text{Br}^-$              | 1.921                                               | 0.785                                            | 1.544                                            | 2.447                                            |
| Morpholine                 | 3.735                                               | 0.62                                             |                                                  |                                                  |
| Benzylamine                | 3.326                                               | 0.124                                            |                                                  |                                                  |
| $\text{N}_2\text{H}_4$     | 3.29                                                | 1.84                                             |                                                  |                                                  |

These data are plotted in fig.(V-17). Generally it can be inferred that reactivity of saturated  $\text{C}^+$ ,  $\text{N}^+$ ,  $\text{O}^+$ ,  $\text{S}^+$  and  $\text{I}^+$  species are very similar and this may be extended to other neighbouring electrophilic centres in the Periodic Table as far as organic nucleophilic reactions are concerned.

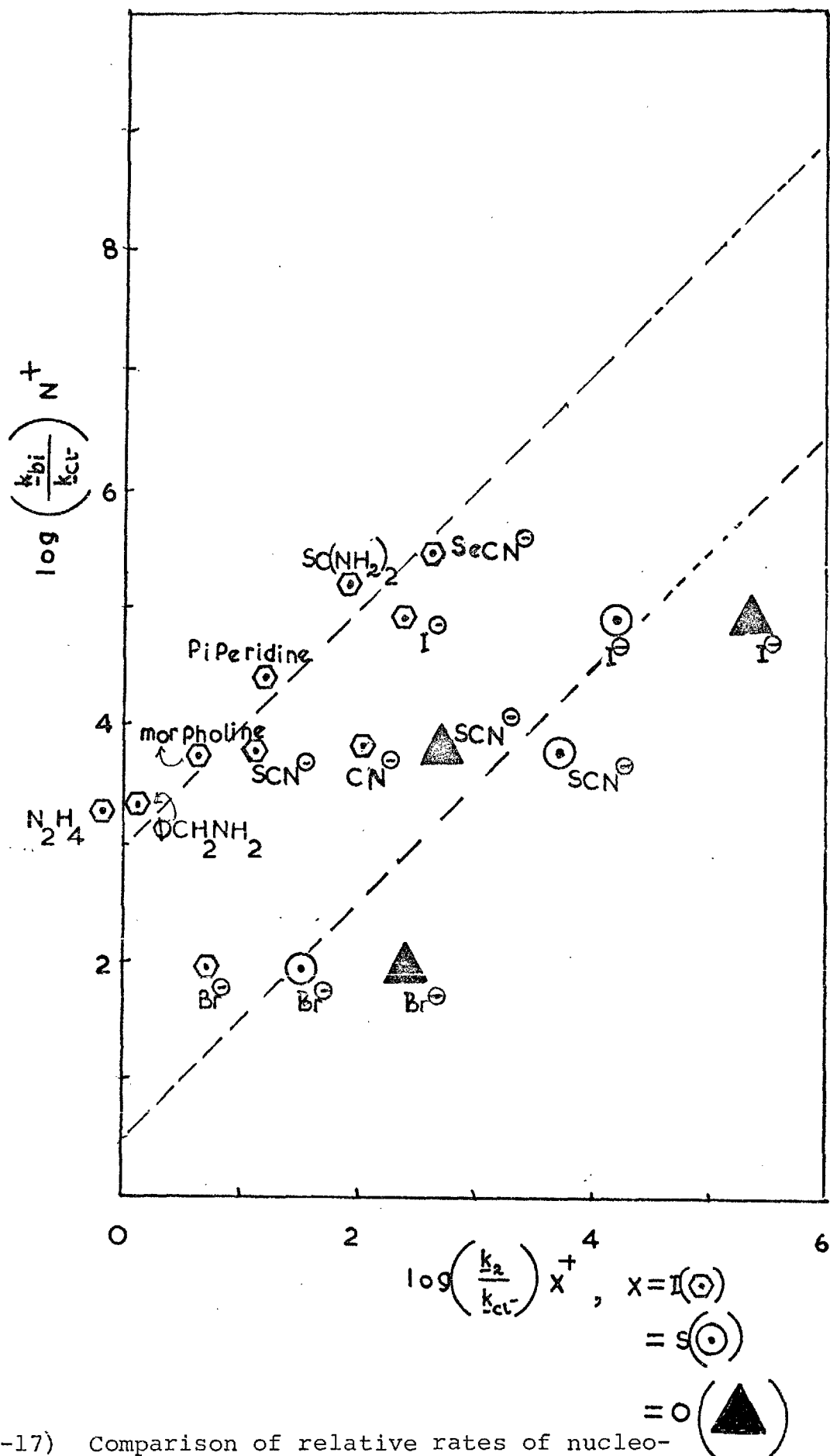


Fig. (V-17) Comparison of relative rates of nucleophiles towards electron-deficient nitrogen in O-(2,4-dinitrophenyl)hydroxylamine with those towards other electrophilic centres ( $I^+$ ,  $S^+$  and  $O^+$ ).

### V.2.7 Order of Nucleophilic Reactivity in Dipolar Aprotic Solvents

As pointed out previously (see Chapter I), the behaviour of an anionic nucleophile in a protic solvent is different from that in a dipolar aprotic solvent. This difference has been explained in terms of preferential solvation.<sup>63</sup> The outcome is that the order of nucleophilic reactivity suffers almost complete reversal when going from a protic to a dipolar aprotic solvent. However, when the polarizability of the nucleophile plays a predominant role in determining reactivity, this reversal may not occur. Belluco<sup>56</sup> and his co-workers have demonstrated that the order of reactivity  $I^- > Br^- > Cl^-$  for monohalide displacement of trans- $\{Pt(P(Et)_3)_2Cl_2\}$  with halide nucleophiles in dimethylsulphoxide, acetone and methanol was the same regardless of the nature of the solvent. This has been confirmed by Baciocchi<sup>30</sup> and his colleague for the dehalogenations of erythro-1-chloro-2-iodo-1,2-diphenylethane by halide ions. The order of reactivity in both methanol and dimethylformamide was the same, viz.  $I^- > Br^- > Cl^-$ . It is therefore expected that substitution at electron-deficient nitrogen compounds (where polarizability is predominant) should not show any reversal in order and such is evident from the data presented in Table (V-10) and Table (V-11).

### V.2.8 Reactions with hydroxide and perhydroxyl ions

As pointed out at the beginning of this chapter, satisfactory first order kinetics could not be obtained in these cases after about 50-60% of reaction. In the case of perhydroxyl ion, its instability at 25°C could be a factor since better results have been obtained at 4°C {see Table (V-4)}. However, as

phenols are known to undergo oxidative dimerisation reactions both in neutral and alkaline solutions, possibility of such side reactions resulting in the observed odd behaviour cannot be ruled out. T.l.c. examination, however, has failed to reveal the presence of any such undesired by-product, probably due to the break up of the latter to 2,4-dinitrophenol during the work-up for the t.l.c.

Attempts to ascertain why the hydroxide reaction does not produce satisfactory first order kinetics were inconclusive. Reactions carried out at different substrate concentrations {see Table (V-3), Expts. 477 and 478} with virtually no change in rate suggest that catalysis by the product(s) of the reaction, if any, is kinetically unimportant. The formation of some peroxycompound or dimerisation product has been suspected but lack of experimental evidence precludes any conclusion.

### V.3 Conclusions

It is clear that the electron-deficient N in O-(2,4-dinitrophenyl)hydroxylamine has properties similar to tetrahedral carbon in methyl halides (in particular to methyl iodide) as far as the softness of the electrophilic centre is concerned. The nitrogen centre in question also seems to be comparable to certain sulphur and oxygen electrophilic centres and this similarity may be extended to substitution at  $I^+$  centres.

It is clear that the polarizability factor is pre-eminent in determining nucleophilic reactivity in both protic and dipolar aprotic solvents.

A better correlation is obtained with electron polarizability alone than with the Edwards double scale equation. A modification of the Edwards equation seems to be required.

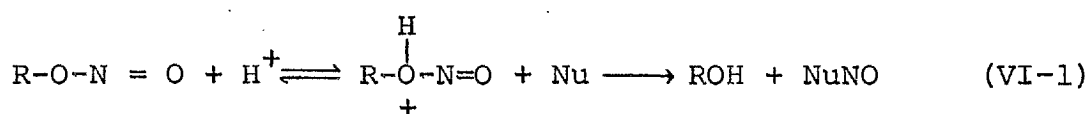
It is also clear that the  $\alpha$ -effects are small for substitution at nitrogen. However, perhydroxyl ion ( $\text{HOO}^\ominus$ ) has shown reasonable rate enhancement towards the nitrogen centre in question in agreement with the proposal of Hudson<sup>42</sup> et al that the  $\alpha$ -nucleophiles of the type  $\text{ROO}^\ominus$  always exhibit the  $\alpha$ -effect. The rate enhancements observed for  $\text{NH}_2\text{NH}_2$ ,  $\text{NH}_2\text{OH}$  are apparently negligible.

As far as the mechanism of these reactions are concerned,  $\text{S}_\text{N}2$  substitution of O-(2,4-dinitrophenyl)-hydroxylamine seems to be remarkably similar to that at carbon as far as effects of temperature and solvents are concerned. The only difference observed here is that steric effects, not surprisingly, are much reduced for the N-substitution.

## CHAPTER VI

### Acidic and Nucleophilic Reactions of Alkylnitrites

Allen<sup>107</sup> had already shown that the hydrolysis of alkylnitrites is markedly catalysed by acids, but nucleophilic reactivity towards this electron-deficient N-centre [eqn. (VI-1)] had not been examined thoroughly.



The key to the present investigation was to find a suitable solvent and a satisfactory anucleophilic (i.e. one which did not catalyse the reaction) buffer. Preliminary experiments showed that 70/30 dioxan-water (v/v) would be a suitable solvent.

#### VI.1 Anucleophilic Buffers

Benzene sulphonic acid-sodium benzene sulphonate buffer with  $p^{\text{H}}$  up to 2.9 showed satisfactory anucleophilic properties. Good first order rates for decomposition of the alkylnitrite were observed and these were independent of the concentration of the buffer anion. Some of the results concerning the hydrolysis of n-amylnitrite are presented in Table (VI-1). Logarithms of the observed rates plotted against respective  $p^{\text{H}}$  values can be seen in fig. (VI-1).

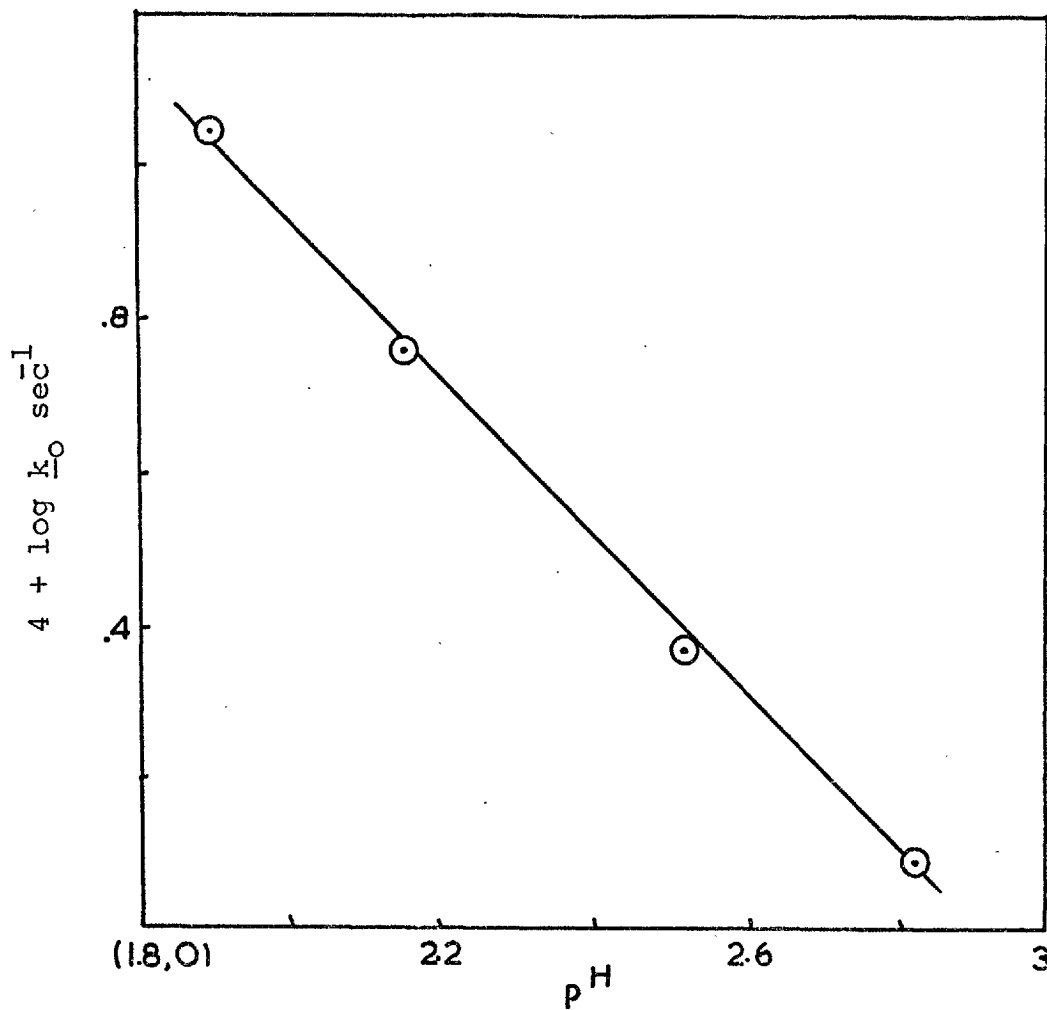


Fig. (VI-1)  
Hydrolysis of n-amyl-nitrite in 70/30 dioxan-water (benzene sulphonic acid buffers) at 0°C.

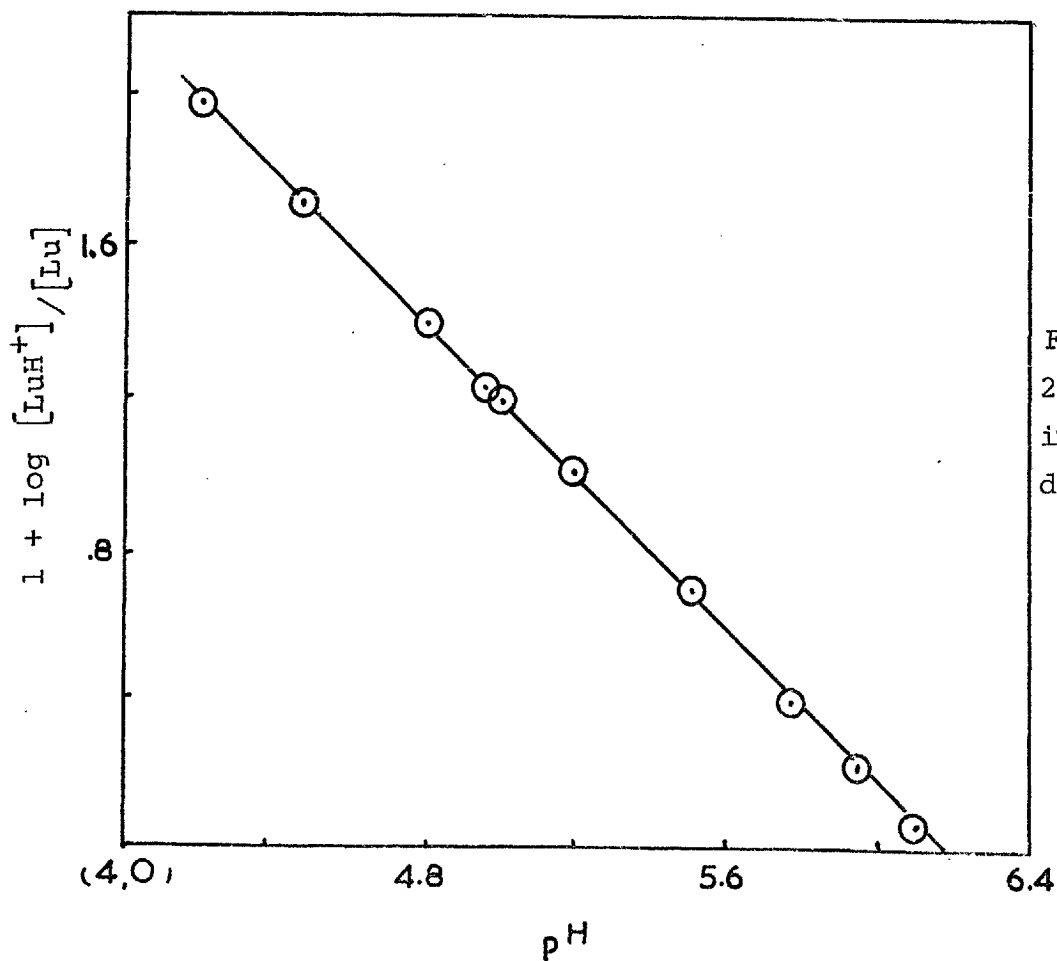


Fig. (VI-2)  
2,6-Lutidine buffers in 70/30 (v/v) dioxan-water at 25°C.

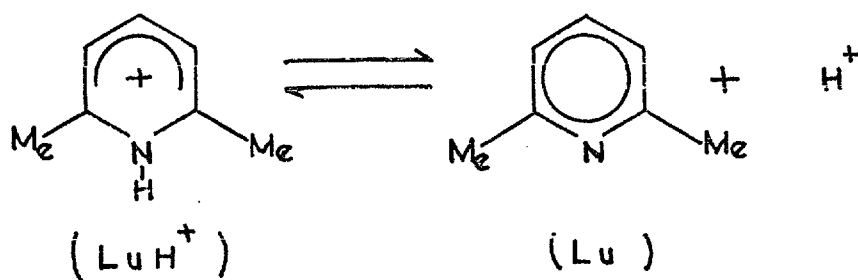
TABLE (VI-1)

Hydrolysis of n-amylnitrite in benzene sulphonic acid buffer  
at  $0^{\circ}\text{C} \pm .1^{\circ}\text{C}$

| Expt. | $[\text{PhSO}_3\text{Na}]$<br>$10^2 \text{ M}$ | $[\text{PhSO}_3\text{H}]$<br>$10^2 \text{ M}$ | $\text{p}^{\text{H}} \text{ a)}$ | $10^4 \text{ k}_o \text{ sec}^{-1}$ |
|-------|------------------------------------------------|-----------------------------------------------|----------------------------------|-------------------------------------|
| 7     | 0.75                                           | 0.75                                          | 1.9                              | 11.2                                |
| 6     | 0.375                                          | 0.375                                         | 2.14                             | 5.67                                |
| 5     | 0.6                                            | 0.15                                          | 2.51                             | 2.3                                 |
| 3     | 0.135                                          | 0.015                                         | 2.82                             | 1.25                                |

a) measured at  $25^{\circ}\text{C}$ .

However, this buffer seemed to be of limited applicability because of its low  $\text{p}^{\text{H}}$  and the 2,6-lutidine buffer system (Scheme VI-1) was, therefore, examined.



Scheme (VI-1) 2,6-Lutidine buffer system

Evidence given in Table (VI-2) shows that the 2,6-lutidine buffers in 70/30 (v/v) dioxan-water gave sensible  $\text{p}^{\text{H}}$  values. In practice, the  $\text{p}^{\text{H}}$  values were operational ones obtained by

TABLE (VI-2)

2,6-Lutidine Buffer (25°C)

| [Lu]<br>M | [LuH <sup>+</sup> ]<br>M | $\frac{[\text{LuH}^+]}{[\text{Lu}]}$ | p <sup>H</sup> at 25°C |
|-----------|--------------------------|--------------------------------------|------------------------|
| 0.011     | 0.1                      | 9.09                                 | 4.2                    |
| 0.02      | "                        | 5.0                                  | 4.475                  |
| 0.041     | "                        | 2.44                                 | 4.8                    |
| 0.062     | "                        | 1.61                                 | 4.975                  |
| 0.08      | "                        | 1.25                                 | 5.09                   |
| 0.101     | "                        | 0.99                                 | 5.195                  |
| 0.2       | "                        | 0.50                                 | 5.485                  |
| 0.401     | "                        | 0.25                                 | 5.775                  |
| 0.602     | "                        | 0.166                                | 5.94                   |
| 0.902     | "                        | 0.111                                | 6.1                    |

calibration of the 'p<sup>H</sup> Meter' with standard buffers in H<sub>2</sub>O. The p<sup>H</sup> given in Table (VI-2) is that measured experimentally. The relationship between buffer ratios and p<sup>H</sup> is shown in fig.(VI-2), the best straight line drawn has a slope of unity.

The 2,6-lutidine buffer also proved anucleophilic. Reactions carried out at different buffer concentrations, but at constant ionic strength (to keep the p<sup>H</sup> constant) showed a remarkably constant rate proving beyond doubt that the buffer anion does not catalyse rate. The data are presented in Table (VI-3).

TABLE (VI-3)

Substrate = n-Butylnitrite

temp. =  $25^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ ,  $p^{\text{H}} = 5.4 \pm 0.1$

$\mu = 0.25$ , adjusted by  $\text{NaClO}_4$ , where necessary.

| Expt. | $[\text{LuH}^+]$<br>M | $[\text{Lu}]$<br>M | $10^5 \underline{k}_o \text{ sec}^{-1}$<br>a) |
|-------|-----------------------|--------------------|-----------------------------------------------|
| 230   | 0.05                  | 0.05               | 1.67                                          |
| 232   | 0.1                   | 0.1                | 1.67                                          |
| 231   | 0.2                   | 0.2                | 1.67                                          |
| 229   | 0.25                  | 0.25               | 1.67                                          |

a)  $\pm 0.05$

## VI.2 Dependence on $p^{\text{H}}$

All kinetic experiments reported below were carried out at  $25^{\circ}\text{C} \pm 0.1^{\circ}\text{C}$ . In absence of any nucleophile, the hydrolysis rates followed eqn. (VI-2)

$$\text{rate} = \underline{k}_2 [\text{substrate}] [\text{H}_3\text{O}^+] \quad (\text{VI-2})$$

where  $\underline{k}_2$  is the rate constant observed for the hydrolysis of alkylnitrite,  $[\text{H}_3\text{O}^+]$  is the hydronium ion concentration and  $[\text{substrate}]$  refers to the stoichiometric concentration of alkylnitrite. Eqn. (VI-2) can be written in the form (VI-3)

$$\text{rate} = \underline{k}_o [\text{substrate}] \quad (\text{VI-3})$$

since for a particular run, the  $[\text{H}_3\text{O}^+]$  concentration was constant.

The variation of  $k_o$  with  $p^H$  of the reaction solution is shown in fig. (VI-3) and the experimental data are given in Table (VI-4).

TABLE (VI-4)

Hydrolysis of n-butyl nitrite catalysed by  $[H_3O^+]$  in 2,6-lutidine buffer at 25°C

Initial  $[n-BuONO] \approx (7 \times 10^{-3} - 2 \times 10^{-2})M$

$[LuH^+] = 0.25 M$

| Expt. | $p^H$ | $10^7 k_o \text{ sec}^{-1}$ |
|-------|-------|-----------------------------|
| 233   | 3.72  | 8283                        |
| 237   | 4.2   | 2510                        |
| 234   | 4.53  | 1167                        |
| 236   | 4.8   | 631                         |
| 235   | 5.19  | 300                         |
| 229   | 5.28  | 167                         |
| 257   | 5.63  | 50                          |
| 258   | 5.9   | 25                          |

The plot is linear (at least up to  $p^H$  5.4) and has a slope of unity. This confirms the validity of eqn. (VI-1) and shows that the reactions are catalysed by  $[H_3O^+]$ .

#### VI.2.1 Catalysis by Bromide ions

Addition of NaBr accelerated the rate of hydrolysis of n-BuONO and this agrees with Allen's observation<sup>107</sup>. The observed pseudo first order rate coefficient  $k_o$ , at constant bromide ion concentration has a linear dependence on the  $p^H$

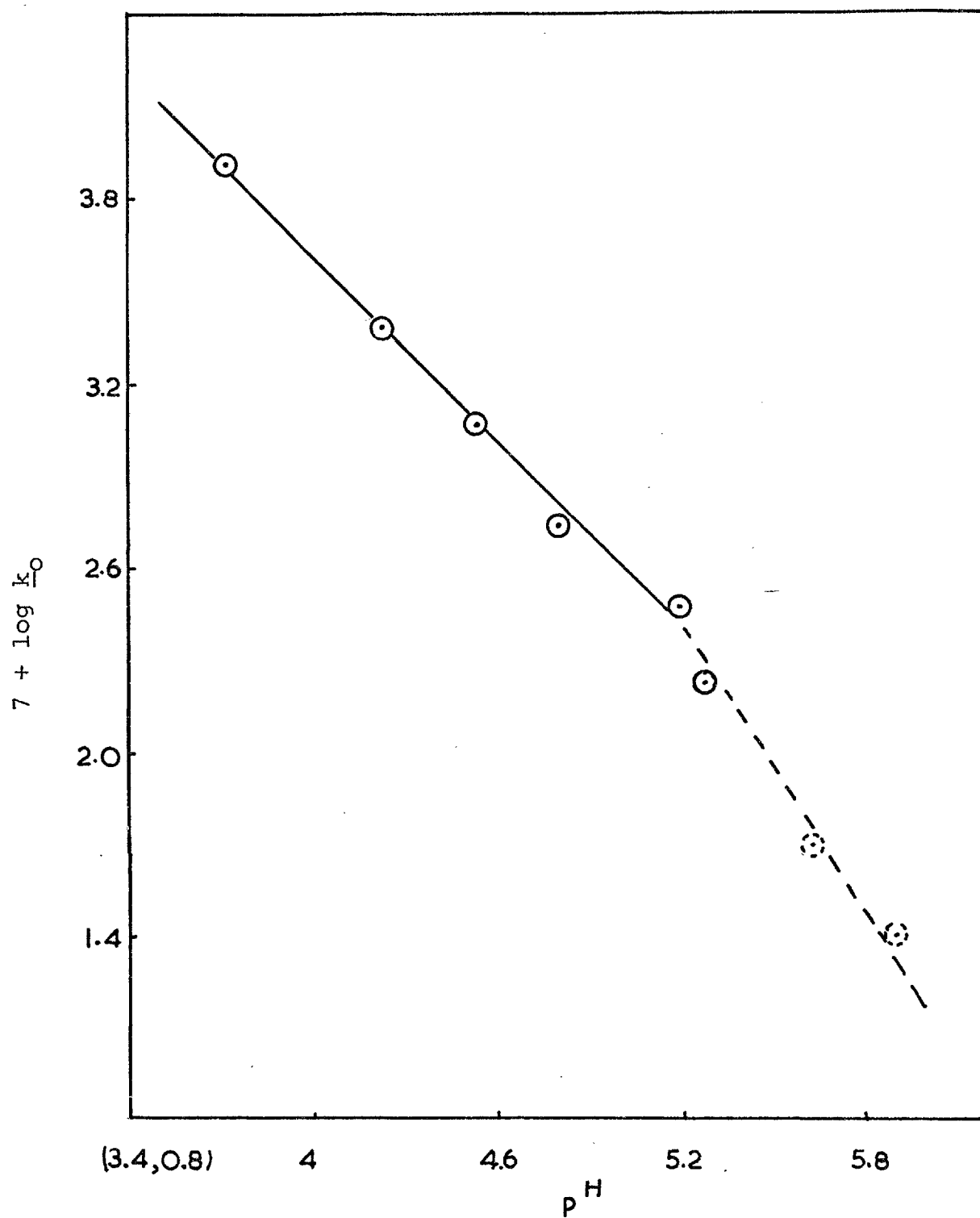


Fig. (VI-3) Hydrolysis of n-butyl nitrite in 70/30 dioxan-water at 25°C (2,6-lutidine buffers).

of the reaction, as illustrated by Table (VI-5). The plot of these data is shown in fig.(VI-4) and the straight line drawn has a slope of unity.

TABLE (VI-5)

Hydrolysis of n-BuONO catalysed by NaBr

Initial [n-BuONO] =  $(7 \times 10^{-3} - 2 \times 10^{-2})M$ , temp. =  $25^{\circ} \pm 0.1^{\circ}C$   
 [NaBr] = 0.1 M,  $\mu = 0.3$ ,  $[LuH^{+}] = 0.2$

| Expt. | $p^H$ | $10^5 \underline{k}_O \text{ sec}^{-1}$ | $10^5 \underline{k}_{\text{water}}^{\text{a)}} \text{ sec}^{-1}$ | $10^5 (\underline{k}_O - \underline{k}_{\text{water}}) \text{ sec}^{-1}$ |
|-------|-------|-----------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------|
| 355   | 4.48  | 28.33                                   | 13.18                                                            | 15.15                                                                    |
| 356   | 4.87  | 11.33                                   | 5.37                                                             | 5.96                                                                     |
| 357   | 5.2   | 5.67                                    | 2.51                                                             | 3.16                                                                     |
| 238   | 5.37  | 3.5                                     | 1.32                                                             | 2.18                                                                     |
| 358   | 5.51  | 2.67                                    | 0.85                                                             | 1.82                                                                     |

a)  $\underline{k}_{\text{water}}$  refers to rate at the  $p^H$  of the experiment in the absence of added nucleophile.

#### VI.2.2 Catalysis by NaSCN

Thiocyanate ion catalysed hydrolysis of n-butylnitrite at constant ionic strength was found to be  $p^H$  dependent. In Table (VI-6) some of the experimental data are presented. A plot of  $\log (\underline{k}_O - \underline{k}_{\text{water}})$  against  $p^H$  also gave a straight line of slope 0.9 (Fig.VI-4).

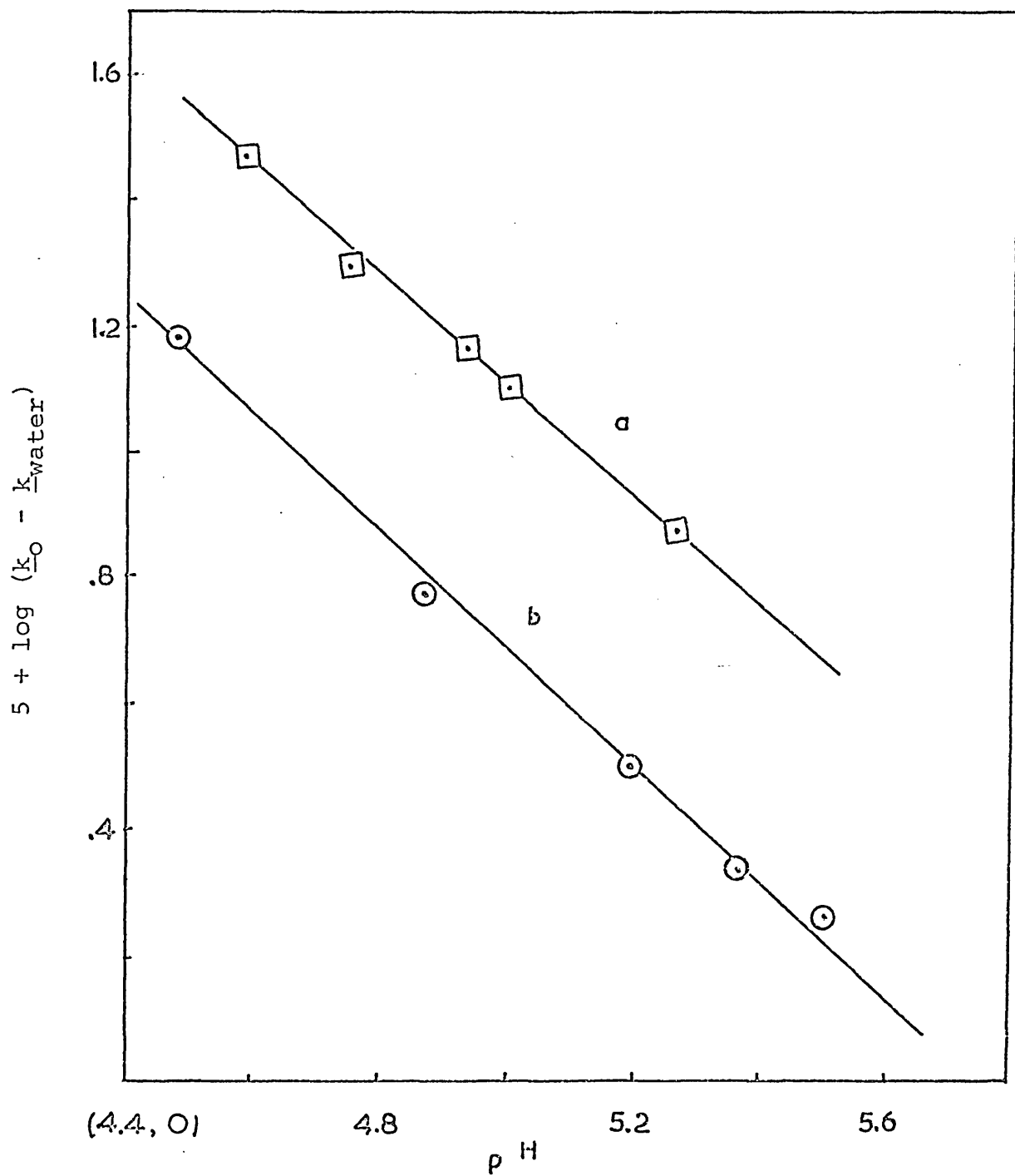


Fig. (VI-4) Hydrolysis of n-butyl nitrite in 70/30 dioxan-water (2,6-lutidine buffers) catalysed by

(a) NaSCN  $\square$

and (b) NaBr  $\circ$

at  $25^{\circ}\text{C}$ .

TABLE (VI-6)

Hydrolysis of n-Butylnitrite catalysed by NaSCN in 2,6-lutidine buffers at 25°C

Initial  $[n\text{-BuONO}] = (7 \times 10^{-3} - 2 \times 10^{-2})\text{M}$ ;  $[\text{NaSCN}] = 0.1\text{ M}$ ;  
 $[\text{LuH}^+] = 0.2\text{ M}$ ;  $\mu = 0.3$

| Expt. | p <sup>H</sup> | $10^5 \underline{k}_O \text{ sec}^{-1}$ | $10^5 \underline{k}_{\text{water}}^{\text{a)}} \text{ sec}^{-1}$ | $10^5 (\underline{k}_O - \underline{k}_{\text{water}}) \text{ sec}^{-1}$ |
|-------|----------------|-----------------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------------|
| 360   | 4.58           | 38.33                                   | 10.47                                                            | 27.86                                                                    |
| 367   | 4.75           | 25.83                                   | 7.0                                                              | 18.83                                                                    |
| 353   | 4.94           | 18.33                                   | 4.57                                                             | 13.76                                                                    |
| 368   | 5.0            | 15.83                                   | 3.98                                                             | 11.85                                                                    |
| 352   | 5.27           | 9.5                                     | 2.0                                                              | 7.5                                                                      |

a)  $\underline{k}_{\text{water}}$  refers to rate at the p<sup>H</sup> of the experiment in the absence of  $\text{SCN}^\ominus$ .

### VI.2.3 Catalysis by Thiourea

Table (VI-7) summarises results of the reactions studied with various thiourea concentrations. The last column (which has been normalised with respect to water) shows the first order dependence on the concentration of thiourea.

TABLE (VI-7)

Hydrolysis of n-BuONO catalysed by thiourea in 70/30 dioxan-water (2,6-lutidine buffer) at 25°C

Initial [n-BuONO] =  $(7 \times 10^3 - 2 \times 10^2)M$ ,

$\mu = 0.15$

| Expt.     | p <sup>H</sup> | [Thiourea]<br>M | $10^5 \underline{k}_o \text{ sec}^{-1}$ | $10^5 \underline{k}_{\text{water}}^{\text{a)}} \text{ sec}^{-1}$ | $10^5 \frac{(\underline{k}_o - \underline{k}_{\text{water}})}{[\text{thiourea}]}$ | $\frac{\underline{k}_{\text{bi}}^{\text{b)}}}{\underline{k}_{\text{H}_2\text{O}}}$ |
|-----------|----------------|-----------------|-----------------------------------------|------------------------------------------------------------------|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|
| 490       | 5.39           | 0.05            | 3                                       | 1.24                                                             | 35.2                                                                              | 475                                                                                |
| c)<br>256 | 5.34           | 0.1             | 4.83                                    | 1.45                                                             | 33.8                                                                              | 389                                                                                |
| 489       | 5.44           | 0.2             | 6.67                                    | 1.05                                                             | 28.1                                                                              | 446                                                                                |

a)  $\underline{k}_{\text{water}}$  refers to rate at the p<sup>H</sup> of the experiment in the absence of the catalyst.

b)  $\underline{k}_{\text{H}_2\text{O}}$  ( $= \underline{k}_{\text{water}}/16.65$ ) refers to bimolecular water rate assuming  $[\text{H}_2\text{O}] = 16.65 \text{ m/l.}$

c)  $\mu = 0.2.$

#### VI.2.4 Catalysis by Azide ions

Some reactions were carried out at various  $p^H$  values keeping the initial concentration of azide ions the same ( $= 0.01 \text{ M}$ ), in order to evaluate the catalytic rate constant due to  $N_3H$ . The data are presented in Table (VI-8).

TABLE (VI-8)

Hydrolysis of n-BuONO catalysed by azide nucleophile at various  $p^H$  values

Initial  $[N_3^-] = 0.01 \text{ M}$ , temp.  $= 25^\circ\text{C}$ ,  $[n\text{-BuONO}] = \text{as in Table (VI-7)}$

| Expt.  | $p^H$ | $10^5 \frac{k_o}{\text{sec}^{-1}}$ | a) $10^5 \frac{k_{\text{water}}}{\text{sec}^{-1}}$ | b) $[N_3^-] 10^5 \text{ M}$ | $\frac{(k_o - k_{\text{water}})}{[N_3^-]} \equiv k_{\text{cat}} \text{ l mole}^{-1} \text{ sec}^{-1}$ | a) $\frac{k_{\text{cat}}}{k_{H_2O}}$ |
|--------|-------|------------------------------------|----------------------------------------------------|-----------------------------|-------------------------------------------------------------------------------------------------------|--------------------------------------|
| 263    | 4.5   | 15.5                               | 12.59                                              | 7.2                         | 0.404                                                                                                 | $53.4 \times 10^3$                   |
| 264    | 4.70  | 12.67                              | 7.94                                               | 11.35                       | 0.42                                                                                                  | $88.1 \times 10^3$                   |
| 265    | 4.78  | 10.5                               | 6.61                                               | 13.6                        | 0.286                                                                                                 | $72.0 \times 10^3$                   |
| 266    | 4.94  | 9.33                               | 4.57                                               | 19.56                       | 0.243                                                                                                 | $88.5 \times 10^3$                   |
| 267    | 5.1   | 8.67                               | 3.16                                               | 28.03                       | 0.196                                                                                                 | $10.3 \times 10^4$                   |
| 270    | 5.35  | 9.67                               | 1.38                                               | 48.78                       | 0.17                                                                                                  | $20.5 \times 10^4$                   |
| 270(b) | 5.36  | 10.0                               | 1.35                                               | 49.9                        | 0.173                                                                                                 | $21.4 \times 10^4$                   |

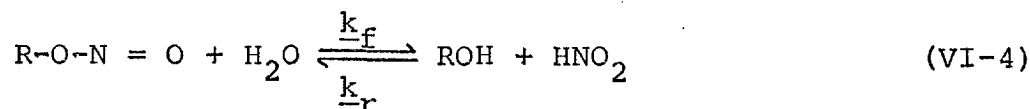
a)  $k_{\text{water}}, k_{H_2O}$  have the same significance as before.

b) calculated from eqn. (VI-12)

It is clear that the variation in  $\frac{k_{\text{cat}}}{k_{\text{H}_2\text{O}}}$  is outside the expected experimental errors and that this term increases with decreasing  $p^{\text{H}}$ . Apparently, the assumption that  $\text{N}_3^-$  attacks  $\text{ROHNO}^+$  in the rate-limiting step will not completely account for the observed rates. Also consideration of additional reaction pathways involving  $\text{N}_3^-$  and neutral  $\text{RONO}$ , and  $\text{N}_3\text{H}$  and  $\text{ROHNO}^+$  do not explain these discrepancies.

### VI.3 Reversibility of n-Butylnitrite Hydrolysis

The hydrolysis reaction is reversible in principle [eqn. (VI-4)] since alkyl nitrites are prepared by the action of  $\text{HNO}_2$  on the corresponding alcohol.



In this case the observed pseudo first order rate coefficient ( $k_o$ ) comprises the sum of the forward and reverse reactions, i.e.  $k_o = k_f + k_r$ , and these data would, therefore, give no direct information on the sensitivity of alkyl nitrites to nucleophilic attack. The contribution of the  $k_r$  term to the observed rate coefficients was, therefore, checked by examining the position of equilibrium for the hydrolysis reaction. The data are given in Table (VI-9) where it is evident that at infinity, the equilibrium is well to the right hand side of eqn. (VI-4) ( $93\% \pm 3\%$ ). Accordingly, the contribution to  $k_o$  from the  $k_r$  term must be negligible and  $k_o$  to a good approximation represents the forward rate of decomposition of alkyl nitrite.

TABLE (VI-9)

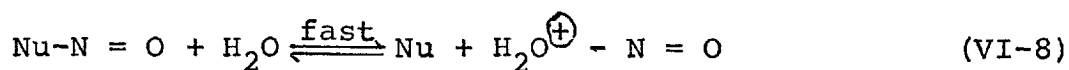
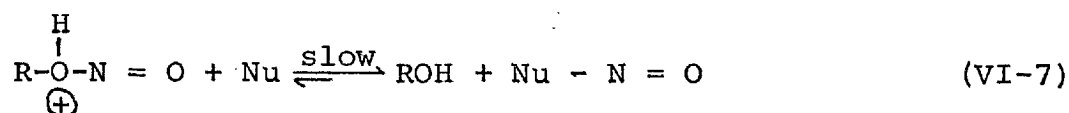
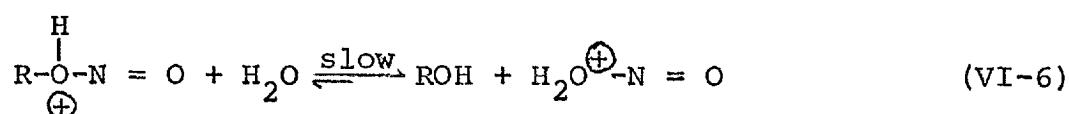
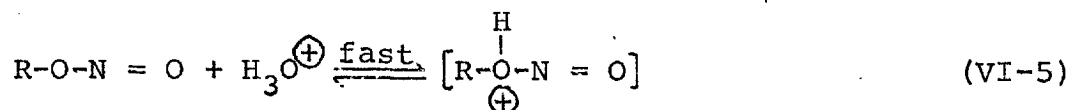
Position of Equilibrium in the hydrolysis of n-BuONO in 70/30 dioxan-water at 25°C

| [Lu]<br>M | [LuH <sup>+</sup> ]<br>M | p <sup>H</sup> | [n-BuONO]<br>10 <sup>2</sup> M | O.D. $\lambda = 360$ nm<br>of the xylene extract |                                       | a)<br>%<br>reaction |
|-----------|--------------------------|----------------|--------------------------------|--------------------------------------------------|---------------------------------------|---------------------|
|           |                          |                |                                | Initial<br>(showed<br>multiplet)                 | Infinite<br>(absence of<br>multiplet) |                     |
| 0.026     | 0.25                     | 4.45           | ~ 0.85                         | 0.355                                            | 0.035                                 | 98                  |
| 0.026     | "                        | "              | ~ 1.42                         | 0.58                                             | 0.045                                 | 97                  |
| 0.25      | "                        | 5.42           | ~ 0.85                         | 0.355                                            | 0.05                                  | 94                  |
| 0.25      | "                        | "              | ~ 1.42                         | 0.58                                             | 0.07                                  | 93                  |

a) A blank solution containing  $\text{NaNO}_2$  ( $1.42 \times 10^{-2}$  M) and n-Butanol ( $\sim 1.42 \times 10^{-2}$  M) was prepared and extracted in the same way as in the equilibrium experiments with xylene and the U.V. spectrum taken. The xylene extract showed an absorbance of 0.03 at  $\lambda = 360$  nm; this fact was taken into consideration when calculating the percent reacted.

#### VI.4 Mechanism of Acid catalysed Hydrolysis

The observed kinetics suggest that protonation of the substrate is necessary for reaction to occur. This is likely to occur in a rapid pre-equilibrium step followed by a rate-determining bimolecular attack of the nucleophilic species present including water as a solvent component. As regards the site of protonation, it is assumed that O-protonation is most probable. The N in an alkylnitrite is flanked by two electronegative oxygen atoms and it is likely that the lone pair is polarized towards the doubly bonded oxygen, making nitrogen deficient in electrons. The following scheme (VI-2) is consistent with the observations made.



Scheme (VI-2) Mechanism for the acid-catalysed decomposition of alkylnitrites

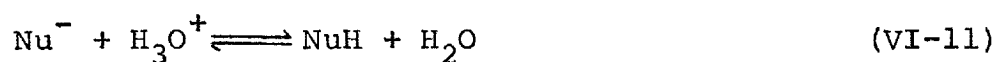
This is in agreement with the previous mechanistic interpretation<sup>107</sup>.

The results for nucleophiles other than bromide and

thiocyanate are summarised in Table (VI-10). Here,  $k_o$  is the overall pseudo first order rate coefficient observed with added nucleophile,  $k_{\text{water}}$  is the specific  $[\text{H}_3\text{O}^+]$  catalysed rate at the  $p^H$  of the experiment and  $k_{bi}$  is the difference between the  $k_o$  and  $k_{\text{water}}$  divided by the actual concentration of the nucleophile [eqn. (VI-10)].

$$k_{bi} = \frac{k_o - k_{\text{water}}}{[\text{Nu}^-]} \quad (\text{VI-10})$$

In the case of basic species (e.g.  $\text{N}_3^-$ ,  $\text{OAc}^-$ ,  $\text{ClCH}_2\text{CO}_2^-$ ,  $\text{NO}_2^-$  and p-toluidine) that underwent protonation [eqn. (VI-11)] under the experimental conditions, the value of  $[\text{Nu}^-]$  was



deduced by means of the Henderson eqn. (VI-12),

$$p^H = pK_A + \log \frac{[\text{Nu}^-]}{[\text{NuH}]} \quad (\text{VI-12})$$

from independent measurement of the  $pK_A$  of NuH (by  $p^H$  titration) in 70/30 (v/v) dioxan-water solutions and the experimental  $p^H$  of the reaction solution. The values of the relevant  $pK_A$  values are listed in Table (VI-10) together with the actual  $[\text{Nu}^-]$  computed.

TABLE (VI-10)

Hydrolysis of n-BuONO catalysed by nucleophiles at 25°C in 70/30 dioxan-water

| Expt. | $p^H$ | Nu              | Initial<br>[Nu]<br>M | $10^5 k_o$<br>$\text{sec}^{-1}$ | $10^5 k_{\text{water}}$<br>$\text{sec}^{-1}$ | $10^5$<br>(difference)<br>$\text{sec}^{-1}$ | $pK_a$ | Effective<br>[Nu]<br>M | $10^5 k_{bi}$<br>$\text{l mole}^{-1} \text{sec}^{-1}$ |
|-------|-------|-----------------|----------------------|---------------------------------|----------------------------------------------|---------------------------------------------|--------|------------------------|-------------------------------------------------------|
| 241   | 5.64  | $N_3^-$         | 0.1                  | 83.33                           | 0.53                                         | 82.8                                        | 6.64   | 0.009                  | 9200.0                                                |
| 254   | 5.21  | L-ascorbate     | 0.1                  | 193.33                          | 2.1                                          | 191.23                                      | ~      | ~0.1                   | 1912.3                                                |
| 249   | 5.76  | $OAc^-$         | 0.1                  | 5.17                            | 0.37                                         | 4.8                                         | 7.04   | 0.0049                 | 979.6                                                 |
| 262   | 5.49  | $ClCH_2CO_2^-$  | 0.1                  | 11.83                           | 0.87                                         | 10.96                                       | 4.92   | 0.0787                 | 139.26                                                |
| 240   | 5.46  | $NO_2^-$        | 0.1                  | 7.0                             | 1.0                                          | 6.0                                         | 5.12   | 0.068                  | 88.23                                                 |
| 248   | 5.48  | $SCN^-$         | 0.1                  | 7.17                            | 0.95                                         | 6.22                                        | -      | 0.1                    | 62.2                                                  |
| 256   | 5.34  | $SC(NH_2)_2$    | 0.1                  | 4.83                            | 1.45                                         | 3.38                                        | -      | 0.1                    | 33.8                                                  |
| 238   | 5.37  | $Br^-$          | 0.1                  | 3.5                             | 1.32                                         | 2.18                                        | -      | 0.1                    | 21.8                                                  |
| 369   | 5.5   | p-toluidine     | 0.2                  | 3.8                             | 0.87                                         | 2.93                                        | 4.11   | 0.2                    | 14.65                                                 |
| 239   | 5.32  | $Cl^-$          | 0.1                  | 2.5                             | 1.52                                         | 0.98                                        | ~      | 0.1                    | 9.8                                                   |
| 485   | 5.5   | p-bromo-aniline | 0.5                  | 0.97                            | 0.87                                         | 0.1                                         | ~      | 0.5                    | 0.2                                                   |

The 2,6-lutidine buffer is anucleophilic towards alkyl-nitrites probably because of steric factors. The O-N-O angle in alkyl nitrite is of the order of  $109^\circ$  and strong Van der Waal's repulsion must occur when 2,6-lutidine approaches the electron-deficient nitrogen, making close contact between the reaction centres difficult. When steric factors are minimised, as in p-toluidine, strong catalysis (compared to that of bromide ion) is observed.

#### VI.5 Order of Nucleophilic Reactivity

It has been the common practice to ascertain nucleophilic reactivity with respect to some standard nucleophile and this practice is followed here. Accordingly, nucleophilic reactivity is defined as the ratio of the second order rate constants ( $k_{bi}$ ) to the rate in 70/30 dioxan-water (v/v) alone of similar  $p^H$ . The relevant ratio is given by eqn.(VI-13). These ratios refer, of course, to reaction in 70/30 (v/v) dioxan-water at  $25^\circ\text{C}$ .

$$\text{Nucleophilic reactivity} = \frac{k_{bi}}{k_{H_2O}} \quad (\text{VI-13})$$

Table (VI-11) lists the relative reactivities of the various nucleophiles towards n-butyl nitrite.

TABLE (VI-11)

Relative nucleophilic reactivities towards n-BuONO

| Nu              | $10^5 k_{bi}$<br>$\text{l mole}^{-1} \text{sec}^{-1}$ | $10^5 k_{H_2O}^a)$<br>$\text{l mole}^{-1} \text{sec}^{-1}$ | $k_{bi}/k_{H_2O}$   |
|-----------------|-------------------------------------------------------|------------------------------------------------------------|---------------------|
| $N_3^-$         | 9200                                                  | 0.032                                                      | $28.75 \times 10^4$ |
| $OAc^-$         | 979.6                                                 | 0.022                                                      | $44.53 \times 10^3$ |
| L-Ascorbate     | 1912.3                                                | 0.126                                                      | $15.18 \times 10^3$ |
| $ClCH_2CO_2^-$  | 139.26                                                | 0.052                                                      | $26.78 \times 10^2$ |
| $NO_2^-$        | 88.23                                                 | 0.06                                                       | $14.7 \times 10^2$  |
| $SCN^-$         | 62.2                                                  | 0.057                                                      | $10.91 \times 10^2$ |
| $SC(NH_2)_2$    | 33.8                                                  | 0.087                                                      | $3.88 \times 10^2$  |
| p-Toluidine     | 14.65                                                 | 0.052                                                      | $2.81 \times 10^2$  |
| $Br^-$          | 21.8                                                  | 0.079                                                      | $2.76 \times 10^2$  |
| $Cl^-$          | 9.8                                                   | 0.091                                                      | $1.08 \times 10^2$  |
| p-Bromo-aniline | 0.2                                                   | 0.052                                                      | 4                   |

a)  $k_{H_2O}$  has the same significance as in Table (VI-7).

The N in the nitrous acidium ion ( $H_2ONO^+$ ), and in the protonated alkyl nitrite ( $RONOH^+$ ) is expected to be similar as far as the electrophilic centre is concerned and both are expected to exhibit a similar order of reactivity. Comparison of the observed order [Table (VI-11)]:  $N_3^- > OAc^- > \text{L-ascorbate} > ClCH_2CO_2^- > NO_2^- > SCN^- > SC(NH_2)_2 > \text{p-toluidine} > Br^- > Cl^- > \text{p-bromoaniline}$  with that of the nitrous acidium ion<sup>74</sup> reveals that this is so. It is to be pointed out that the observed order cannot be explained solely in terms of basicity or the

polarizability but by a combination of both, although the former seems to be more important. There is reason to believe that the electron-deficient N in alkyl nitrite is very similar to that in carbonyl carbon. The covalent radii of carbon (0.77 Å) and nitrogen (0.75 Å) are very similar and the N=O bond length (1.22 Å) in RONO and C=O (1.215 Å) in aldehydes are also very similar. Electronegativity increases in the order  $C < N < O$ , i.e. oxygen is more electronegative than both carbon and nitrogen. From this it can be assumed that polarization of the N=O bond in  $R-O-N=O$  and  $C=O$  in aldehydes and ketones takes place similarly towards oxygen.

#### VI.6 Correlation of Nucleophilic Reactivity

Relevant Edwards<sup>21</sup> parameters are presented in Table (VI-12) and a plot of  $\frac{1}{E_N} \log \frac{k_{bi}}{k_{H_2O}}$  versus  $H/E_N$  is shown in fig. (VI-5).

TABLE (VI-12)

#### Edwards Parameters

| Nu             | $\frac{1}{E_N}$ | $\frac{k_{bi}}{k_{H_2O}}$ | $\log \frac{k_{bi}}{k_{H_2O}}$ | $\frac{1}{E_N} \log \frac{k_{bi}}{k_{H_2O}}$ | $H/E_N$ |
|----------------|-----------------|---------------------------|--------------------------------|----------------------------------------------|---------|
| $Cl^-$         | 0.81            | 108                       | 2.033                          | 1.65                                         | -2.42   |
| $Br^-$         | 0.66            | 276                       | 2.441                          | 1.61                                         | -3.97   |
| $NO_2^-$       | 0.58            | 1470                      | 3.17                           | 1.84                                         | +2.94   |
| $N_3^-$        | 0.63            | 287500                    | 5.45                           | 3.44                                         | +4.08   |
| $OAc^-$        | 1.053           | 44527                     | 4.65                           | 4.89                                         | +6.8    |
| $SCN^-$        | 0.55            | 1091                      | 3.04                           | 1.67                                         | +0.55   |
| $SC(NH_2)_2$   | 0.46            | 388                       | 2.59                           | 1.19                                         | +0.37   |
| $ClCH_2CO_2^-$ | 1.26            | 2678                      | 3.43                           | 4.32                                         | +5.74   |

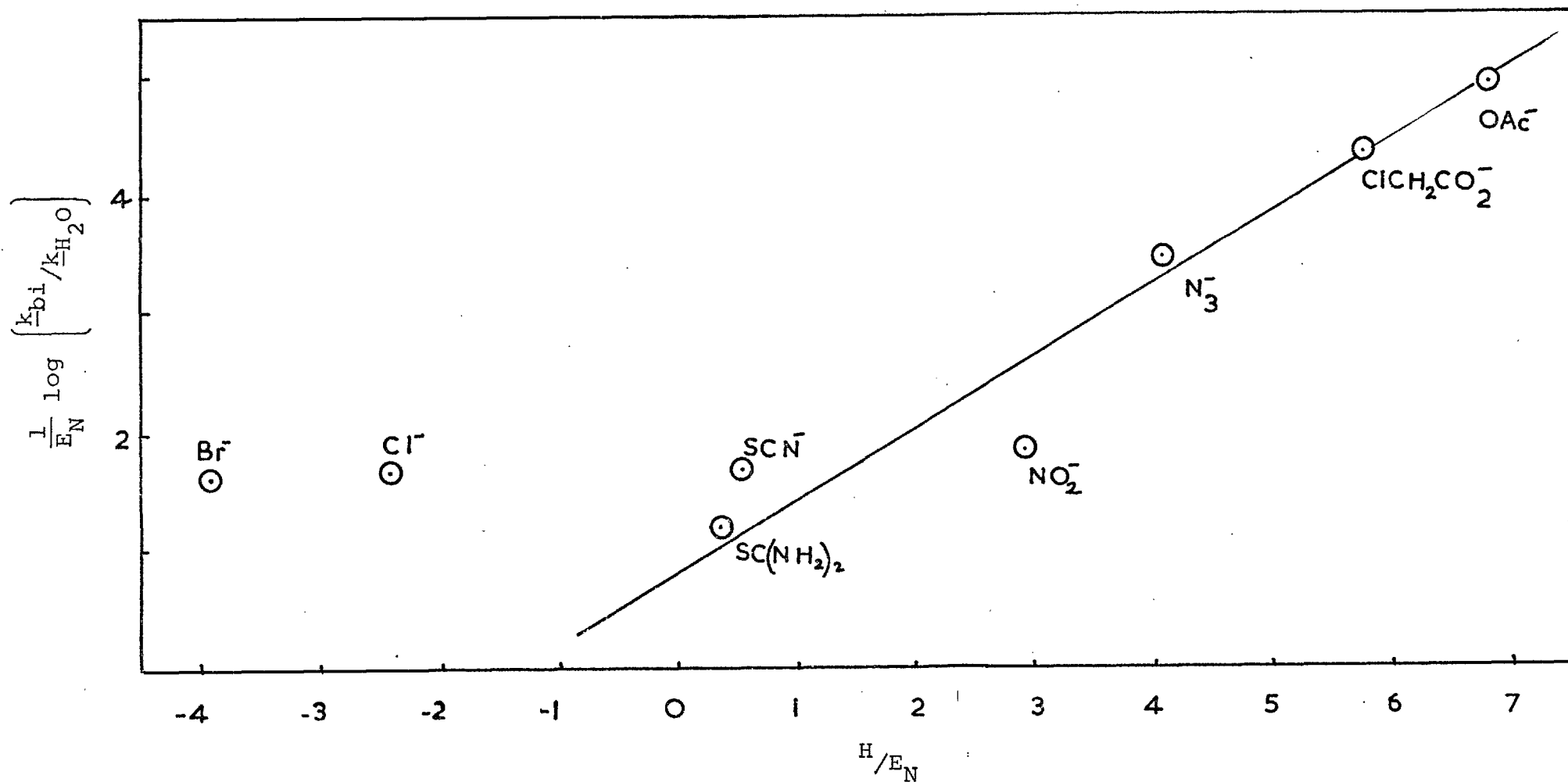


Fig. (VI-5) A plot of Edwards linear free-energy eqn. for reactions of n-butyl nitrite in 70/30 dioxan-water (2,6-lutidine buffers) with nucleophiles at 25°C.

The best straight line drawn has an intercept ( $= \alpha$ ) and slope ( $= \beta$ ) of 0.75 and 0.62 respectively. The positive and reasonably high  $\beta$  value indicates the importance of the basicity factor for these reactions. This also suggests that the nitrogen centre in alkyl nitrites is moderately hard. The relatively high reactivity of hard bases (like acetate and chloroacetate) and low reactivity of soft nucleophiles (like thiourea and thiocyanate) seem to support this view.

An interesting point from fig. (VI-5) is that the Edwards relationship<sup>21</sup> seems to fail for nucleophiles with negative  $pK_A$  values. Thus points for  $Cl^-$  and  $Br^-$  are well off the line as observed previously for substitution of O-(2,4-dinitrophenyl)-hydroxylamine (Chapter V).

#### VI.7 Conclusions

The 2,6-lutidine buffer system is an anucleophilic buffer system which behaves satisfactorily even in a mixed solvent like dioxan-water.

The order of nucleophilic reactivity towards n-butyl nitrite is very similar to that for the nitrous acidium ion. Both the basicity and polarizability factors seem to be important but the former appears to be pre-eminent. The electron-deficient nitrogen centre also appears to be comparable to carbonyl carbon as far as the 'hardness' of the electrophilic centres are concerned.

## CHAPTER VII

### Acidic and Nucleophilic Reactions of Oxaziridines

From a study of the nucleophilic reactivity towards electron-deficient N in both O-(nitroaryl)hydroxylamine and alkyl nitrites, it has been noted that structural features determine the relative softness of the N concerned. In alkyl nitrites, the N-centre is hard and comparable to carbonyl carbon, while in O-(nitroaryl)hydroxylamines, the N is moderately soft. In this chapter, nucleophilic attack of a soft nucleophile on the electron-deficient N of 2,3,3-triethyloxaziridine together with results of the acid hydrolysis of 2-benzyl-3,3-diethyloxaziridine are reported and discussed.

All the kinetic experiments reported in this chapter were carried out at  $25^{\circ} \pm 0.1^{\circ}\text{C}$  and the rates followed eqn. (VII-1)

$$\text{rate} = k_o [\text{substrate}] \quad (\text{VII-1})$$

where  $k_o$  is the rate constant observed for the ring opening reactions and [substrate] refers to the stoichiometric concentration of oxaziridine.

The second order rate coefficient,  $k_2^{\text{cat}}$ , for the catalyst studied, eqn. (VII-2)

$$\text{Rate} = k_2^{\text{cat}} [\text{Oxaziridine}] [\text{catalyst}] \quad (\text{VII-2})$$

was obtained from the slope of the best straight line for the plot of  $k_o$  versus [catalyst].

## VII.1 Kinetic Results

### VII.1.1 Acid Hydrolysis

The ring opening of 2-benzyl-3,3-diethyloxaziridine was studied under acidic conditions between 0 - 1.09 M  $\text{HClO}_4$  at  $25^\circ\text{C}$  in 50-50 EtOH-water (v/v). These results are presented in Table (VII-1) and the rate profile is shown in fig.(VII-1).

TABLE (VII-1)

Hydrolysis of 2-Benzyl-3,3-diethyloxaziridine in aqueous ethanolic  $\text{HClO}_4$  at  $25^\circ \pm 0.1^\circ\text{C}$

| Expt. | $[\text{HClO}_4]$<br>10 M | $10^4 \underline{k}_o \text{ sec}^{-1}$ |
|-------|---------------------------|-----------------------------------------|
| 188   | 0                         | 0.18                                    |
| 189   | 1.0                       | 1.25                                    |
| 190   | 2.0                       | 2.52                                    |
| 192   | 3.5                       | 5.22                                    |
| 191   | 5.0                       | 7.48                                    |
| 197   | 6.46                      | 11.2                                    |
| 193   | 8.0                       | 15.78                                   |
| 194   | 10.1                      | 19.57                                   |
| 196   | 10.9                      | 22.9                                    |

The ring opening rates for the above oxaziridine in aqueous-ethanolic solution buffered by sodium acetate-acetic acid are to be found in Table (VII-2).

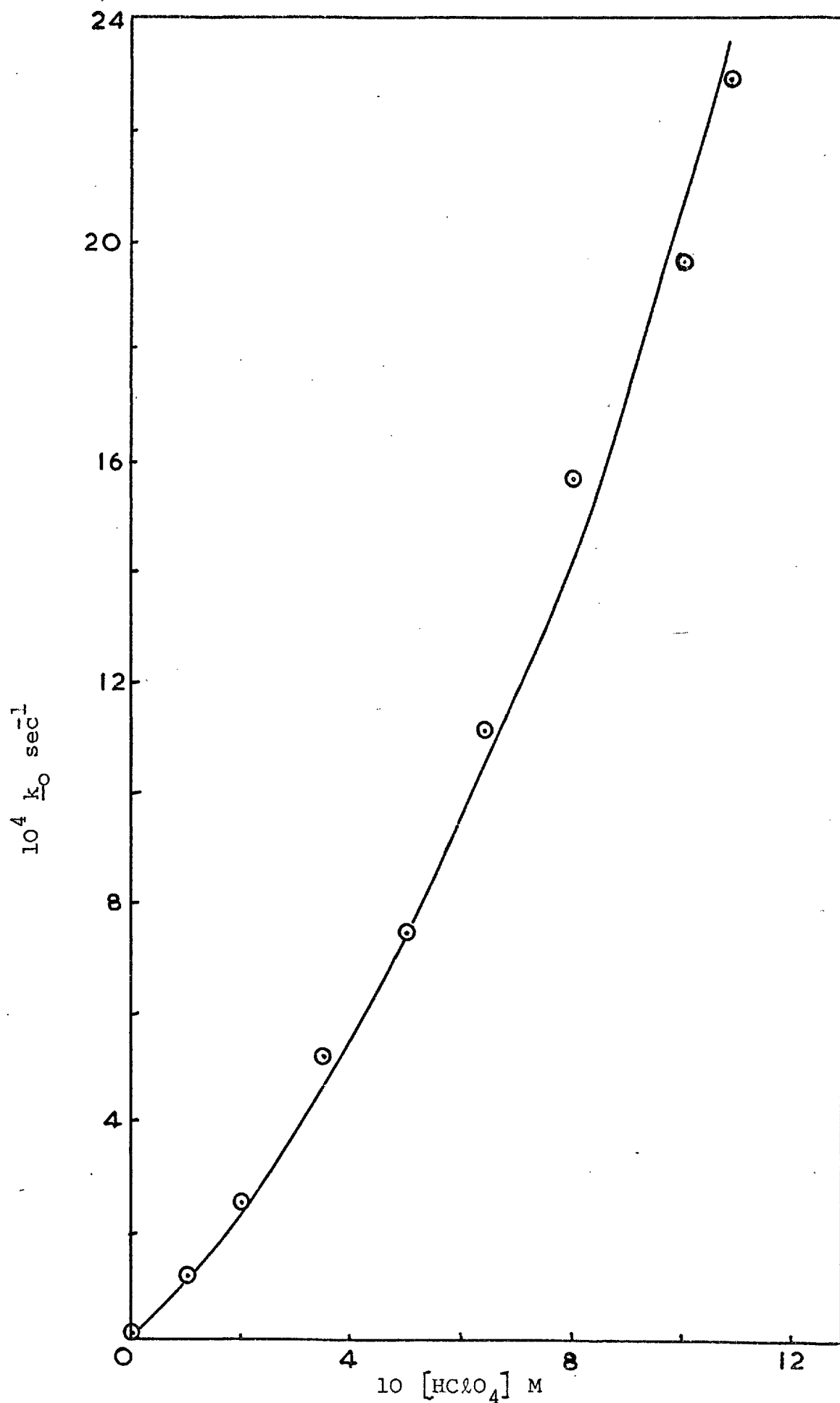


Fig. (VII-1) Acid hydrolysis of 2-benzyl-3,3-diethyloxaziridine  
in 50:50 EtOH-water at 25°C.

TABLE (VII-2)

Ring opening of 2-Benzyl-3,3-diethyloxaziridine in sodium acetate-acetic acid buffer at 25°C in 50-50 aqueous-ethanol (v/v) solution

| Expt. | $[\text{OAc}^-]/[\text{HOAc}]$ | $[\text{OAc}^-]$ | $10^4 k_o \text{ sec}^{-1}$ |
|-------|--------------------------------|------------------|-----------------------------|
| 209   | 1:1                            | 0.1              | 0.4                         |
| 210   | "                              | 0.02             | 0.23                        |
| 213   | "                              | 0.05             | 0.30                        |
| 211   | 5:1                            | 0.5              | 1.12                        |
| 212   | "                              | 0.1              | 0.43                        |
| 214   | "                              | 0.25             | 0.70                        |

Plots of  $k_o$  versus  $[\text{OAc}^-]$  gave straight lines [fig. (VII-2)] of slopes  $2.14 \times 10^4 \text{ l mol}^{-1} \text{ sec}^{-1}$  and  $1.71 \times 10^4 \text{ l mol}^{-1} \text{ sec}^{-1}$  for the 1:1 and 5:1 buffers respectively.

Reactions in various EtOH-water solutions

Reactions were also carried out in various EtOH-water mixtures, at constant  $[\text{HClO}_4]$  at 25°C and these results are summarised in Table (VII-3).

TABLE (VII-3)

Hydrolysis of 2-Benzyl-3,3-diethyloxaziridine in various EtOH-water mixtures (v/v) in 1.01 M  $\text{HClO}_4$  at 25°C

| Expt. | $[\text{HClO}_4]$<br>M | Water:EtOH<br>(v/v) | $10^4 k_o \text{ sec}^{-1}$ |
|-------|------------------------|---------------------|-----------------------------|
| 201   | 1.01                   | 20:80               | 14.92                       |
| 202   | "                      | 40:60               | 16.83                       |
| 196   | "                      | 50:50               | 19.57                       |
| 204   | "                      | 60:40               | 21.93                       |
| 205   | "                      | 80:20               | 22.13                       |
| 203   | "                      | 96:4                | 19.78                       |

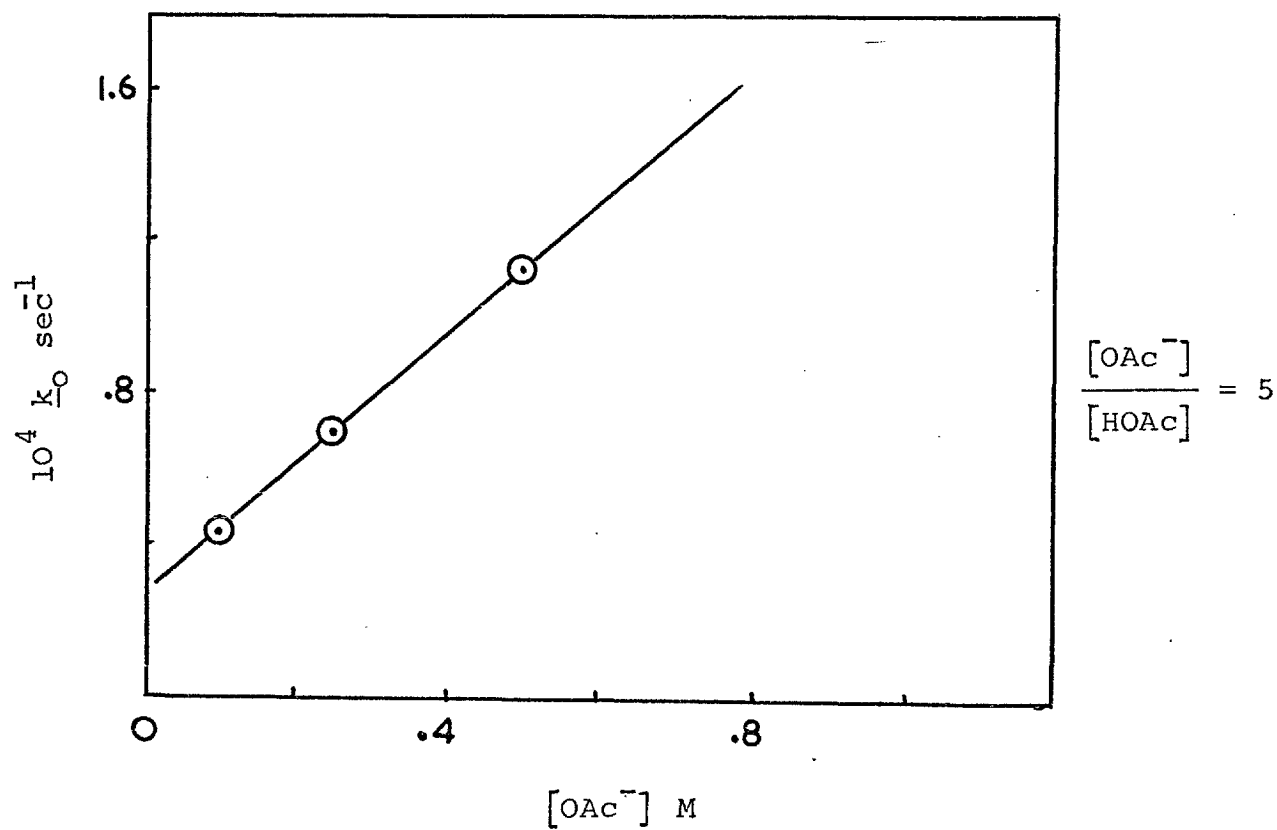
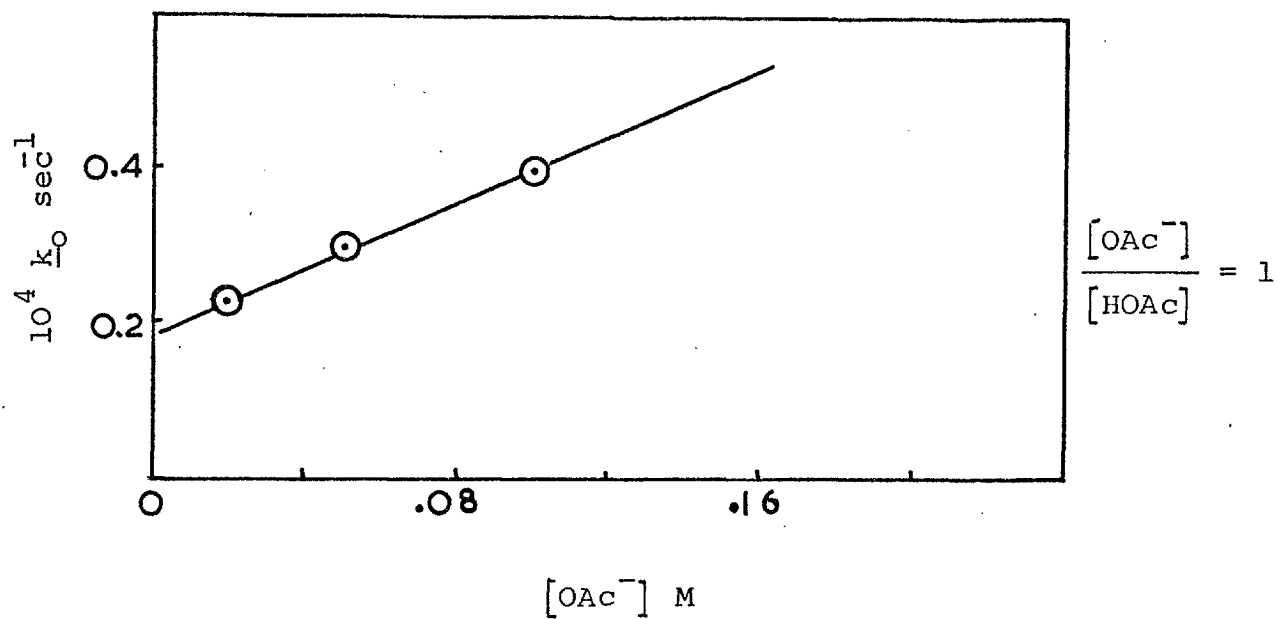


Fig. (VII-2) Hydrolysis of 2-benzyl-3,3-diethyl-oxaziridine (in 50:50 EtOH-water) in sodium acetate-acetic acid buffers at 25°C.

Reactions in various dioxan-water mixtures

The ring opening reactions of 2-benzyl-3,3-diethyloxaziridine were carried out in various dioxan-water (v/v) mixtures in 1.01 M  $\text{HClO}_4$  at  $25^\circ\text{C}$  and these results are presented in Table (VII-4).

TABLE (VII-4)

Hydrolysis of 2-Benzyl-3,3-diethyloxaziridine in various dioxan-water (v/v) mixtures

$$[\text{HClO}_4] = 1.01 \text{ M, temp.} = 25^\circ \pm 0.1^\circ\text{C}$$

| Expt. | Water:dioxan<br>(v/v) | $10^4 \text{ } k_o \text{ sec}^{-1}$ |
|-------|-----------------------|--------------------------------------|
| 206   | 20:80                 | 20.2                                 |
| 207   | 50:50                 | 17.9                                 |
| 208   | 70:30                 | 19.4                                 |

The effect of ionic strength on the hydrolysis of 2-benzyl-3,3-diethyloxaziridine was also investigated in the presence of equimolar quantities of  $\text{NaCl}$  and  $\text{NaClO}_4$ . These results are summarised in Table (VII-5).

TABLE (VII-5)

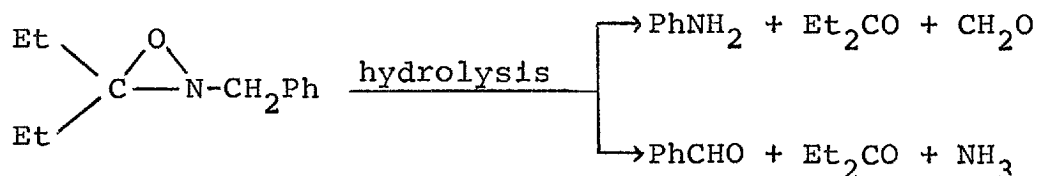
Hydrolysis of 2-Benzyl-3,3-diethyloxaziridine in the presence of salts in 50:50 ethanol:water at  $25^\circ\text{C}$

$$\mu = 1.0$$

| Expt. | [Salt]<br>0.9 M  | $[\text{HClO}_4]$<br>M | $10^4 \text{ } k_o \text{ sec}^{-1}$ |
|-------|------------------|------------------------|--------------------------------------|
| 198   | $\text{NaCl}$    | 0.1                    | 2.33                                 |
| 199   | $\text{NaClO}_4$ | 0.1                    | 2.83                                 |

### VII.1.2 Product Analysis

The hydrolysis of 2-benzyl-3,3-diethyloxaziridine gives two main products<sup>110</sup> viz. benzaldehyde and aniline, depending on the conditions [Scheme (VII-1)].



Scheme (VII-1) Hydrolysis of 2-benzyl-3,3-diethyloxaziridine

Aniline was estimated from a previously determined relationship between the absorbance of the azo dye solution obtained by coupling diazotised aniline with R-salt and the concentration of aniline. Table (VII-6) and the fig.(VII-3) illustrate the relationship. Benzaldehyde was estimated from its U.V. absorption (for details see Chapter XI).

TABLE (VII-6)

Optical densities of various standard solutions of diazotized aniline coupled with R-salt

| $10^5$ [Aniline] M | Absorbance of the dye solution<br>(100 ml) |
|--------------------|--------------------------------------------|
| 1.305              | 0.32                                       |
| 1.38               | 0.35                                       |
| 1.96               | 0.46                                       |
| 2.07               | 0.495                                      |
| 2.35               | 0.56                                       |
| 2.61               | 0.62                                       |
| 2.76               | 0.68                                       |

Results of the product analysis are presented in Table (VII-7).

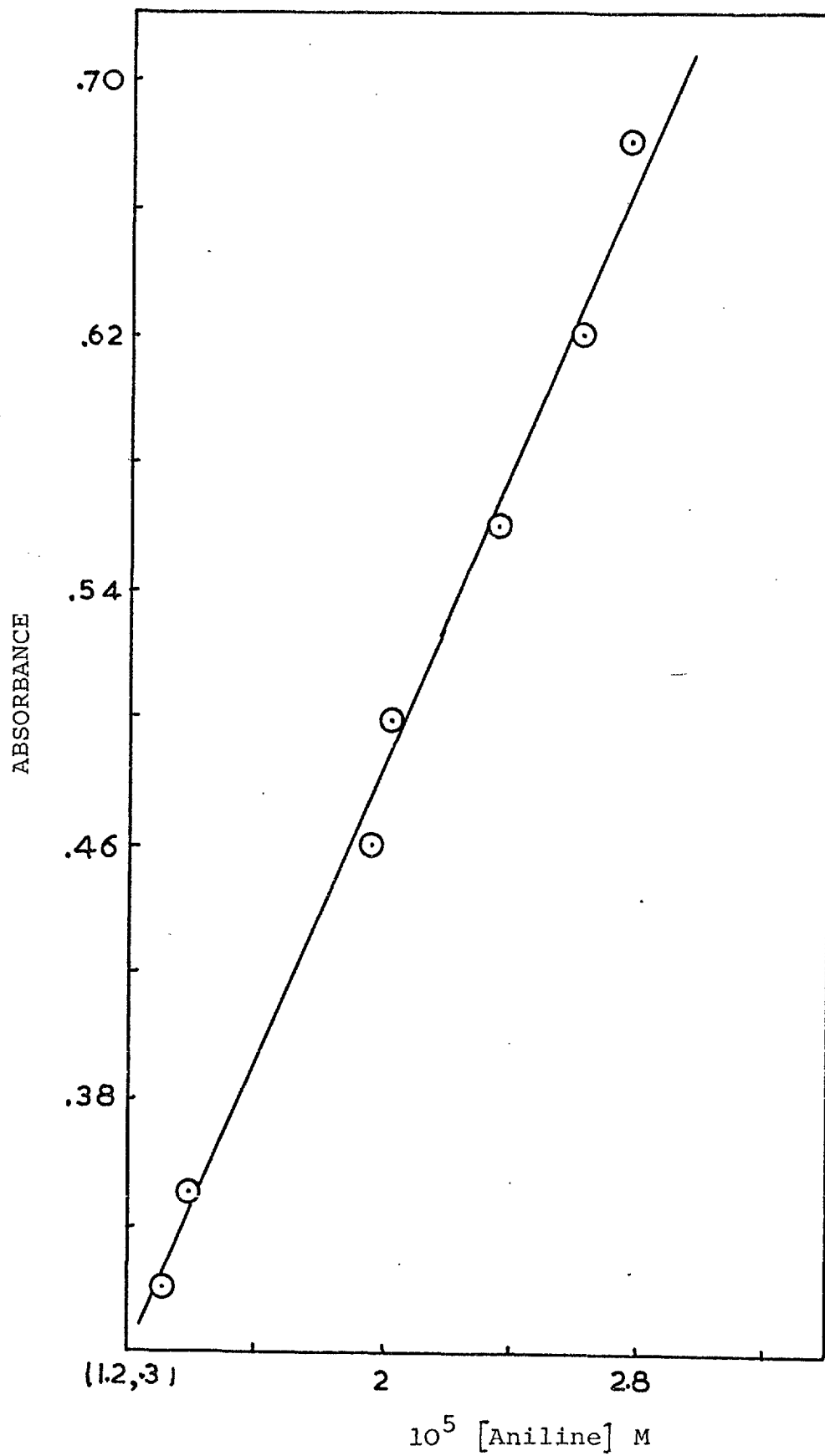


Fig. (VII-3) Absorbance of diazotised aniline, coupled with R-salt against [aniline].

TABLE (VII-7)

Estimation of aniline and benzaldehyde; hydrolysis of 2-benzyl-3,3-diethyloxaziridine at 25°C

| [HClO <sub>4</sub> ]<br>M | Solvent (v/v)      | [Salt]                   | 10 <sup>3</sup> [PhNH <sub>2</sub> ]<br>M | 10 <sup>3</sup> [PhCHO] | % PhNH <sub>2</sub> | % PhCHO |
|---------------------------|--------------------|--------------------------|-------------------------------------------|-------------------------|---------------------|---------|
| 0                         | 50:50; EtOH-water  | -                        | 0                                         | 1.85                    | 0                   | 100     |
| 0.10                      | " "                | -                        | 0.92                                      | 0.86                    | 52                  | 48      |
| 0.20                      | " "                | -                        | 1.07                                      | 0.70                    | 60                  | 40      |
| 0.35                      | " "                | -                        | 1.20                                      | 0.61                    | 68                  | 32      |
| 0.50                      | " "                | -                        | 1.22                                      | 0.53                    | 69                  | 31      |
| 0.80                      | " "                | -                        | 1.35                                      | 0.43                    | 76                  | 24      |
| 1.0                       | " "                | -                        | 1.39                                      | 0.38                    | 79                  | 21      |
| 1.01                      | 80:20 "            | -                        | 1.07                                      | 0.73                    | 60                  | 40      |
| "                         | 60:40 "            | -                        | 1.30                                      | 0.46                    | 73                  | 27      |
| "                         | 40:60 "            | -                        | 1.43                                      | 0.33                    | 81                  | 19      |
| "                         | 20:80 "            | -                        | 1.56                                      | 0.28                    | 88                  | 12      |
| 0.10                      | 50:50 "            | 0.9 M NaCl               | 0.57                                      | 1.01                    | 37                  | 63      |
| "                         | " "                | 0.9 M NaClO <sub>4</sub> | 1.16                                      | 0.52                    | 69                  | 31      |
| 1.01                      | 80:20 dioxan-water | -                        | 2.2                                       | 2.4                     | 45                  | 55      |
| "                         | 50:50 "            | -                        | 3.3                                       | 1.5                     | 67                  | 33      |
| "                         | 30:70 "            | -                        | 4.0                                       | 0.9                     | 81                  | 19      |

### VII.1.3 Catalysis by Selenocyanate

Potassium selenocyanate was found to catalyse the ring opening reactions of 2,3,3-triethyloxaziridine in 0.01 M borax buffer and the observed rates have a linear dependence on the concentration of selenocyanate, as illustrated by Table (VII-8). The plot of these data is shown in fig. (VII-4).

TABLE (VII-8)

Hydrolysis of 2,3,3-triethyloxaziridine catalysed by selenocyanate in 0.01 M aqueous borax buffer at 25°C

| Expt. | $10^3 [\text{SeCN}^-] \text{ M}$ | $10^3 k_o \text{ sec}^{-1}$ |
|-------|----------------------------------|-----------------------------|
| 484   | 4.1                              | 0.42                        |
| 481   | 10.6                             | 1.22                        |
| 483   | 20.8                             | 2.367                       |

$$k_2^{\text{SeCN}^-} = 0.11 \text{ l.mole}^{-1} \text{ sec}^{-1}$$

### VII.2 Discussion

The rate profile for the hydrolysis of 2-benzyl-3,3-diethyloxaziridine in 50-50 ethanol-water (v/v) containing various amounts of  $\text{HClO}_4$  [fig. (VII-1)] is not properly understood. The rate increases faster than expected with increasing acid concentration and when  $[\text{HClO}_4] = 1.09 \text{ M}$ , the observed rate is almost double the expected value. The effect of ionic strength has not been considered in these runs and may have attributed some positive uplift to the rates.

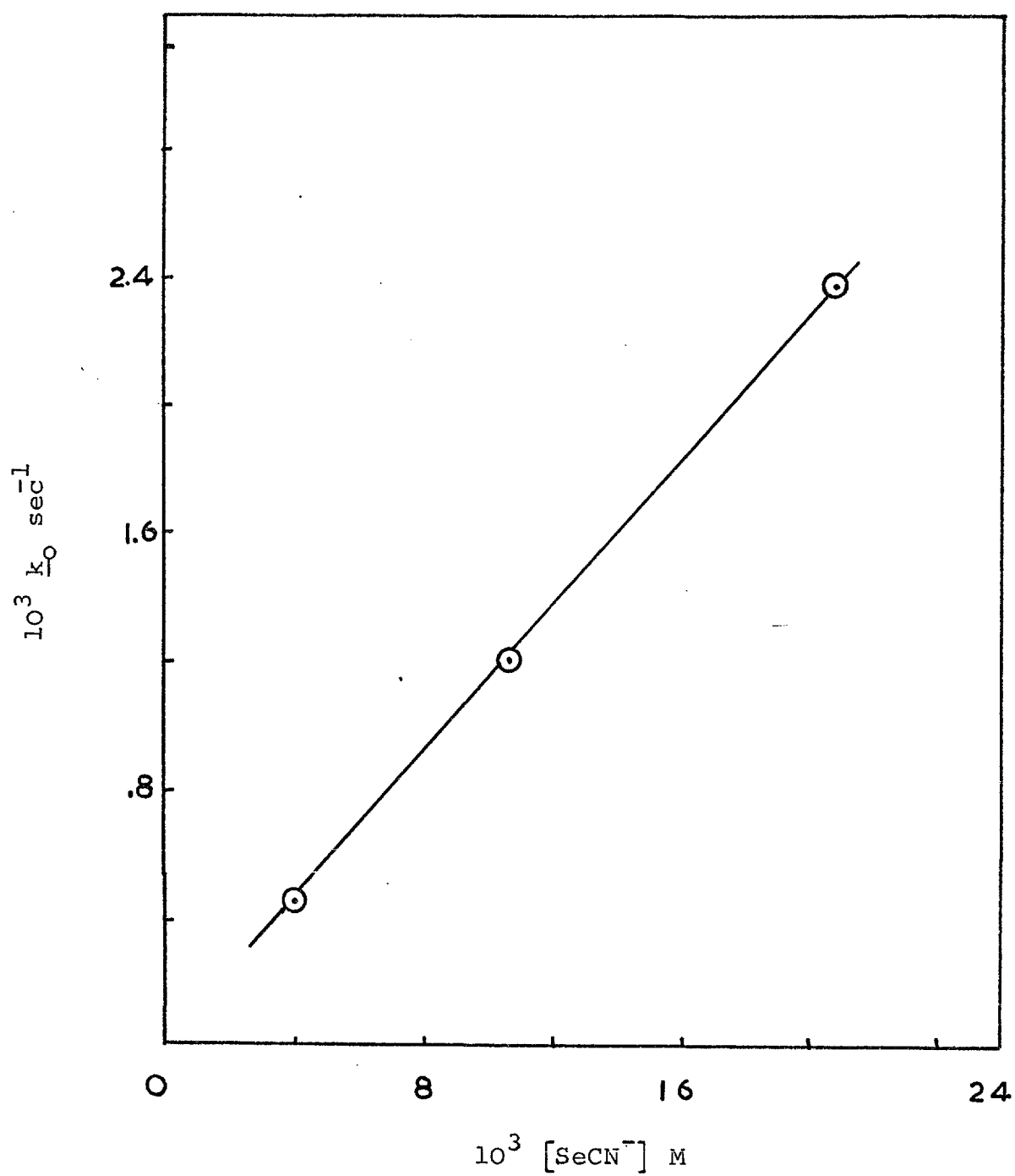
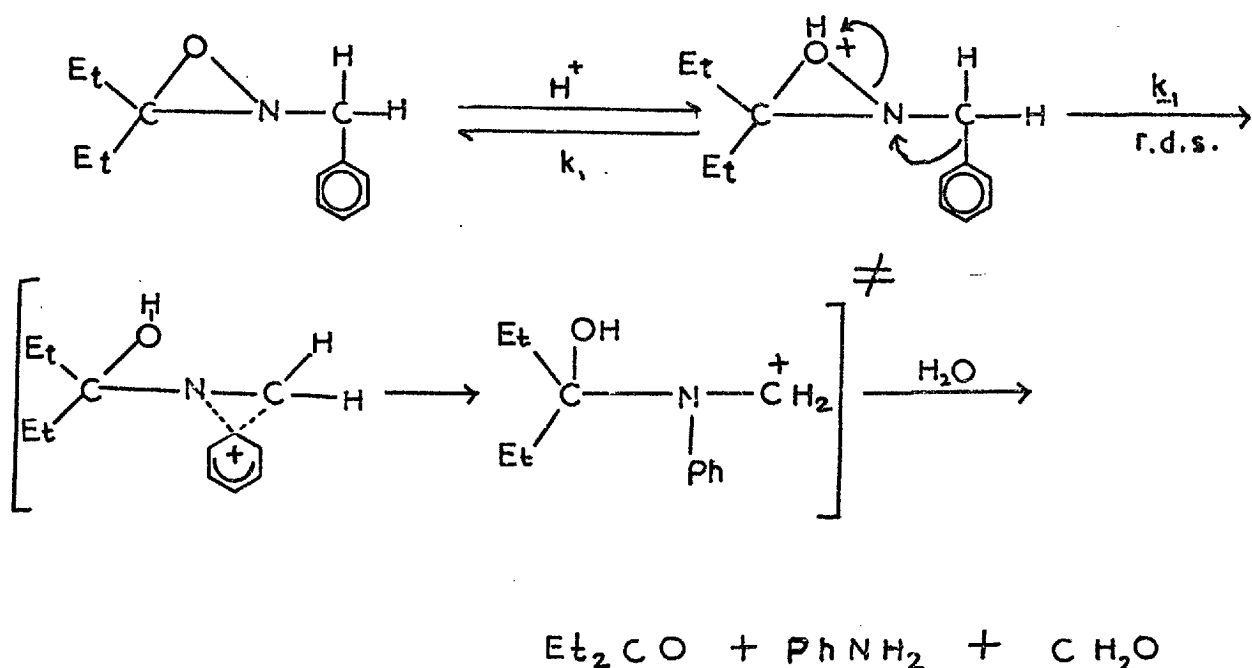


Fig. (VII-4) Hydrolysis of 2,3,3-triethyloxaziridine catalysed by selenocyanate in 0.01 M borax buffers at 25°C.

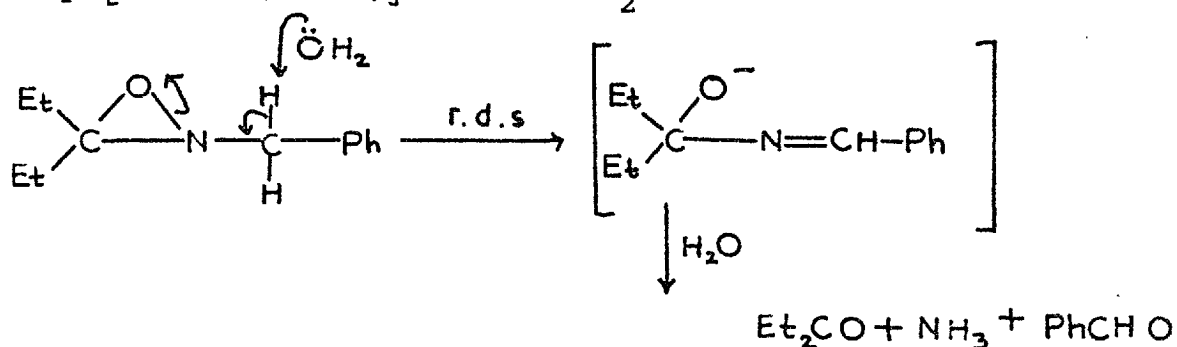
As previously suggested by Lobo<sup>110</sup>, O-protonation, rather than N-protonation, seems to lead successfully to the ring opening of oxaziridines.

The fact that the yields of aniline are negligible [Table (VII-7)] when the reactions are carried out at zero  $\text{HClO}_4$  concentration, suggests that aniline formation is favoured by the acid catalysed pathway, as in Scheme (VII-2), and, conversely,



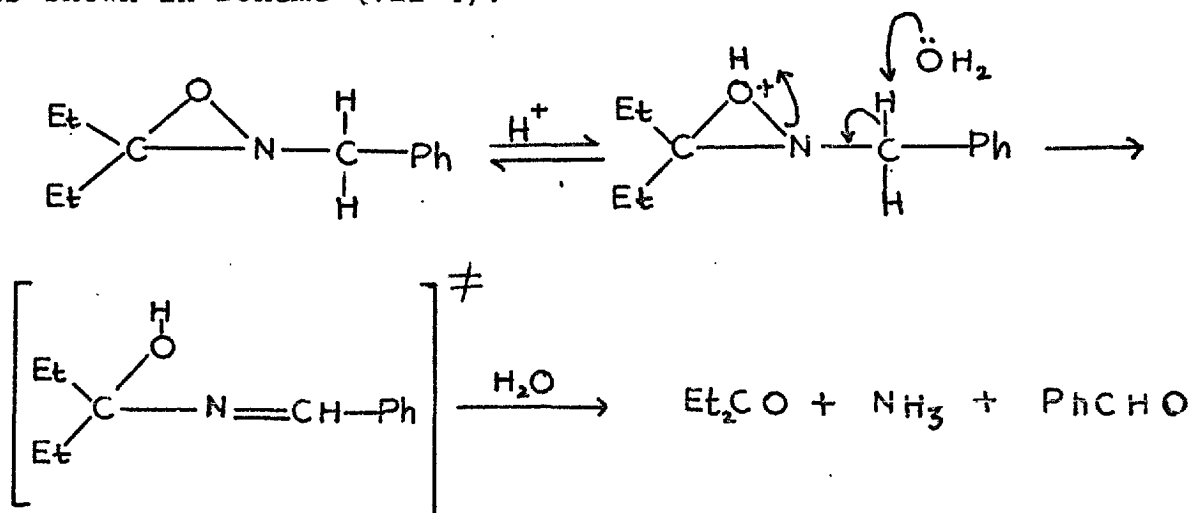
Scheme (VII-2) Aniline formation via the acid catalysed pathway

that benzaldehyde formation is favoured by a base-catalysed pathway [Scheme (VII-3)] in which  $\text{H}_2\text{O}$  acts as the base.



Scheme (VII-3) Formation of benzaldehyde via the base-catalysed pathway

From Table (VII-7) it can be seen that at 0.1 M  $\text{HClO}_4$ , benzaldehyde formation drops to 48% and on this basis, at 0.2 M  $\text{HClO}_4$ , benzaldehyde formation may be expected to be around 25%, similarly at 0.35 M and 0.8 M  $\text{HClO}_4$ , approximately 15% and 7% respectively would be expected. In practice, however, the amount of benzaldehyde is about 15% higher in each case. Lobo<sup>110</sup> has reported the yield of benzaldehyde to be 5.9% even at 4.43 M  $\text{HClO}_4$ . This clearly suggests that some benzaldehyde is formed via the acid-catalysed pathway as well as shown in Scheme (VII-4).



Scheme (VII-4) Formation of benzaldehyde via the acid-catalysed pathway

Reactions carried out in acetic acid-sodium acetate buffers [see Table (VII-2) and fig.(VII-2)] were used to calculate the catalytic rate constants for acetate ion ( $k_{\text{OAc}^-}$ ) and acetic acid ( $k_{\text{AcOH}}$ ). It was assumed that

$$\begin{aligned}
 \text{rate} &= k_{\text{O}} [\text{oxaziridine}] \\
 &= k_{\text{AcOH}} [\text{AcOH}] [\text{oxaziridine}] + k_{\text{OAc}^-} [\text{OAc}^-] [\text{oxaziridine}]
 \end{aligned}
 \tag{VII-3}$$

$$\text{or } k_o = k_{\text{AcOH}} [\text{AcOH}] + k_{\text{OAc}^-} [\text{OAc}^\ominus] \quad (\text{VII-4})$$

$$\text{or } \frac{k_o}{[\text{OAc}^-]} \equiv \text{slope} = k_{\text{AcOH}} \frac{[\text{AcOH}]}{[\text{OAc}^\ominus]} + k_{\text{OAc}^-} \quad (\text{VII-5})$$

When the buffer ratio was 5:1, the slope was found to be  $1.71 \times 10^4 \text{ mole}^{-1} \cdot \text{l.} \cdot \text{sec}^{-1}$ , and with a buffer ratio of 1:1, the slope was found to be  $2.14 \times 10^4 \text{ mole}^{-1} \cdot \text{l.} \cdot \text{sec}^{-1}$ . Thus from eqn. (VII-5), values of  $k_{\text{OAc}^-}$  and  $k_{\text{AcOH}}$  are  $1.6 \times 10^4 \text{ mole}^{-1} \cdot \text{l.} \cdot \text{sec}^{-1}$  and  $0.54 \times 10^4 \text{ mole}^{-1} \cdot \text{l.} \cdot \text{sec}^{-1}$  respectively. This shows that  $k_{\text{OAc}^-}$  is about 3 times more effective than  $k_{\text{AcOH}}$ . Together with the assumption that the formation of benzaldehyde occurs by both the base-catalysed and the acid-catalysed pathways, these rates account for the higher than expected yield of benzaldehyde [see Table (VII-7)].

When the concentration of  $\text{HClO}_4$  is constant, but the water concentration in the solvent is increased, a gradual increase in aniline formation is observed [Table (VII-7)]. Keeping in mind the fact that aniline formation is favoured by the acid-catalysed pathway via a charged transition state, whereas benzaldehyde formation apparently involves a neutral transition state, this observation may be explained in terms of the increased proton-donating properties of the medium<sup>122</sup> (at higher water concentration) together with increased dielectric-constant of the solvent. The ratios of aniline to benzaldehyde under these conditions have been plotted in fig. (VII-5).

The fact that aniline formation is favoured by the increase in  $\text{HClO}_4$  concentration in 50-50 (v/v) EtOH-water may be explained in terms of the increase in concentration of

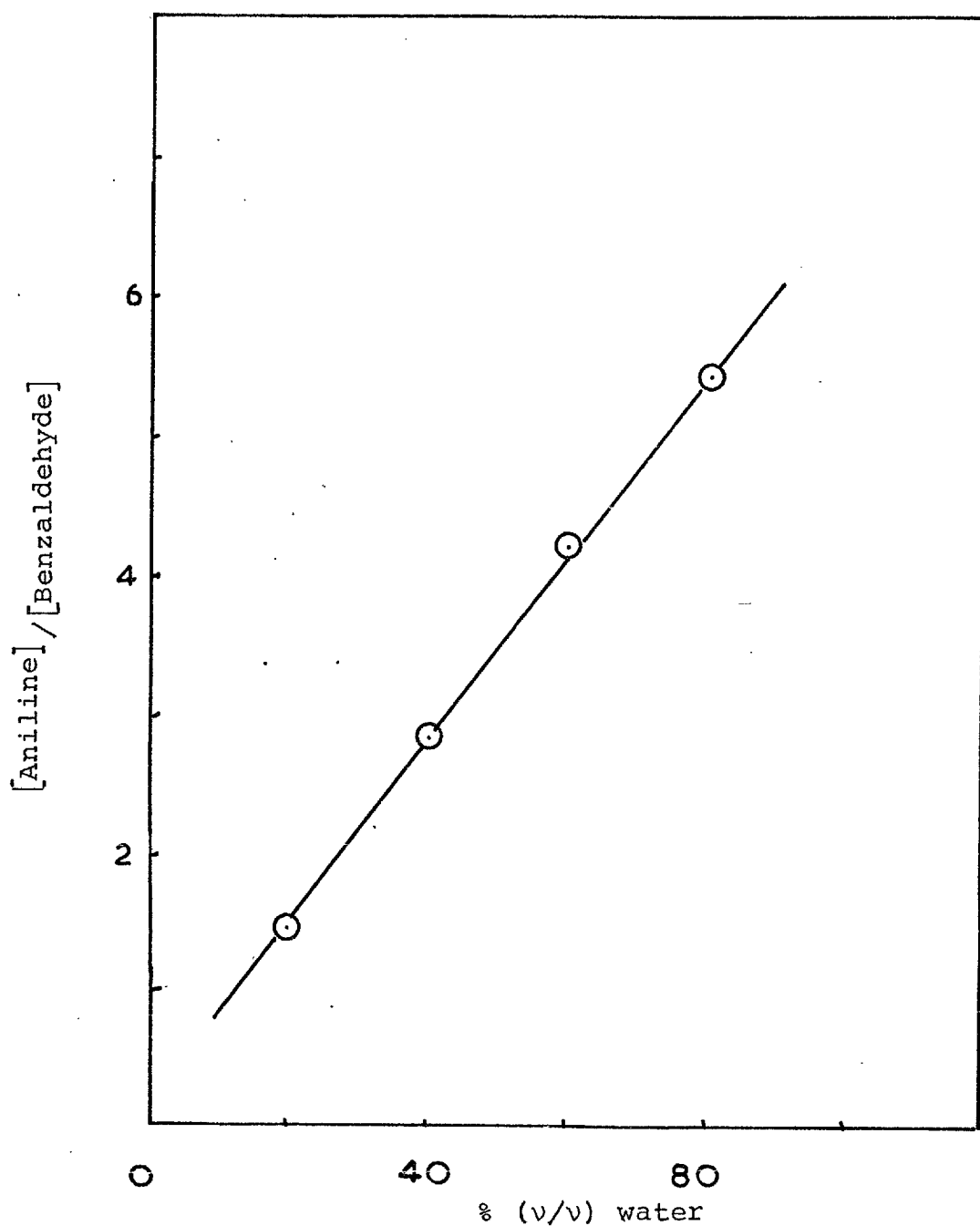


Fig. (VII-5) A plot of  $\frac{[\text{aniline}]}{[\text{benzaldehyde}]}$  vs. % (v/v) water for the hydrolysis of 2-benzyl-3,3-diethyl-oxaziridine in various EtOH-water mixtures at 25°C;  $[\text{HClO}_4] = 1 \text{ M.}$

O-conjugate acid of the oxaziridine. The fig. (VII-6) shows a plot of the ratios of aniline to benzaldehyde versus  $[\text{HClO}_4]$ .

### VII.2.1 Nucleophilic reactivity

Nucleophilic reactivity towards the electron-deficient nitrogen in 2,3,3-triethyloxaziridine has not been studied in as much detail as towards the O-nitroaryl hydroxylamines. However, from the studies of O-(2,4-dinitrophenyl)hydroxylamine and alkyl nitrites it is evident that the nitrogen of 2,3,3-triethyloxaziridine should be a soft electrophilic centre and as such, soft polarizable nucleophiles should be highly reactive towards it. Potassium selenocyanate was used as a nucleophile [see Table (VII-8)] and from a plot of observed rate vs. the concentrations of the nucleophile [see fig. (VII-4)], catalytic rate constant  $k_2^{\text{SeCN}^-}$  was calculated to be  $0.11 \text{ mole}^{-1} \cdot \text{l. sec}^{-1}$ . Comparison with the catalytic rate constants reported by Lobo<sup>110</sup> [see Table (IV-1)] reveals that  $\text{SeCN}^-$  is more reactive than all the other nucleophiles examined so far in agreement with the prediction that the nitrogen is a relatively soft electrophilic centre.

### VII.3 Conclusions

It is clear that the nitrogen centre in 2,3,3-triethyloxaziridine is a relatively soft electrophilic centre and the ring opening reactions are facilitated by soft nucleophiles.

In the case of 2-benzyl-3,3-diethyloxaziridine, aniline formation increases with increasing  $\text{HClO}_4$  concentration in 50-50 EtOH- $\text{H}_2\text{O}$  (v/v). Aniline formation also increases with increase in water concentration in the mixed solvent at a fixed  $\text{HClO}_4$

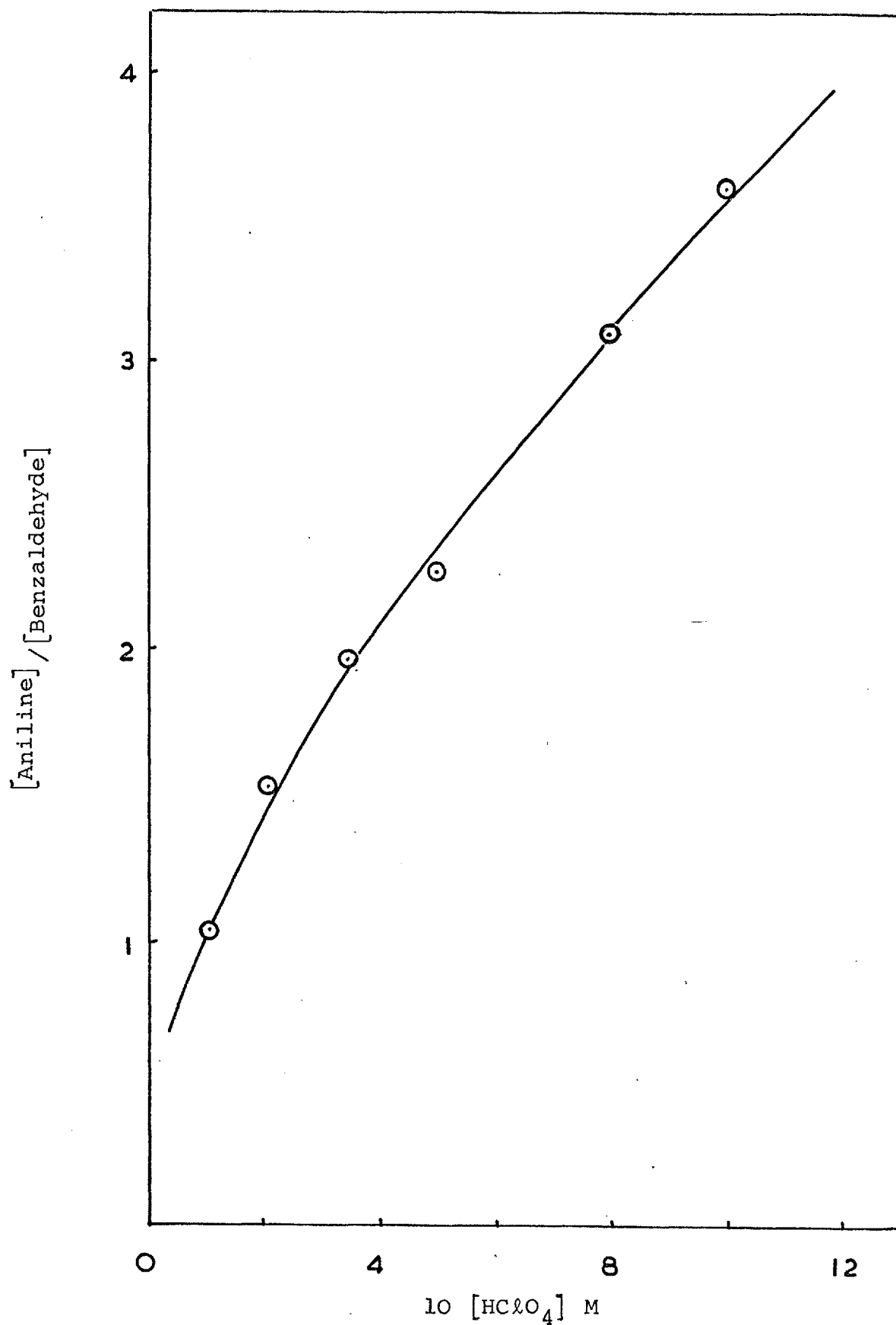


Fig. (VII-6) A plot of  $[\text{aniline}]/[\text{benzaldehyde}]$  vs.  $[\text{HClO}_4]$  for the hydrolysis of 2-benzyl-3,3-diethyloxaziridine in 50:50 EtOH-water at  $25^\circ\text{C}$ .

concentration. Aniline formation seems to take place via the acid-catalysed pathway only, whereas benzaldehyde formation proceeds via both the base-catalysed and the acid-catalysed pathways.

## CHAPTER VIII

### Summaries of the Results

Three different electron-deficient N-centres present in O-(nitroaryl)-hydroxylamines, alkylnitrites and oxaziridines have been investigated (the latter in less detail) with special interest to their nucleophilic reactivities.

Examination of the relative reactivities of various nucleophiles towards O-(2,4-dinitrophenyl)-hydroxylamine suggests that the N-atom of this substrate is a moderately soft electrophilic centre similar to that found in methyl-iodide. Further, comparison of these data with those available for other non-carbon electrophilic centres, viz. peroxide oxygen, sulphenyl sulphur and  $I^+$  species, suggests that reactivities are similar and not entirely different as once thought. The polarizability factor is pre-eminent in these reactions and electron-polarizability alone gives a better correlation than the Edwards oxi-base scale. The nucleophilic reactivity order for solvent water remains unaffected (at least in cases of  $Cl^-$ ,  $Br^-$  and  $I^-$ ) on going to dimethyl sulphoxide, in agreement with previous findings<sup>30,56</sup>. Soft nucleophiles, especially those with selenium and sulphur centres, prove to be very effective nucleophiles and hard bases like acetate and chloride are relatively ineffective, in agreement with the HSAB principle.

$\alpha$ -Nucleophiles like  $NH_2OH$ ,  $NH_2NH_2$  show no striking reactivity and seem to be no better than other nitrogen bases of similar basicity. However, perhydroxyl ion ( $HO_2^-$ ) is significantly more reactive than  $OH^-$ .

Product analysis, activation data and the kinetic effects of varying dielectric-constant suggest these reactions proceed via an  $S_N2$  pathway. However, only a small steric inhibition has been observed which refers mainly to the incoming group suggesting that the steric environment about N is more free than that found for substitution of comparable carbon compounds.

Nitrogen in alkyl nitrites appears to be moderately hard and the basicity factor is of overriding importance. The order of relative reactivities is similar to that reported for nitrous acidium ion<sup>74</sup>. 2,6-Lutidine buffers show nucleophilic properties in these reactions. It seems that the reactions involve the protonated alkyl nitrite followed by nucleophilic attack by nucleophilic species including  $H_2O$  present as solvent. No evidence has been found in favour of an  $S_N1$  pathway.

Nitrogen in 2,3,3-triethyloxaziridine also appears to be moderately soft which is evident from its facile reaction with a soft nucleophile, selenocyanate.

As far as the products of the acid-hydrolysis of 2-benzyl-3,3-diethyloxaziridine is concerned, it has been assumed that aniline formation proceeds via the acid-catalysed pathway and that of benzaldehyde via both the acid and base-catalysed (water present in the solvent acts as a base) pathways. Aniline formation seems to involve a charged transition state and is favoured by high dielectric and proton-donating properties of the medium, whereas benzaldehyde formation seems to involve a neutral transition state.

PART 3

EXPERIMENTAL

### Experimental Details

In the following chapters, experimental methods concerning O-nitroarylhydroxylamines, alkyl nitrites and oxaziridines are given.

All the U.V. spectra were recorded either in a Unicam SP-1800 or a SP-700 spectrophotometer. I.R. spectra were recorded usually as a thin film or as a Nujol mull between two sodium chloride plates with a Perkin Elmer Infrared spectrophotometer 700. N.M.R. spectra were obtained with a Varian A-60 (by Mrs. A.I. Boston and Mr. J. Moor) or with a Varian HA-100 (by Mr. S.J. Roberts). Mass spectra were measured on a M.S.9 high resolution mass spectrometer (by Mrs. J. Lee) using direct sample injection. Water was deionized by percolation through an Elgastat column {Elga Products Ltd., Bucks.}. A Beckman LS200 liquid scintillation counter was used to measure the decomposition of tritiated alkyl nitrite. In all iodometric titrations, a semi-automatic burette system was used. The refractive indices were measured with a Higler and Watts Refractometer under ordinary light. Melting points were taken on a Kofler melting point apparatus or a Gallenkamp m.p. apparatus and are uncorrected. Microanalyses were performed by the analysts of the Imperial College Chemistry Department Microanalysis Service. The pH measurements and titrations were carried out with a Radiometer (PHM26, Titrator 11, Titrigraph type SBR2C) pH Titrator. Thin layer chromatography was carried out on silicagel plates or polygram MN silicagel N-HR/UV254 layers.

## CHAPTER IX

### O-Nitroarylhydroxylamines

An account of experimental methods concerning O-(2,4-dinitrophenyl)-hydroxylamine and its N-methyl derivative together with typical examples of kinetic runs are given in this chapter.

#### IX.1 Kinetic Methods

##### IX.1.1 The Substrate Solution

O-(2,4-dinitrophenyl)-hydroxylamines are sparingly soluble in water. A few crystals of the compound were therefore placed in a 100 ml. conical flask and about 50 ml. of boiled-out water was added. The flask was then stoppered and the solution stirred with a magnetic stirrer for about an hour; after standing for some time this solution was filtered and made up to the mark in a 100 ml. volumetric flask. This solution, or a suitable dilution of it, was called the substrate solution.

##### IX.1.2 The Reaction Solution

In most cases, reaction solutions were prepared in 50 ml. volumetric flasks by weighing one of the reactants directly into the flask or by very carefully transferring it from a weighing boat and dissolving it in a minimum volume of boiled-out water. The required volume of B.D.H. standard sodium hydroxide solution was then added from a 10 ml. graduated burette; the ionic strength was adjusted to a predetermined value by adding anhydrous  $\text{NaClO}_4$  where necessary. Finally, the volume was made up to the mark with boiled-out water.

The stoppered flask was then immersed in a thermostatted tank to equilibrate thermally. The temperature of this tank was usually maintained at  $25^{\circ} \pm 0.1^{\circ}\text{C}$ . Some reactions were also carried out at other temperatures where indicated.

### IX.1.3 Methods of Following Reactions

#### IX.1.3.1 Sampling Method

After about 45 minutes, 10 ml. of the reaction solution was pipetted into a 25 ml. graduated measuring cylinder to be diluted to 12.5 ml. with water. The spectrum of this solution was taken to represent the baseline. In most cases, its absorbance was zero.

To start the reaction, 10 ml. of the substrate solution was added to the reaction flask, which was shaken thoroughly and then returned to the thermostatted tank. The substrate concentration was of the order of ca  $1.4 \times 10^{-4}$  mole  $\text{lit}^{-1}$  in most cases. About 3 ml. of the kinetic solution was then immediately withdrawn and transferred to the appropriate spectrophotometric cell. The absorption of this solution was recorded generally from  $\lambda = 290$  to  $410$  nm with either a Unicam SP1800 or SP 700 spectrophotometer. The reference cell contained water. The time of removing the first aliquot was taken as time zero. Successive aliquots of ca 3 ml. were withdrawn at various timed intervals, placed in the appropriate cell and the U.V. spectrum recorded as above. Good isosbestic points were observed in most cases (Fig. IX-1). Appearance of the 2,4-dinitro phenolate peak at  $\lambda = 360$  or  $400$  nm {Scheme (IX-1)} was used to compute rate constants (section IX.1.4).

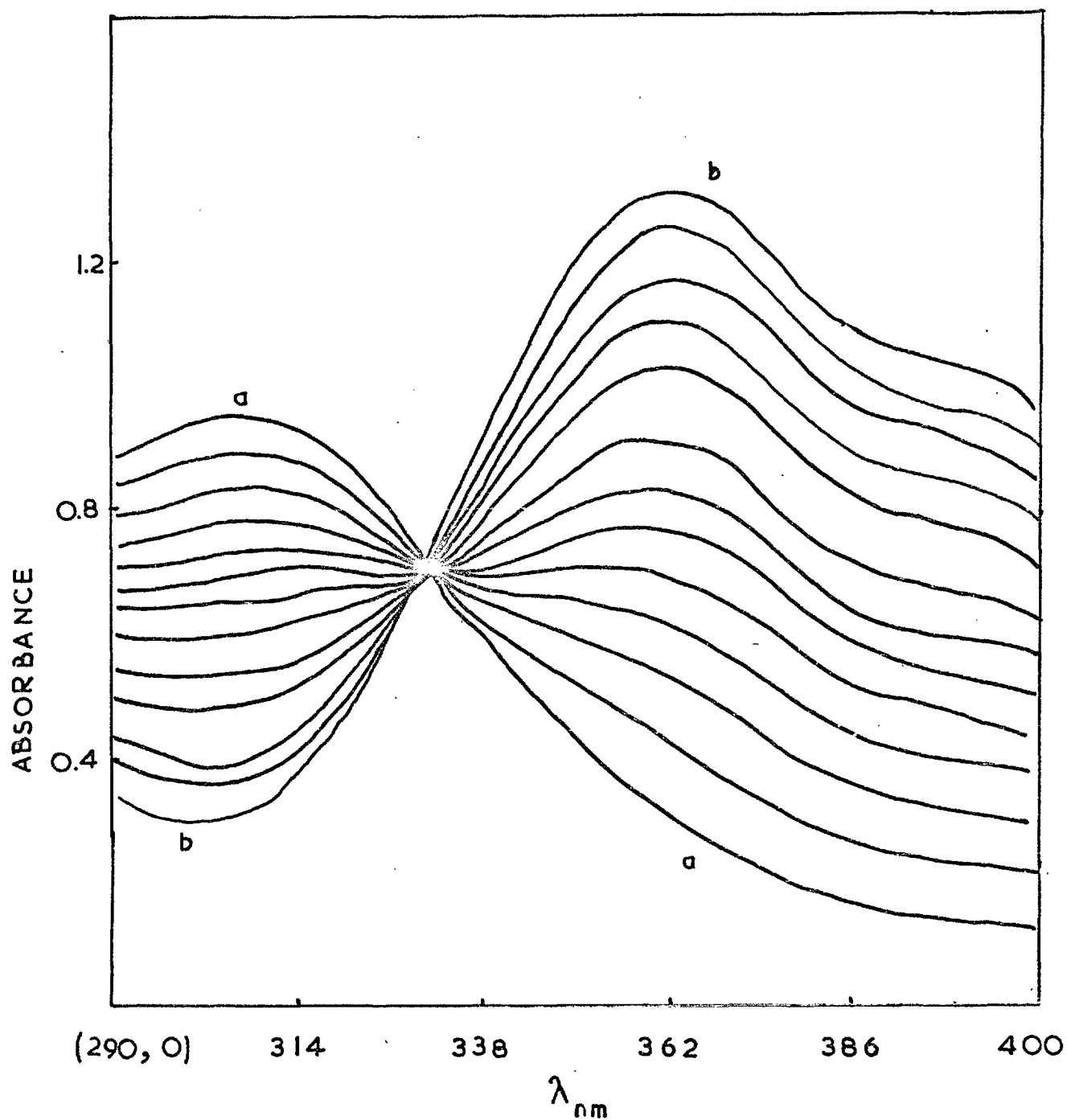
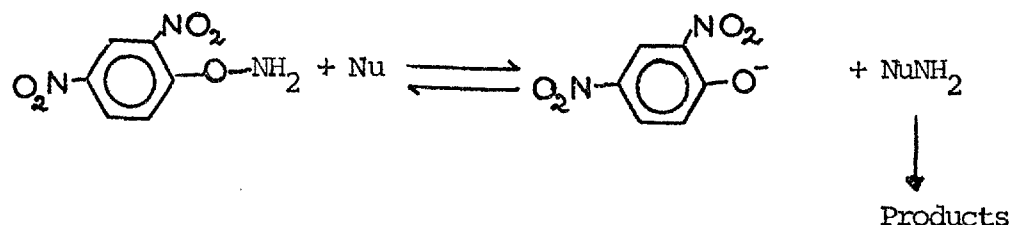


Fig. (X-1) Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by NaSCN (0.05 M) in water at 25°C. ( $\mu = 1.0$ ).

( a and b refer to spectra at  $t = 0$  and  $t = \infty$  respectively)



Scheme (IX-1) Decomposition of O-(2,4-dinitrophenyl)-hydroxylamine by nucleophilic species

An 'infinity' point was taken after about 10 half-lives and usually indicated complete hydrolysis of the substrate.

#### IX.1.3.2 Direct Spectrophotometric Method

When the rate of reaction was too fast to make accurate sampling feasible, the reaction was followed directly in the thermostatted quartz spectrophotometric cells of a Unicam SP-1800 spectrophotometer. The instrument was either programmed to superimpose spectra at various timed intervals for a given range (generally from  $\lambda = 290$  to 410 nm) or to record continuously at a fixed wavelength characteristic of the product.

#### IX.1.4 Calculation of the Rate Coefficient

Since the 2,4-dinitrophenolate ion has a strong absorption at  $\lambda = 360$  nm where the substrate absorption is very low, this wavelength was found suitable for calculation of the rate coefficients. However, in some cases calculations were also carried out at other wavelengths. Since the concentration of the product is gradually increasing with time, and that of the substrate is decreasing, the method of calculation must allow

for change in both. The following equations illustrate the method employed.

$$\text{O.D.}_t = (a - x)\epsilon_s + x\epsilon_p \quad (\text{IX-1})$$

where  $\text{O.D.}_t$  = optical density (absorbance) at time 't'

$a$  = initial concentration of the substrate

$x$  = concentration of product formed at time 't'

$\epsilon_s$  = extinction coefficient of the substrate

$\epsilon_p$  = extinction coefficient of the product .

$$\therefore \text{O.D.}_t - a\epsilon_s = x(\epsilon_p - \epsilon_s) \quad (\text{IX-2})$$

$$\text{or } x = \frac{\text{O.D.}_t - a\epsilon_s}{\epsilon_p - \epsilon_s}$$

$$\begin{aligned} \text{or } a - x &= a - \frac{(\text{O.D.}_t - a\epsilon_s)}{(\epsilon_p - \epsilon_s)} \\ &= \frac{a\epsilon_p - a\epsilon_s - \text{O.D.}_t + a\epsilon_s}{\epsilon_p - \epsilon_s} \\ &= \frac{a\epsilon_p - \text{O.D.}_t}{\epsilon_p - \epsilon_s} \quad (\text{IX-3}) \end{aligned}$$

Since  $\text{O.D.}_\infty = a\epsilon_p$  and  $\text{O.D.}_0 = a\epsilon_s$ , where  $\text{O.D.}_\infty$  and  $\text{O.D.}_0$  refer to the optical density of the reaction mixture at time  $t = \infty$  and  $t = 0$ , respectively; eqn. (IX-3) can be written as:

$$a - x = \frac{\text{O.D.}_\infty - \text{O.D.}_t}{\epsilon_p - \epsilon_s}$$

$$\begin{aligned}
 \therefore \frac{a}{a-x} &= \frac{\frac{a}{O.D._{\infty} - O.D._t}}{\frac{\epsilon_p - \epsilon_s}{\epsilon_p - \epsilon_s}} \\
 &= \frac{a(\epsilon_p - \epsilon_s)}{O.D._{\infty} - O.D._t} \\
 &= \frac{a\epsilon_p - a\epsilon_s}{O.D._{\infty} - O.D._t}
 \end{aligned}$$

Thus:

$$\frac{a}{a-x} = \frac{O.D._{\infty} - O.D._0}{O.D._{\infty} - O.D._t}$$

Thus  $k_o$ , the observed first order rate coefficient, was usually obtained from the slope  $\left( = 2.303/k_o \right)$  of plots of  $\log \frac{O.D._{\infty} - O.D._0}{O.D._{\infty} - O.D._t}$  versus time. In a few cases,  $k_o$  was calculated directly from the first order rate expression eqn. (IX-4).

$$k_o = \frac{2.303}{(t - t_o)} \log \frac{O.D._{\infty} - O.D._0}{O.D._{\infty} - O.D._t} \quad (IX-4)$$

IX.1.5 Typical Kinetic Runs

TABLE (IX-1)

Hydrolysis of O-(2,4-dinitrophenyl)hydroxylamine catalysed by NaSCN followed by direct spectrophotometric method

Expt. 389

Initial  $[\text{NaSCN}] = 0.10 \text{ M}$ ;  $[\text{NaOH}] = 0.001 \text{ M}$

$\mu = 1.0$  adjusted by  $\text{NaClO}_4$ , temp. =  $25^\circ \pm 0.1^\circ \text{C}$

| Time (min) | O.D. $\lambda_{360\text{nm}}$ | (O.D. $_{\infty}$ - O.D. $_t$ ) | $\frac{\text{O.D.}_{\infty} - \text{O.D.}_0}{\text{O.D.}_{\infty} - \text{O.D.}_t}$ | % reaction | $10^2 k_o \text{ min}^{-1}$ |
|------------|-------------------------------|---------------------------------|-------------------------------------------------------------------------------------|------------|-----------------------------|
| 0          | 0.49                          | -                               | -                                                                                   | -          | -                           |
| 1          | 0.64                          | 1.29                            | 1.12                                                                                | 10.6       | 11.3                        |
| 2          | 0.78                          | 1.15                            | 1.25                                                                                | 20.0       | 11.2                        |
| 3          | 0.91                          | 1.02                            | 1.41                                                                                | 29.0       | 11.4                        |
| 4          | 1.02                          | 0.91                            | 1.58                                                                                | 36.8       | 11.5                        |
| 5          | 1.12                          | 0.81                            | 1.78                                                                                | 43.8       | 11.5                        |
| 6          | 1.20                          | 0.73                            | 1.97                                                                                | 49.2       | 11.3                        |
| 7          | 1.30                          | 0.63                            | 2.28                                                                                | 56.2       | 11.8                        |
| 8          | 1.36                          | 0.56 <sub>7</sub>               | 2.54                                                                                | 60.7       | 11.7                        |
| 10         | 1.49                          | 0.44                            | 3.27                                                                                | 69.4       | 11.8                        |
| 12         | 1.57 <sub>5</sub>             | 0.35 <sub>5</sub>               | 4.05                                                                                | 75.3       | 11.6                        |
| 15         | 1.68                          | 0.25                            | 5.76                                                                                | 82.6       | 11.7                        |
| 20         | 1.78                          | 0.15                            | 9.60                                                                                | 89.6       | 11.3                        |
| $\infty$   | 1.93                          | -                               | -                                                                                   | -          | -                           |

Mean value of  $k_o = 11.5 \times 10^{-2} \text{ min}^{-1}$   
 $= 19.16 \times 10^{-4} \text{ sec}^{-1}$

TABLE (IX-2)

Hydrolysis of O-(2,4-dinitrophenyl)hydroxylamine catalysed by sodium azide followed by sampling method

Expt. 383

Initial  $[\text{NaN}_3] = 0.10 \text{ M}$ ;  $[\text{NaOH}] = 0.001 \text{ M}$

$\mu = 1.0$ , adjusted by  $\text{NaClO}_4$ ; temp. =  $25^\circ \pm 0.1^\circ \text{C}$

| Time<br>(min) | O.D.<br>$\lambda_{362\text{nm}}$ | $\text{O.D.}_\infty - \text{O.D.}_t$ | $\frac{\text{O.D.}_\infty - \text{O.D.}_0}{\text{O.D.}_\infty - \text{O.D.}_t}$ | % reaction | $10^2 \underline{k}_O$<br>$\text{min}^{-1}$ |
|---------------|----------------------------------|--------------------------------------|---------------------------------------------------------------------------------|------------|---------------------------------------------|
| 0.0           | 0.33                             | -                                    | -                                                                               | -          | -                                           |
| 7.5           | 0.52                             | 1.24                                 | 1.15                                                                            | 13.3       | 1.90                                        |
| 16.5          | 0.73                             | 1.03                                 | 1.39                                                                            | 28.1       | 1.99                                        |
| 25.5          | 0.90                             | 0.86                                 | 1.66                                                                            | 39.8       | 1.98                                        |
| 34.5          | 1.04                             | 0.72                                 | 1.99                                                                            | 49.7       | 1.98                                        |
| 44.5          | 1.18                             | 0.58                                 | 2.47                                                                            | 59.4       | 2.02                                        |
| 56.5          | 1.30                             | 0.46                                 | 3.11                                                                            | 67.8       | 2.00                                        |
| 75.5          | 1.44                             | 0.318                                | 4.50                                                                            | 77.7       | 1.98                                        |
| 103.5         | 1.58                             | 0.179                                | 7.99                                                                            | 87.5       | 2.00                                        |
| 164.5         | 1.69 <sub>5</sub>                | 0.065                                | 22.0                                                                            | 95.5       | 1.87                                        |
| $\infty$      | 1.76                             | -                                    | -                                                                               | -          | -                                           |

Mean value of  $\underline{k}_O = 1.96 \times 10^{-2} \text{ min}^{-1}$   
 $= 3.26 \times 10^{-4} \text{ sec}^{-1}$

TABLE (IX-3)

Hydrolysis of O-(2,4-dinitrophenyl)hydroxylamine catalysed by n-butylamine followed by direct spectrophotometric method

Expt. 401

Initial  $[n\text{-BuNH}_2] = 0.102 \text{ M}$ ,  $[\text{NaOH}] = 0.001 \text{ M}$ ,

$p^H \sim 11.6$ ,  $\mu = 1.0$ , adjusted by  $\text{NaClO}_4$ , temp. =  $25^\circ\text{C} \pm 0.1^\circ\text{C}$

| Time (min) | O.D. $\lambda_{360\text{nm}}$ | O.D. $_{\infty} - \text{O.D.}_t$ | $\frac{\text{O.D.}_{\infty} - \text{O.D.}_0}{\text{O.D.}_{\infty} - \text{O.D.}_t}$ | % reaction | $10^2 k_O \text{ min}^{-1}$ |
|------------|-------------------------------|----------------------------------|-------------------------------------------------------------------------------------|------------|-----------------------------|
| 0          | 0.265                         | -                                | -                                                                                   | -          | -                           |
| 2          | 0.385                         | 1.09                             | 1.11                                                                                | 9.67       | 5.06                        |
| 4          | 0.50                          | 0.97                             | 1.24                                                                                | 19.5       | 5.41                        |
| 6          | 0.58 <sub>4</sub>             | 0.89                             | 1.36                                                                                | 26.4       | 5.10                        |
| 8          | 0.68 <sub>4</sub>             | 0.79                             | 1.53                                                                                | 36.7       | 5.32                        |
| 10         | 0.77                          | 0.70                             | 1.72                                                                                | 41.9       | 5.40                        |
| 12         | 0.84                          | 0.63                             | 1.91                                                                                | 47.7       | 5.30                        |
| 14         | 0.92                          | 0.55                             | 2.19                                                                                | 54.3       | 5.50                        |
| 16         | 0.96                          | 0.51                             | 2.36                                                                                | 57.6       | 5.30                        |
| 20         | 1.05                          | 0.42                             | 2.87                                                                                | 65.2       | 5.20                        |
| 24         | 1.13                          | 0.338                            | 3.57                                                                                | 72.0       | 5.20                        |
| 28         | 1.19                          | 0.28                             | 4.30                                                                                | 76.8       | 5.20                        |
| 34         | 1.26                          | 0.21                             | 5.74                                                                                | 82.6       | 5.10                        |
| 40         | 1.30                          | 0.167                            | 7.22                                                                                | 86.1       | 4.90                        |
| $\infty$   | 1.47                          | -                                | -                                                                                   | -          | -                           |

Mean value of  $k_O = 5.2 \times 10^{-2} \text{ min}^{-1}$   
 $= 8.66 \times 10^{-4} \text{ sec}^{-1}$

TABLE (IX-4)

Hydrolysis of O-(2,4-dinitrophenyl)-hydroxylamine catalysed by selenourea followed by direct spectrophotometric method

Expt. 437

Initial  $[\text{SeC}(\text{NH}_2)_2] = 0.0008 \text{ M}$ ,  $[\text{NaOH}] = 0.001 \text{ M}$ ,

$\mu = 1.0$ , adjusted by  $\text{NaClO}_4$ , temp. =  $25^\circ\text{C} \pm 0.1^\circ\text{C}$

{Since selenourea is not very stable in water, the reaction was carried out as soon as possible, the reaction flask was covered with silver paper to minimise decomposition by light. The substrate concentration was maintained to about  $0.7 \times 10^{-4} \text{ m/l}$ }

| Time (sec) | O.D. $\lambda_{360\text{nm}}$ | O.D. $_{\infty} - \text{O.D.}_t$ | $\frac{\text{O.D.}_{\infty} - \text{O.D.}_0}{\text{O.D.}_{\infty} - \text{O.D.}_t}$ | % reaction | $10^4 k_{\text{O}} \text{ sec}^{-1}$ |
|------------|-------------------------------|----------------------------------|-------------------------------------------------------------------------------------|------------|--------------------------------------|
| 0          | 0.415                         | -                                | -                                                                                   | -          | -                                    |
| 5          | 0.445                         | 0.355                            | 1.08                                                                                | 7.7        | 161                                  |
| 10         | 0.47                          | 0.33                             | 1.166                                                                               | 14.2       | 153                                  |
| 15         | 0.49                          | 0.31                             | 1.24                                                                                | 19.4       | 143                                  |
| 20         | 0.52                          | 0.28                             | 1.35 <sub>5</sub>                                                                   | 26.2       | 151                                  |
| 25         | 0.54                          | 0.26                             | 1.46                                                                                | 31.4       | 150                                  |
| 30         | 0.55                          | 0.25                             | 1.55                                                                                | 35.6       | 146                                  |
| 35         | 0.57                          | 0.23                             | 1.67                                                                                | 40.2       | 147                                  |
| 40         | 0.58 <sub>5</sub>             | 0.21 <sub>5</sub>                | 1.79                                                                                | 44.1       | 145                                  |
| 45         | 0.60                          | 0.20                             | 1.90                                                                                | 47.5       | 143                                  |
| 50         | 0.61                          | 0.19                             | 2.03                                                                                | 50.6       | 141                                  |
| 55         | 0.62 <sub>7</sub>             | 0.17                             | 2.22                                                                                | 55.0       | 145                                  |
| 60         | 0.63 <sub>5</sub>             | 0.16 <sub>5</sub>                | 2.33                                                                                | 57.1       | 141                                  |
| 65         | 0.65                          | 0.15                             | 2.53                                                                                | 60.5       | 142                                  |
| 70         | 0.66                          | 0.13                             | 2.92                                                                                | 65.7       | 152                                  |
| 85         | 0.68 <sub>5</sub>             | 0.115                            | 3.35                                                                                | 70.1       | 142                                  |
| $\infty$   | 0.80                          | -                                | -                                                                                   | -          | -                                    |

Mean value of  $k_{\text{O}} = 146 \times 10^{-4} \text{ sec}^{-1}$

#### IX.1.6 Differential U.V. Absorption Method

Some reactions were carried out in dimethylsulphoxide solvent (DMSO) using the substrate O-(2,4-dinitrophenyl)-N-methyl-hydroxylamine. Since there is a slow spontaneous reaction in this solvent, the usual method of following the reaction had to be modified. A very concentrated solution of the substrate was prepared in DMSO and kept in the 'fridge. The reaction solutions were prepared in volumetric flasks and maintained in the thermostatted tank to equilibrate thermally. When the Unicam SP 700 was used, the thermo-jacketted quartz cells were first well balanced with pure DMSO in both. The solution cell was then emptied, cleaned, dried and the reaction solution was then transferred to it. The volume of DMSO in the reference cell and the volume of the reaction solution in the solution cell were maintained the same. The concentrated substrate solution was then taken out of the 'fridge, placed inside a desiccator for some time and then with a micro-litre syringe, an equal amount of the substrate solution was added to both the cells. After stoppering and mixing thoroughly, the absorbance was recorded at a fixed wavelength at various timed intervals. The method of calculating  $k_0$  was the same as that described previously.

#### IX.1.7 Infinity Reading

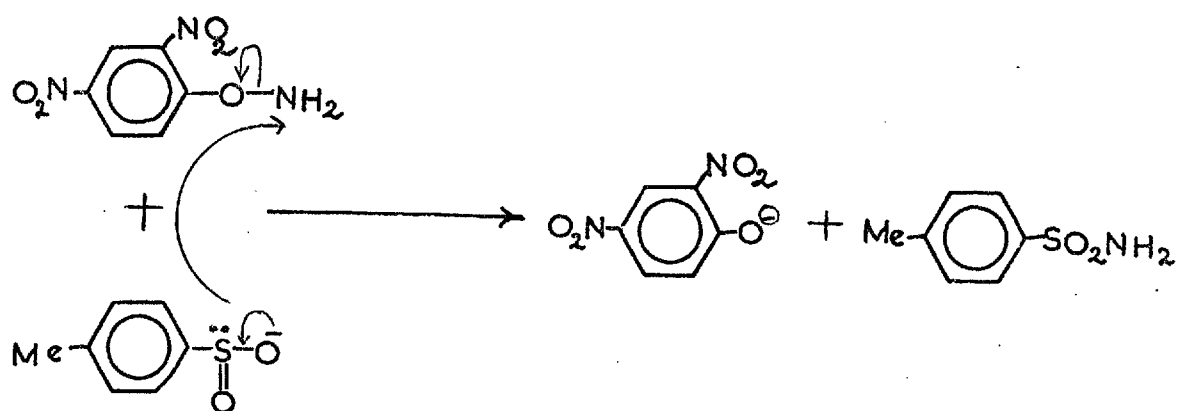
Infinity readings were taken after about 10 half-lives of the reaction. In some cases, its value was checked against the theoretical infinity at that wavelength. Agreement was usually within  $\pm 5\%$ . In most of the reactions, the experimental infinity point (i.e. absorption after 10 half-lives) was used for calculation.

#### IX.1.8 Precision of the Measured Rate Coefficients

Water used was deionized and boiled to remove any dissolved oxygen and  $\text{CO}_2$ . This was always maintained under nitrogen. This minimised various side effects. In most cases good isosbestic points were obtained and the theoretical and experimental infinity points were in good agreement. The only source of error could be the small contribution from other products of the reaction at the wavelength of the calculation. The effect of U.V. light on the reaction solution has been ignored. In the case of very fast reactions, there could be a small time error. However, percentage of error should be below  $\pm 10\%$ . In the case of reactions with perhydroxyl ion ( $\text{HO}_2^\ominus$ ) and hydroxide ion ( $\text{OH}^\ominus$ ) catalysts, good kinetics could not be obtained after about 50% of reaction. The reason for this could not be finally established. However, the initial rates of both reactions were first order with respect to catalyst concentrations. Accordingly, the error in these runs would be as high as  $\pm 20\%$ .

#### IX.2 Product Analysis

The observation of the 'infinity' solutions shows that 2,4-dinitrophenolate ion is formed in nearly quantitative yield. It was desirable to establish the product derived from the amino fragment, but in most cases this proved difficult because of the small amount of material obtained from a kinetic experiment. The reaction with sodium p-toluenesulphinate {Scheme (IX-2)}, however, proved more amenable because the product, p-toluenesulphonamide, could be estimated spectrophotometrically. The reaction was carried out in the usual way with  $[\text{Na-p-toluenesulphinate}] = 0.05 \text{ M}$  and  $[\text{substrate}] = 9.2 \times 10^{-4} \text{ M}$ .



Scheme (IX-2) Formation of p-toluenesulphonamide from the corresponding sulphinate and the substrate

The neutralized aqueous reaction mixture was extracted with ether and a t.l.c. was carried out with the ethereal solution on a silica-gel plate developed by  $\text{CHCl}_3$ ; p-toluenesulphonamide was identified by spotting the plate with authentic sample.

#### IX.2.1 Quantitative Estimation of p-Toluenesulphonamide

In the absence of a suitable colorimetric method, an extraction procedure was attempted. When a neutral aqueous solution of p-toluenesulphonamide, sodium p-toluenesulphinate, 2,4-dinitrophenol and O-(2,4-dinitrophenyl)-hydroxylamine was extracted successively three times with about an equal volume of dichloromethane, it was observed that quantitative extraction of p-toluenesulphonamide was possible. In other words, sodium-p-toluenesulphinate remained completely in the aqueous phase, whereas p-toluenesulphonamide went completely into the organic phase. However, some of the 2,4-dinitrophenol and O-(2,4-dinitrophenyl)-hydroxylamine also passed

into the organic phase. This created a problem, but it was solved as described below. In actual practice, the organic phase was evaporated to dryness, the residue was dissolved in 0.1 N NaOH in a volumetric flask and the U.V. spectrum of the alkaline solution was taken against 0.1 N NaOH from  $\lambda = 220$  to 390 nm. From the absorbance at  $\lambda = 358$  nm, the amount of 2,4-dinitrophenol present in the organic phase was estimated (from its known extinction coefficient). Its contribution at  $\lambda = 226$  nm was deducted to estimate the concentration of p-toluenesulphonamide. A trial experiment showed that the method was accurate within  $\pm 3\%$ .

Procedure: In a 50 ml. volumetric flask, sodium-p-toluene-sulphinate (0.446 g; 0.05 M) was weighed, dissolved and the volume was made up to the mark with  $9.2 \times 10^{-4}$  M solution of O-(2,4-dinitrophenyl)-hydroxylamine in water. The volumetric flask was stoppered and immersed in the  $25^{\circ}\text{C}$  thermostatted tank.

After about 18 hours, 20 ml. of the reaction mixture was pipetted into a separatory funnel and extracted very carefully with 3 x 15 ml. portions of dichloromethane into a 250 ml. volumetric flask. The combined extract was then evaporated to dryness by means of an oil pump. The residue was dissolved in 0.1 N NaOH solution (shaken for some time) and finally the volume was made up to the mark with 0.1 N NaOH solution. The U.V. spectrum of the solution was taken against 0.1 N NaOH solution.

Calculation: Absorbance at  $\lambda_{358\text{nm}} = 0.044$   
 $\epsilon_{358}$  (2,4-dinitrophenol) in 0.1 N NaOH (123 )  
 $= 14.79 \times 10^3$

Amount of 2,4-dinitrophenol that has come over to the organic phase was estimated from the relation,  $O.D. = \epsilon \times c \times l$  where  $c$  is the concentration of 2,4-dinitrophenol present in the organic phase, other symbols have their usual significance,

$$\text{or, } 0.044 = 14.79 \times 10^3 \times c \times 1.0$$

$$\text{or, } c = \frac{0.044}{14.79 \times 10^3}$$

$$= 2.97 \times 10^{-6} \text{ m/l}$$

$$O.D. (\lambda = 226) = 0.66$$

$$O.D. (226) = \epsilon_{226} (\text{p-tol.sulphonamide}) \times [\text{p-toluenesulphonamide}]$$

$$+ \epsilon_{226} (2,4\text{-dinitrophenol}) \times [2,4\text{-dinitrophenol}]$$

$$\text{or } 0.66 = 9832 \times [\text{p-toluenesulphonamide}]$$

$$+ 10.23 \times 10^3 \times 0.297 \times 10^{-5} \quad (123, 124)$$

$$\text{or } 0.66 = 9832 [\text{p-toluenesulphonamide}] + 0.0303$$

$$\text{or } [\text{p-toluenesulphonamide}] = \frac{0.6297}{9832} = 0.64 \times 10^{-4} \text{ m/l}$$

Since the original solution has been diluted 12.5 times, the actual concentration of p-toluenesulphonamide in the reaction mixture was

$$0.64 \times 10^{-4} \times 12.5 \text{ m/l} \quad \text{i.e., } 8.0 \times 10^{-4} \text{ m/l}.$$

The expected concentration of p-toluenesulphonamide was  $9.2 \times 10^{-4} \text{ m/l}$ .

∴ p.c. of p-toluenesulphonamide formed =  $87 \pm 3\%$ .

### IX.3 Purification of Reagents

Distilled water was deionized by percolation through an 'Elgastat column', then boiled for about 10 minutes. It was then kept always under nitrogen.

p-Dioxane was purified by Vogel's Procedure<sup>125</sup>. DMSO was first dried by 4A molecular sieve and then fractionally distilled under normal pressure. The middle fraction was collected and kept in a sealed container in contact with 4A molecular sieve.

Analar grade  $\text{NaNO}_2$ ,  $\text{NaCl}$ ,  $\text{KI}$ ,  $\text{Na}_2\text{S}_2\text{O}_3$ , phenol, pyridine were used without further purification. B.D.H. standard  $\text{NaOH}$  solutions were used where necessary, occasionally their strengths were checked by titration against B.D.H. standard hydrochloric acid.

Analar grade hydrogenperoxide (100 volume) (supplied by Hopkins and Williams) was used without further purification. The amount of hydrogen peroxide in the prepared solution was estimated by a standard procedure<sup>126</sup>.

Hydroxylamine hydrochloride was recrystallised from  $\text{MeOH}$ , washed with  $\text{Et}_2\text{O}$  and finally dried at  $130^\circ$ .

Potassium selenocyanate was prepared by the method of Waitkins et al<sup>127</sup> and its purity was checked by micro analysis data; (reqd:-  $\text{C} = 8.33\%$ ;  $\text{N} = 9.72\%$ ; obtd:-  $\text{C} = 8.33\%$ ,  $\text{N} = 9.88\%$ ).

Analar grade sodiumacetate-trihydrate was converted to the anhydrous salt<sup>128</sup>. Analar grade  $\text{NaClO}_4$  was heated in an oven at  $120^\circ$  to remove water.

Sodium p-toluenesulphinate (supplied by Aldrich Chemicals) and selenourea (K & K Lab.) were used without further purification. 2,6-Lutidine, aniline, n-butyl amine, diethylamine, morpholine, piperidine were fractionally distilled under normal pressure after drying from the appropriate drying agents.

LiBr, NaBr,  $\text{NaN}_3$ , NaCN were dried in the oven at the recommended temperatures, and then cooled in desiccators. t-Butyloxycarbonylazide, N-methyl-hydroxylamine hydrochloride and 2,4-dinitrofluorobenzene (supplied by Ralph N. Emanuel) were used as such. All the reagents were stored in desiccators over silica gel or the appropriate drying agents whenever possible or in the 'fridge when necessary.

#### IX.4 Preparation of Substrates

##### IX.4.1 O-(2,4-dinitrophenyl)-hydroxylamine

This was prepared by the method of Sheradsky et al<sup>78</sup> as outlined in Schemes (II-1), (II-2) and (II-3) in Chapter II. Various stages in the preparation were as follows:

##### Preparation of t-butyl-N-hydroxy carbamate

This was prepared according to the procedure of Carpino<sup>129</sup> et al from hydroxylamine hydrochloride (13 g), t-butylazidoformate (20 g) and sodium hydroxide (22.4 g). The yield of the crude product was 14.5 gm. which was then recrystallised from pet-ether (60-80°) to give clean white crystals of melting point 55 - 56°C (Lit.<sup>129</sup> 56 - 58°C).

##### Preparation of t-butyl-N-(2,4-dinitrophenoxy) carbamate

This was prepared by the method of Sheradsky et al<sup>78</sup> from 2,4-dinitrofluoro benzene (13.95 g), t-butyl-N-hydroxy carbamate (10 g), KOH (4.2 g) in 150 ml. of abs. EtOH to give 18 g of

crude product. Recrystallisation from EtOAc-petether (40 - 60°) gave yellow crystals m.p. 73 - 74°C (Lit.<sup>78</sup> 74 - 75°C).

I.R.; - NH - (str.) 3250 cm<sup>-1</sup>; c = O, 1725 cm<sup>-1</sup>

#### Preparation of O-(2,4-dinitrophenyl)-hydroxylamine<sup>78</sup>

t-Butyl-N-(2,4-dinitrophenoxy)-carbamate (2 g) was dissolved in trifluoroacetic acid (10 ml.) and left at room temperature for 30 minutes. It was then poured into cold water, neutralised with NaHCO<sub>3</sub> and filtered. The crude product (1 g) was finally recrystallised from EtOH-water to get orange-yellow crystals. These were recrystallised twice to get a single spot on the silica gel t.l.c. plate developed by CHCl<sub>3</sub>.

#### IX.4.2 Preparation of O-(2,4-dinitrophenyl)-N-methyl hydroxylamine

This was prepared according to the procedure of Sheradsky<sup>78</sup> et al exactly as in Schemes (II-1), (II-2) and (II-3) (Chapter II) except that hydroxylamine hydrochloride was replaced by N-methyl-hydroxylamine hydrochloride.

#### Preparation of t-butyl-N-methyl-N-hydroxy carbamate

Use was made of House et al<sup>130</sup> procedure in which t-butyl-azidoformate (10.85 g), N-methylhydroxylaminehydrochloride (6.95 g) and sodium hydroxide (11.4 g) reacted to give 6 g of the carbamate. This was then fractionally distilled.

B.P., 48 - 49°C (ca 0.3 mm., Lit.<sup>130</sup> 50 - 50.5°C; 0.3 mm.)

#### Preparation of t-butyl-N-(2,4-dinitrophenoxy)-N-methyl carbamate

This was prepared<sup>78</sup> by reacting t-butyl-N-methyl-N-hydroxy carbamate (6 g), 2,4-dinitrofluorobenzene (7.5 g), KOH (2.25 g) in abs. EtOH (100 ml.) to get after recrystallisation from pet-ether (40 - 60°) yellow crystals of m.p. 90° (Lit.<sup>78</sup>

94 - 95°). I.R. 1740  $\text{cm}^{-1}$  ( $\text{>C=O}$ ).

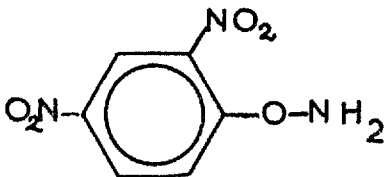
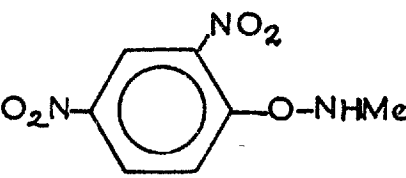
Preparation of O-(2,4-dinitrophenyl)-N-methylhydroxylamine

This was prepared<sup>78</sup> from t-butyl-N-(2,4-dinitrophenoxy)-N-methyl carbamate (3 g) and trifluoroacetic acid (15 ml ) to give after recrystallisation from EtOH-water, yellow crystals which proved to give a single spot on silica t.l.c. developed by  $\text{CHCl}_3$ .

IX.5 Physical Properties

Some of the physical properties of O-nitroaryl hydroxylamines are presented in Table (IX-5).

TABLE (IX-5)

| Compound                                                                            | M.P. °C |                    | I.R.                                                                                 | U.V.                                                            | Micro                                                                                              | Mass                  |
|-------------------------------------------------------------------------------------|---------|--------------------|--------------------------------------------------------------------------------------|-----------------------------------------------------------------|----------------------------------------------------------------------------------------------------|-----------------------|
|                                                                                     | obs.    | Lit. <sup>78</sup> | $\nu_{\text{cm}}^{-1}$<br>(Nujol/mull)                                               | (water)                                                         | Analysis                                                                                           | Spectrum              |
|    | 108-109 | 112-114            | 3310 )<br>) -NH <sub>2</sub><br>3250 ) (Str.)<br><br>1610 -NH <sub>2</sub><br>(bend) | $\lambda_{\text{max}}^{\text{nm}(\epsilon)}$<br>304<br>(10,000) | Found:<br>C = 36.98%<br>H = 2.64%<br>N = 21.21%<br>Req'd:<br>C = 36.2%<br>H = 2.53%<br>N = 21.1%   | -                     |
|  | 73-74   | 74                 | 3280 >N-H<br>(Str.)                                                                  | $\lambda_{\text{max}}^{\text{nm}}$<br>305 <sub>nm</sub>         | Found:<br>C = 39.39%<br>H = 3.28%<br>N = 19.57%<br>Req'd:<br>C = 39.45%<br>H = 3.31%<br>N = 19.71% | M <sup>+</sup><br>213 |

## CHAPTER X

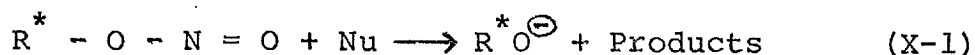
### Alkyl nitrites

An account of the experimental details concerning the reactions of alkyl nitrites is given in this chapter.

#### X.1 Kinetic Methods

##### X.1.1 Liquid Scintillation Counting

Attempts were made to use this method for following the reactions of alkyl nitrites in 70/30 dioxan-water according to eqn. (X-1)

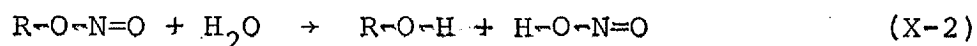


where Nu = a suitable nucleophile and  $R^* - O - N = O$  indicates tritiated alkyl nitrite.

It was assumed that the organic extract of the reaction mixture would contain the unhydrolysed alkyl nitrite only and, thus, the  $R^* O^{\ominus}$  could be counted in a Liquid Scintillation Counter. In practice, almost constant counts were obtained for samples extracted at various time intervals. An attempt was also made to use tritiated ethyl nitrite, a very volatile alkyl nitrite. It was hoped to remove the unreacted ethyl nitrite in the organic extract by bubbling nitrogen at a slow speed, and thereby obtain a sensible counting, but unfortunately this too proved a failure.

##### X.1.2 $p^H$ Stat Titration

Attempts were made to titrate the liberated nitrous acid [eqn. (X-2)], with a ' $p^H$  Stat Titrator'.



Individual runs showed good pseudo first order kinetics but runs carried out at different  $p^{\text{H}}$  values could not be correlated in any way. Various modifications were attempted involving the use of new electrodes and salt-bridges, but no success was achieved. It was believed that the low solubility of alkyl nitrites made the preparation of a homogeneous solution difficult.

### X.1.3 U.V. Spectrophotometric Method

When an alkaline solution of 70/30 dioxan-water (v/v) containing alkyl nitrite was extracted with xylene, it was observed that at least 98% of alkyl nitrite passed to the organic layer. The Beer-Lambert law was obeyed by the alkyl nitrite in the xylene solution. It was, therefore, apparent that the hydrolysis of alkyl nitrites could be followed quantitatively by estimating the alkyl nitrite concentration spectrophotometrically. The hydrolysis was known to be catalysed by both acids and nucleophilic species, but maintenance of the reaction solution at a constant  $p^{\text{H}}$  was a major problem. This was solved by using anucleophilic buffers, two of which were found suitable.

#### X.1.3.1 Benzene sulphonic acid-sodium benzene sulphonate buffer system

A stock solution of the buffer was prepared by weighing out sodium benzene sulphonate (2.7g) in a 100 ml. volumetric flask (to make a 0.15 M solution) and 10 ml. of 0.15 M  $\text{HClO}_4$  solution was added. The volume was then made up to the mark

with water. An aliquot (less than 30 ml.) of this stock solution was then pipetted into a 100 ml. volumetric flask, 70 ml. of dried dioxan was added and the volume was made up to the mark with water. The flask was numbered and immersed into a thermostatted tank of ice-water maintained at  $0^{\circ} \pm 0.1^{\circ}\text{C}$ . A few drops of alkyl nitrite was then added to the flask to make an approximately  $1 \times 10^{-2}$  M solution. The solution was then shaken thoroughly and returned to the thermostatted tank to equilibrate thermally.

5 ml. of this reaction mixture was then immediately pipetted into a 60 ml. shaking bottle containing 15 ml. of aqueous alkali (sufficient to neutralise the nitrous acid present in the aliquot of the reaction mixture) and 10 ml. of xylene. It was then stoppered, shaken for 1 minute and allowed to stand. The time of pipetting the first aliquot was taken as time zero. The U.V. spectrum of the upper xylene layer was recorded against the xylene extract of the blank solution. Aliquots of the reaction mixture were pipetted at timed intervals, extracted in the way described and their U.V. spectrum recorded. The infinity spectrum was recorded after about 10 half-lives and indicated approximately 96-97% reaction.

#### X.1.3.2 2,6-Lutidine Buffer System

Although the benzene sulphonic acid-sodium benzene sulphonate buffer system was found to be anucleophilic, its low  $p^{\text{H}}$  range was a disadvantage because of the fast reaction rates obtained. The 2,6-lutidine buffer system, having a  $p^{\text{H}}$  range from 4 to 6, proved more satisfactory.

Preparation of the Reaction Solutions: A typical example is described below.

$\text{HClO}_4$  (212.2 ml. of 0.943 M) in 70/30 dioxan-water and 2,6-lutidine (47 ml.) were mixed in a 1 litre volumetric flask and the final volume was made up to the mark with 70/30 dioxan-water (v/v). The required amount of nucleophilic catalyst was then weighed into a 100 ml. volumetric flask and the volume was made up to the mark with the buffer solution after the dissolution of the catalyst. However, in the case of the reactions carried out at different  $p^H$  values without any external catalyst, the required amount of 2,6-lutidine and standard  $\text{HClO}_4$  in 70/30 dioxan-water were added in a 100 ml. volumetric flask and the volume was made up to the mark with 70/30 dioxan-water.

The procedure used for the kinetic runs involving sampling and xylene extraction, followed by U.V. assay of unreacted alkyl nitrite was similar to that described previously for the benzene sulphonic acid-sodium benzene sulphonate buffer [section (X.1.3.1)] except that the thermostatted tank was maintained at  $25^\circ \pm 0.1^\circ\text{C}$ .

#### X.1.4 Infinity Readings

In the case of some reactions (for example, the reaction with thiourea as the catalyst), infinity readings (after about 10 half-lives) were almost zero at the wavelength ( $\lambda_{\text{max}}$ ) of calculation. However, in the case of slow runs, the infinity readings were not zero, but showed no fine structure characteristic of alkyl nitrites. Some reactions were also carried out in sealed ampoules at both the lowest and highest  $p^H$  values used for kinetic studies, which indicated that the reactions nearly went to completion and that the infinity absorption was due to the traces of sodium nitrite and n-butyl alcohol (derived from

alkylnitrite) which passed into the xylene layer.

#### X.1.5 Calculation of Rate Coefficients

The optical density at  $\lambda = 358$  nm of the xylene extract at time zero corresponded to the initial concentration of alkylnitrite (a) and that at time 't' corresponded to (a - x).  $\log (O.D._{t_0} - O.D._t)$ , which corresponded to  $\log \left( \frac{a}{a - x} \right)$ , was, therefore, plotted against time; the slope being  $\left[ 2.303 / k_o \right]$ . Rate constants were calculated from the slope of the best straight line. In some cases, rate constants were calculated from the integrated first order rate expression

$$k_o = \frac{2.303}{(t - t_0)} \log \frac{O.D._{t_0} - O.D._\infty}{O.D._{t_0} - O.D._t} \quad (X-3)$$

The pseudo first order rate constants thus obtained related to both background water rate and to catalysis by the nucleophile. The second order catalytic rate constants were evaluated after deducting the water rate determined previously in a number of independent runs. The concentration of nucleophile in the free base form was calculated from a knowledge of the total concentration of the nucleophile, its  $pK_a$  and the measured  $p^H$ . Titrations were used to determine  $pK_a$  values [Section (X.1.9)].

#### X.1.6 Typical Examples

Typical kinetic runs with benzene sulphonic acid and 2,6-lutidine (Lu) buffers are tabulated below.

TABLE (X-1)

Hydrolysis of n-amylnitrite in 70/30 dioxan-water (v/v) buffered by benzene sulphonic acid-sodium benzene sulphonate

Expt. 3

Initial  $[\text{PhSO}_3\text{H}] = 0.015 \times 10^{-2} \text{ M}$ ;  $[\text{PhSO}_3\text{Na}] = 0.135 \times 10^{-2} \text{ M}$

temp. =  $0^\circ\text{C} \pm 0.1^\circ\text{C}$ ;  $\text{p}^{\text{H}} = 2.82$  (room temp.)

| Time<br>(min) | O.D. $\lambda_{358}$<br>nm | log O.D. | % reaction | $10^3 \frac{k_o}{\text{min}^{-1}}$ |
|---------------|----------------------------|----------|------------|------------------------------------|
| 0             | 1.51                       | 0.179    | -          | -                                  |
| 5.3           | 1.45                       | 0.161    | 3.9        | 7.7                                |
| 11.3          | 1.39                       | 0.143    | 7.9        | 7.3                                |
| 21.8          | 1.28                       | 0.107    | 15.3       | 7.6                                |
| 32.5          | 1.19                       | 0.075    | 21.2       | 7.3                                |
| 50.5          | 1.03                       | 0.013    | 31.8       | 7.5                                |
| 71.9          | 0.85                       | 1.929    | 43.7       | 7.9                                |
| 114.0         | 0.64                       | 1.806    | 57.6       | 7.5                                |

Mean value of  $\frac{k_o}{\text{min}^{-1}} = 7.5 \times 10^{-3} \text{ min}^{-1}$   
 $= 1.25 \times 10^{-4} \text{ sec}^{-1}$

TABLE (X-2)

Hydrolysis of n-butyl nitrite in 70/30 dioxan-water buffered by 2,6-lutidine buffer system

Expt. 237

$[\text{Lu}] = 0.026 \text{ M}, \quad [\text{LuH}^+] = 0.25 \text{ M}$

$\mu = 0.25 \quad p^{\text{H}} = 4.2 \quad \text{temp.} = 25^{\circ} \pm 0.1^{\circ}\text{C}$

| Time<br>(min) | O.D. $\lambda_{358}$<br>nm | log O.D.      | % reaction | $10^3 k_o$<br>$\text{min}^{-1}$ |
|---------------|----------------------------|---------------|------------|---------------------------------|
| 0.0           | 0.291                      | $\bar{1}.464$ | -          | -                               |
| 7.6           | 0.26                       | $\bar{1}.415$ | 10.8       | 14.7                            |
| 15.7          | 0.235                      | $\bar{1}.371$ | 19.2       | 13.5                            |
| 25.5          | 0.206                      | $\bar{1}.315$ | 29.0       | 13.4                            |
| 37.7          | 0.167                      | $\bar{1}.224$ | 42.5       | 14.7                            |
| 50.6          | 0.145                      | $\bar{1}.161$ | 50.2       | 13.7                            |
| 75.5          | 0.107                      | $\bar{1}.031$ | 63.1       | 13.1                            |
| 98.3          | 0.075                      | $\bar{2}.875$ | 74.2       | 13.8                            |

Mean value of  $k_o = 13.8 \times 10^{-3} \text{ min}^{-1}$   
 $= 2.3 \times 10^{-4} \text{ sec}^{-1}$

TABLE (X-3)

Hydrolysis of n-butylnitrite catalysed by sodium azide

Expt. 241

[Lu] = 0.2 M, [LuH<sup>+</sup>] = 0.2 M, initial [NaN<sub>3</sub>] = 0.1 M  
p<sup>H</sup> = 5.64      μ = 0.30      temp = 25° ± 0.1°C

| Time<br>(min) | O.D. λ <sub>358</sub><br>nm | log O.D. | % reaction | 10 <sup>3</sup> $\frac{k_o}{\text{min}^{-1}}$ |
|---------------|-----------------------------|----------|------------|-----------------------------------------------|
| 0.0           | 0.367                       | 1.565    | -          | -                                             |
| 2.9           | 0.315                       | 1.498    | 14.2       | 52.1                                          |
| 5.0           | 0.266                       | 1.457    | 21.9       | 49.5                                          |
| 9.0           | 0.231                       | 1.364    | 37.1       | 51.1                                          |
| 12.0          | 0.198                       | 1.298    | 45.9       | 51.0                                          |
| 15.0          | 0.173                       | 1.237    | 53.0       | 50.2                                          |
| 21.8          | 0.125                       | 1.097    | 65.9       | 49.3                                          |
| 28.1          | 0.09                        | 2.954    | 75.5       | 50.0                                          |

Mean value of  $\frac{k_o}{\text{min}^{-1}}$  = 50 × 10<sup>3</sup> min<sup>-1</sup>  
= 8.33 × 10<sup>4</sup> sec<sup>-1</sup>

TABLE (X-4)

Hydrolysis of n-butyl nitrite catalysed by thiourea

Expt. 256

[Lu] = 0.2 M      Initial [SC(NH<sub>2</sub>)<sub>2</sub>] = 0.1 M      temp = 25<sup>0</sup>±0.1<sup>0</sup>C  
 [LuH<sup>+</sup>] = 0.2 M      μ = 0.2      p<sup>H</sup> = 5.34

| Time<br>(min) | O.D. <sub>λ<sub>358</sub></sub> | log O.D. | % reaction | 10 <sup>3</sup> $\frac{k_o}{\text{min}^{-1}}$ |
|---------------|---------------------------------|----------|------------|-----------------------------------------------|
| 0.0           | 0.465                           | 1.667    | -          | -                                             |
| 29.0          | 0.428                           | 1.632    | 7.8        | 2.8                                           |
| 71.3          | 0.379                           | 1.579    | 18.4       | 2.8                                           |
| 110.2         | 0.340                           | 1.532    | 26.9       | 2.8                                           |
| 170.1         | 0.280                           | 1.447    | 39.8       | 2.9                                           |
| 230.0         | 0.227                           | 1.357    | 51.1       | 3.1                                           |
| 326.7         | 0.173                           | 1.237    | 62.9       | 3.0                                           |
| 440.2         | 0.120                           | 1.081    | 74.1       | 3.0                                           |

Mean value of  $\frac{k_o}{\text{min}^{-1}} = 2.9 \times 10^3 \text{ min}^{-1}$   
 $= 0.48 \times 10^4 \text{ sec}^{-1}$

#### X.1.7 Measurement of $p^H$

The  $p^H$  values of the reaction solutions were operational ones and not absolute  $p^H$  values. The  $p^H$  Meter was calibrated with 0.05 M potassium hydrogen phthalate at 25°C. The  $p^H$  of the reaction solution in 70/30 dioxan-water was then measured.

#### X.1.8 Precision of the Measured Rate Constants

The reproducibility was of the order of  $\pm 5\%$  in most cases. The reactions have been assumed to reach completion and any back reaction has been neglected. This may lead to some error. Another probable source of error could arise from evaluation of the water rate beyond  $p^H = 5.3$  but this should be very small. The extraction procedure is satisfactory but subject to volume errors. In the case of very slow runs involving substituted anilines, the error could be higher than  $\pm 5\%$ .

#### X.1.9 Measurement of $pK_a$ values

The  $pK_a$  values of the conjugate acids of some of the catalysts used were determined in 70/30 dioxan-water at 25°C. Generally a 0.1 M solution of the catalyst was prepared in 70/30 dioxan-water and titrated against a strong ( $\sim 2$  M) solution of  $HClO_4$  in 70/30 dioxan-water using a Radiometer  $p^H$  Titrator. In the case of sodium thiocyanate, however, a 0.01 M solution of NaSCN was prepared and an equivalent amount of  $HClO_4$  (in 70/30 dioxan-water) was added. The resulting 0.01 M HSCN was titrated against 0.1 M NaOH in 70/30 dioxan-water. From the acid-base titration curve obtained,  $pK_a$  values were calculated using the Henderson [eqn. (X-4)].

$$p^H = pK_a - \log \frac{[Acid]}{[Salt]} \quad (X-4)$$

A few typical examples are furnished in Table (X-5) and Table (X-6).

TABLE (X-5)

Expt. 339(ii)

[NaOAc] = 0.1 M

| Titrant; 2M HClO <sub>4</sub><br>in 70/30 dioxan-<br>water<br>(ml) | p <sup>H</sup>    | [HA]<br>M | [A <sup>-</sup> ]<br>M | $\frac{[HA]}{[A^-]}$ | $\log \frac{[HA]}{[A^-]}$ | pK <sub>a</sub> |
|--------------------------------------------------------------------|-------------------|-----------|------------------------|----------------------|---------------------------|-----------------|
| 0.1                                                                | 8.1               | 0.01      | 0.09                   | 1/9                  | -0.95                     | 7.15            |
| 0.2                                                                | 7.7               | 0.02      | 0.08                   | 2/8                  | -0.60                     | 7.10            |
| 0.3                                                                | 7.42 <sub>5</sub> | 0.03      | 0.07                   | 3/7                  | -0.36                     | 7.06            |
| 0.4                                                                | 7.20              | 0.04      | 0.06                   | 4/6                  | -0.17                     | 7.03            |
| 0.5                                                                | 6.97 <sub>5</sub> | 0.05      | 0.05                   | 1                    | 0                         | 6.975           |
| 0.6                                                                | 6.85              | 0.06      | 0.04                   | 6/4                  | +0.17                     | 7.02            |
| 0.7                                                                | 6.7               | 0.07      | 0.03                   | 7/3                  | +0.36                     | 7.06            |
| 0.8                                                                | 6.45              | 0.08      | 0.02                   | 8/2                  | +0.60                     | 7.05            |
| 0.9                                                                | 6.3               | 0.09      | 0.01                   | 9/1                  | +0.95                     | 6.95            |
| 1.0                                                                | 5.9               | 0.10      | 0                      | -                    | -                         | -               |

Mean value of pK<sub>a</sub> = 7.04

pK<sub>a</sub> from half-neutralisation point = 7.0

TABLE (X-6)

Expt. 342(i)

$[\text{NaN}_3] = 0.01 \text{ M}$

| Titrant; 0.2 M<br>$\text{HClO}_4$ in 70/30<br>dioxan-water<br>(ml) | $\text{p}^{\text{H}}$ | $[\text{HA}]$<br>M | $[\text{A}^-]$<br>M | $\frac{[\text{HA}]}{[\text{A}^-]}$ | $\log \frac{[\text{HA}]}{[\text{A}^-]}$ | $\text{pK}_a$ |
|--------------------------------------------------------------------|-----------------------|--------------------|---------------------|------------------------------------|-----------------------------------------|---------------|
| 0.10                                                               | 7.55                  | 0.001              | 0.009               | 1/9                                | -0.95                                   | 6.60          |
| 0.20                                                               | 7.20                  | 0.002              | 0.008               | 2/8                                | -0.60                                   | 6.60          |
| 0.30                                                               | 7.00                  | 0.003              | 0.007               | 3/7                                | -0.36                                   | 6.64          |
| 0.40                                                               | 6.80                  | 0.004              | 0.006               | 4/6                                | -0.17                                   | 6.63          |
| 0.50                                                               | 6.65                  | 0.005              | 0.005               | 1                                  | 0                                       | 6.65          |
| 0.60                                                               | 6.45                  | 0.006              | 0.004               | 6/4                                | +0.17                                   | 6.62          |
| 0.70                                                               | 6.25                  | 0.007              | 0.003               | 7/3                                | +0.36                                   | 6.71          |
| 0.80                                                               | 6.07 <sub>5</sub>     | 0.008              | 0.002               | 8/2                                | +0.60                                   | 6.67          |
| 0.90                                                               | 5.72 <sub>5</sub>     | 0.009              | 0.001               | 9/1                                | +0.95                                   | 6.67          |

Mean  $\text{pK}_a = 6.64$

## X.2 Purification of Reagents

The purification of those reagents not mentioned in section (IX.3) is described below.

p-Dioxane used was peroxide-free and obtained by percolation through a column of grade I alumina.

Analar grade  $\text{HClO}_4$ , n-butanol and abs. EtOH were used as such. G.P.R. grade reagents such as xylene, benzyl alcohol, n-amyl alcohol, n-propyl alcohol and sodium benzene sulphonate were used without further purification. Sodium chloroacetate and ascorbic acid were dried under vacuum. p-Toluidine (G.P.R. grade) was sublimed under vacuum. p-Bromo aniline (Hopkins & Williams, 99%) was used as such.

## X.3 Preparation of Alkylnitrites

All alkylnitrites were prepared by nitrosation<sup>84,85</sup> of the corresponding alcohol. A typical example is described briefly below.

### Preparation of n-Butylnitrite

Analar sodium nitrite (21.3 g) was dissolved in water (94 ml.) and stirred in an ice-salt bath. A cold mixture of conc.  $\text{H}_2\text{SO}_4$  (15.6 g), analar n-butanol (28.3 g) and water (6.25 ml.) was added to the above solution at a controlled speed and allowed to stand for 1.5 hours. It was then filtered, washed with a solution of sodium chloride (6.25 g) and  $\text{NaHCO}_3$  (0.5 g) in water (25 ml.) twice; yield 23 gms. It was dried with anhydrous magnesium sulphate and fractionally distilled under normal pressure and the middle fraction collected. n-Butylnitrite was stored away from light in a sealed container in the ice-box of the 'fridge.

### Preparation of Tritium Labelled Alkyl nitrites

The corresponding aldehydes were first labelled with tritium by stirring the aldehyde with THO in a slightly acidic or alkaline solution. The labelled aldehydes were then reduced catalytically with 'Raney Nickel',<sup>131</sup> under pressure and temperature to the corresponding alcohol which were then nitrosated to the alkyl nitrite<sup>84,85</sup>.

### X.4 Physical Characteristics of Alkyl nitrites

Some of the physical properties of n-butyl nitrite and n-amyl nitrite are tabulated below [Table (X-7)].

TABLE (X-7)

| Compd.              | Boiling Point<br>(°C)      |                           | Refractive<br>Index |                                  | I.R. data<br>$\nu_{\max}$ $\text{cm}^{-1}$<br>(liq.film) | U.V. data                                                                                                                                    | Micro<br>Analysis<br>%                                                                   | N.M.R. data     |                              |                                           |                     |
|---------------------|----------------------------|---------------------------|---------------------|----------------------------------|----------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|-----------------|------------------------------|-------------------------------------------|---------------------|
|                     | obs.<br>(normal<br>press.) | Lit <sup>132</sup><br>Lit | obs.<br>$n_D^{22}$  | Lit <sup>132</sup><br>$n_D^{20}$ |                                                          |                                                                                                                                              |                                                                                          | Solv.           | Chemical<br>Shift( $\tau$ )  | Multiplicity <sup>a)</sup><br>of<br>Peaks | Integration         |
| n-Butyl-<br>nitrite | 77.5                       | 77.8<br>(760<br>nm)       | 1.3755              | 1.3762                           | 1608)<br>) -N=O<br>1648) str.                            | $\lambda_{\max}$ nm( $\epsilon$ )<br>solv.<br>(n-hexane)<br>315 (26.0)<br>324 (36.3)<br>334 (56.8)<br>346 (80.5)<br>358 (90.2)<br>372 (74.2) | Found:<br>C = 46.21<br>H = 8.54<br>N = 13.31<br>Reqd:<br>C = 46.5<br>H = 8.7<br>N = 13.5 | $\text{CDCl}_3$ | 9.06<br><br>8.43<br><br>5.30 | 3<br><br>m<br><br>3                       | 3<br><br>4<br><br>2 |
| n-Amyl-<br>nitrite  | 104.0                      | 104.5<br>(763<br>nm)      | 1.3847              | 1.3851                           | 1610)<br>) -N=O<br>1650) str.                            | $\lambda_{\max}$ (nm)<br>solv.<br>(xylene)<br>315, 325,<br>334.5, 346,<br>358, 372                                                           | -                                                                                        | $\text{CDCl}_3$ | 9.07<br><br>8.53<br><br>5.28 | 3<br><br>m<br><br>3                       | 3<br><br>6<br><br>2 |

a) Referred to the TMS signal (internal standard)

m = multiplet; chemical shift referred to the centre of the multiplet

## CHAPTER XI

### Oxaziridines

A brief account of the experimental details concerning the hydrolysis of oxaziridines is described in this chapter.

#### XI.1 Kinetic Method

The kinetic method used was that of Lobo<sup>110</sup>; only a brief description is, therefore, given here.

Various EtOH-water (v/v) solutions containing known amounts of  $\text{HClO}_4$  were prepared and maintained at  $25^\circ\text{C}$  in a thermostatted tank. The oxaziridine substrate was added directly to the reaction flask to give an approximately  $1 \times 10^{-2}$  M solution. The solution was then shaken thoroughly and returned to the thermostatted tank. 10 ml. of the reaction mixture was then pipetted into a mixture of 10 ml. of 10% KI, 5 ml. of glacial acetic acid and ca 0.5 g  $\text{NaHCO}_3$  in a 250 ml. conical flask. After stoppering, this was allowed to stand in the dark for about 5 minutes and then titrated against standard sodium thiosulphate solution to the sodium starch glycollate end point. Aliquots of reaction mixture were pipetted at various timed intervals and the iodine liberated by the unhydrolysed oxaziridine was titrated as described above.

Infinity readings taken after 10 half-lives were usually zero and indicated complete hydrolysis of the oxaziridine.

### XI.1.1 Calculation of Rate Coefficients

The first order rate coefficient ( $k_o$ ) is defined by the eqn. (XI-1).

$$\text{Rate} = \frac{-d [\text{oxaziridine}]}{dt} = k_o [\text{oxaziridine}]_t \quad (\text{XI-1})$$

In practice,  $k_o$  was calculated from the integrated first order rate expression (XI-2),

$$k_o = \frac{2.303}{(t - t_o)} \log \frac{\text{titre}_o - \text{titre}_\infty}{\text{titre}_t - \text{titre}_\infty} \quad (\text{XI-2})$$

where,  $\text{titre}_o$ ,  $\text{titre}_t$  and  $\text{titre}_\infty$  represent the concentration of oxaziridine at time zero,  $t$ , and  $t_\infty$  respectively in terms of the volume of the standard thiosulphate solution required to titrate the liberated  $\text{I}_2$ .

### XI.1.2 Typical Kinetic Runs

Three typical kinetic runs are tabulated below.

TABLE (XI-1)

Hydrolysis of 2-Benzyl-3,3-diethyl oxaziridine in 50:50 EtOH-water (v/v)

Expt. 188

$[\text{HClO}_4] = 0.0 \text{ m}$ , temp. =  $25^\circ \pm 0.1^\circ\text{C}$ , titrant = 0.006 N

sodiumthiosulphate solution

| Time<br>(min) | Titre<br>(ml) | log Titre | % reaction | $10^3 \underline{k}_O \text{ min}^{-1}$ |
|---------------|---------------|-----------|------------|-----------------------------------------|
| 0             | 3.25          | 0.512     | -          | -                                       |
| 66.3          | 3.025         | 0.481     | 6.9        | 1.0                                     |
| 120           | 2.825         | 0.451     | 13.0       | 1.1                                     |
| 180           | 2.6           | 0.415     | 20.0       | 1.2                                     |
| 251           | 2.45          | 0.389     | 24.6       | 1.1                                     |
| 330           | 2.275         | 0.357     | 30.0       | 1.0                                     |
| 435           | 2.0           | 0.301     | 38.5       | 1.11                                    |
| 1883          | 0.70          | 1.845     | 78.5       | 1.11                                    |
| $T_\infty$    | 0.0           | -         | -          | -                                       |

$$\begin{aligned} \text{Mean value of } \underline{k}_O &= 1.1 \times 10^3 \text{ min}^{-1} \\ &= 1.83 \times 10^5 \text{ sec}^{-1} \end{aligned}$$

TABLE (XI-2)

Hydrolysis of 2-Benzyl-3,3-diethyl oxaziridine in 50:50 EtOH-water (v/v)

Expt. 197

$[\text{HClO}_4] = 0.646 \text{ M}$ , temp. =  $25^\circ \pm 0.1^\circ \text{C}$ ,

titrant = 0.006 N sodiumthiosulphate solution

| Time<br>(min) | Titre<br>(ml) | log titre | % reaction | $10^3 \underline{k}_o \text{ min}^{-1}$ |
|---------------|---------------|-----------|------------|-----------------------------------------|
| 0             | 4.70          | 0.672     | -          | -                                       |
| 2.8           | 3.90          | 0.591     | 17.0       | 67.0                                    |
| 5.85          | 3.20          | 0.505     | 31.9       | 65.7                                    |
| 10.3          | 2.35          | 0.371     | 50         | 67.3                                    |
| 13.5          | 1.90          | 0.279     | 59.6       | 67.0                                    |
| 15.7          | 1.55          | 0.190     | 67         | 70.5                                    |
| 20.3          | 1.20          | 0.079     | 74.5       | 67.0                                    |
| $T_\infty$    | 0.00          | -         | -          | -                                       |

Mean value of  $\underline{k}_o = 67.0 \times 10^3 \text{ min}^{-1}$   
 $= 1.12 \times 10^3 \text{ sec}^{-1}$

TABLE (XI-3)

Hydrolysis of 2,3,3-Triethyloxaziridine in water catalysed by Potassium Selenocyanate in 0.01 M sodium tetra borate (buffer) solution

Expt. 481

$[\text{SeCN}^-] = 10.6 \times 10^{-3} \text{ M}$ ;  $p^H \sim 9.1$ ; temp. =  $25^\circ \pm .1^\circ \text{C}$ ;

titrant = 0.005 N sodiumthiosulphate solution

| Time<br>(min) | Titre<br>(ml) | log Titre | % reaction | $10^2 \underline{k}_o \text{ min}^{-1}$ |
|---------------|---------------|-----------|------------|-----------------------------------------|
| 0.0           | 16.40         | 1.215     | -          | -                                       |
| 2.0           | 14.10         | 1.150     | 14         | 7.48                                    |
| 3.1           | 13.25         | 1.120     | 19.2       | 7.03                                    |
| 5.1           | 11.40         | 1.057     | 24.4       | 7.16                                    |
| 8.0           | 8.30          | 0.920     | 49.4       | 8.49                                    |
| 14.0          | 5.90          | 0.770     | 64.0       | 7.32                                    |
| 26.0          | 3.05          | 0.488     | 81.4       | 6.51                                    |

Mean value of  $\underline{k}_o = 7.3 \times 10^{-2} \text{ min}^{-1}$   
 $= 1.22 \times 10^{-3} \text{ sec}^{-1}$

### XI.1.3 Precision of Measured Rate Coefficients

In the case of reactions involving selenocyanate, the end point of the thiosulphate titration was indistinct due to the liberation of red selenium and starch indicator had to be added at the beginning of titration. The percentage error might be as high as  $\pm 15\%$  in this case.

### XI.2 Product Analysis

Lobo<sup>110</sup> identified the products of hydrolysis of 2-benzyl-3,3-diethyl oxaziridine in detail. The aim of the present work was to estimate the two major products viz. aniline and benzaldehyde and determine the favoured pathway.

Aniline was estimated by diazotisation followed by coupling with R-salt (2-Naphthol-3,6-disulphonic acid, sodium salt) in borax buffer, and benzaldehyde by U.V. assay at  $\lambda = 250 \text{ nm}$ .

#### A typical example

A  $0.884 \times 10^{-2} \text{ M}$  stock solution of 2-benzyl-3,3-diethyl oxaziridine was prepared in 95% EtOH by diluting a concentrated solution. 1.5 ml. of  $1.708 \text{ M HClO}_4$ , 11 ml. of water, 7.5 ml. of 95% EtOH and 5 ml. of  $0.884 \times 10^{-2} \text{ M}$  stock solution of oxaziridine were placed in a 25 ml. volumetric flask which was immersed in a thermostatted tank maintained at  $25^\circ\text{C}$  and the reaction allowed to reach completion.

#### Estimation of Aniline

2.5 ml. of the reaction mixture was then withdrawn into a 100 ml. volumetric flask containing 5 ml. of dil. HCl (prepared from 4 ml. of conc. HCl/100 ml. water) and immersed in an ice-salt bath. 5 ml. of a 25% solution of  $\text{NaNO}_2$  in

water (cooled to 0°C) was then added dropwise (with constant stirring by means of a small magnetic stirrer), and the temperature of the solution maintained at around 0°C. After 7-8 minutes, 75 ml. of cold saturated borax solution was added, followed by 10 ml. of a 2.4% solution of 2-Naphthol-3,6-di-sulphonate (Na-salt) in water. The dye solution was kept at room temperature for a short time before the volume was made up to the mark with distilled water. The absorbance of the dye solution at  $\lambda = 490$  nm was then measured. The concentration of aniline in the reaction mixture was calculated from the previously determined linear relationship between the O.D. of the dye solution and the concentration of aniline (see Chapter VII).

#### Estimation of Benzaldehyde

2.5 ml. of the reaction mixture was pipetted in a 50 ml. volumetric flask; 22.45 ml. of water, 1.3 ml. of 1.708 M  $\text{HClO}_4$  were added and the volume made up to the mark with 95% EtOH. The absorbance of the solution was then measured against a suitable blank solution. The relationship,

$$\text{O.D.}_{\lambda 250} = \epsilon_{250}^B \times C_B + \epsilon_{250}^A \times C_A \quad (\text{XI-3})$$

was used<sup>110</sup>

where  $\epsilon_{\lambda}^B, \epsilon_{\lambda}^A$  = extinction coefficients at  $\lambda = 250$  nm of benzaldehyde and aniline respectively  
and  $C_A, C_B$  = concentrations of aniline and benzaldehyde respectively.

$\epsilon_{\lambda 250}^B$  and  $\epsilon_{\lambda 250}^A$  were determined in 50-50 EtOH-water containing 0.05 M  $\text{HClO}_4$  ( $1.29 \times 10^4$  and 126 respectively). It was then possible to evaluate  $C_B$  [eqn. (XI-3)], computing  $C_A$  from the

coupling procedure described above.

### XI.3 Purification of Reagents

Purification of most of the reagents used has been described in the previous chapters (see Chapters IX and X).

Ethanol (James Burrough Ltd. B.P. 66.6) was used without further purification. Benzylamine, ethylamine and diethylketone were dried prior to use. The benzaldehyde, glacial acetic acid and sodiumthiosulphate used were of analar grade. R-salt used was of Hopkins and Williams' laboratory reagent grade. The hydrogen peroxide (90%) used in the preparation of peracetic acid was supplied by Laporte Industries Ltd.

### XI.4 Preparation of Substrates

A typical preparation is described below.

#### Preparation of 2,3,3-Triethyloxaziridine

Isoamylidene-ethylamine was prepared by condensing diethylketone (86.13 g; 1 mole) and ethylamine (49.5 g; 1 mole) in a 250 ml. stoppered conical flask according to the procedure of Campbell et al<sup>133</sup>. On distillation, 25g of imine B.P. [30° (ca 0.35 mm), Lit.<sup>134</sup> 52-54° (54 mm);  $n_{25.4}^D$  1.4228, Lit.<sup>134</sup>  $n_{20}^D$  1.4230] was collected.

The imine (25g) was then converted to the oxaziridine by the Emmons Procedure<sup>134</sup>; yield 12g. This was then fractionally distilled.

#### Preparation of 2-Benzyl-3,3-diethyloxaziridine

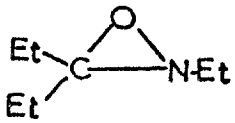
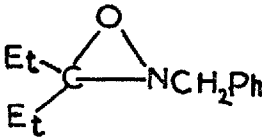
This was prepared in an analogous way to that described above, except that Isoamylidene-benzylamine was prepared from benzylamine (107.2 gm; 1 mole) and diethyl ketone (86.2 gm; 1 mole).

#### XI.5 Physical Characteristics of Oxaziridines

Some of the physical characteristics of 2,3,3-triethyl oxaziridine and 2-benzyl-3,3-diethyl oxaziridines are described in Table (XI-4).

TABLE (XI-4)

## Physical Characteristics of Oxaziridines

| Compound                                                                           | B.P. °C                                                                                              | Refractive Index<br>( $n_{tO_C}$ )                       | Active Oxygen<br>Exptl./Theoretical | N.M.R. Data       |                                      |                                |                  | Micro Analysis<br>%                                                                          |
|------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------|----------------------------------------------------------|-------------------------------------|-------------------|--------------------------------------|--------------------------------|------------------|----------------------------------------------------------------------------------------------|
|                                                                                    |                                                                                                      |                                                          |                                     | Solv.             | Chem.-Shift<br>( $\tau$ )            | Multiplicity<br>of peaks       | Integration      |                                                                                              |
|   | 40 (10 mm)<br>Lit. <sup>110</sup><br>40 (10 mm)                                                      | $n_{21}$ 1.4212<br>Lit. <sup>110</sup> $n_{20.5}$ 1.4218 | 0.94                                | -                 | -                                    | -                              | -                | Found:<br>C = 64.65<br>H = 11.62<br>N = 11.08<br>Required:<br>C = 65<br>H = 11.7<br>N = 10.8 |
|  | 63-64°C<br>(Ca $1 \times 10^{-4}$ mm)<br>Lit. <sup>110</sup><br>75-76<br>( $1.35 \times 10^{-4}$ mm) | $n_{24}$ 1.5095<br>Lit. <sup>110</sup> $n_{22.2}$ 1.5258 | 1.018                               | CDCl <sub>3</sub> | 9.10<br>8.92<br>8.23<br>6.06<br>2.63 | 3 )<br>)<br>3 )<br>m<br>1<br>1 | 6<br>4<br>2<br>5 | Found:<br>C = 75.55<br>H = 9.17<br>N = 7.2<br>Required:<br>C = 75.4<br>H = 8.9<br>N = 7.3    |

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