Kinetic studies of nitrosations by alkyl nitrites

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Kinetic Studies of Nitrosations by Alkyl Nitrites

by

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To My Parents

Memorandum

The work for this thesis has been carried out in the Department of Chemistry at the University of Durham between October 1985 and July 1988. It is the original work of the author unless otherwise stated. None of this work has been submitted for any other Degree.

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ABSTRACT

The reactions of tertiary butyl nitrite and isopropyl nitrite in aqueous acid solution have been studied. In the case of isopropyl nitrite the rates of reaction with hydrazoic acid, sulphamic acid, thioglycolic acid and N-methylaniline are markedly reduced by the addition of propan-2-ol. This has been explained in terms of a rapid hydrolysis of the alkyl nitrite to yield an equilibrium concentration of nitrous acid which then effects nitrosation. Analysis of the results gives values for the equilibrium constant for isopropyl nitrite hydrolysis and for the rate constants for nitrous acid nitrosation of the substrate, which are in good agreement with the literature values obtained by direct measurement. For tertiary butyl nitrite the extent of hydrolysis is so large and rapid that the kinetics are identical to those obtained using nitrous acid.

The reactions of isopropyl nitrite in isopropanol and tertiary butyl nitrite in tertiary butanol with thiourea and thioglycolic acid have been studied. In both cases the reactions are acid catalysed and the results are consistent with a direct reaction between the protonated alkyl nitrite and the substrate. The reactions with thioglycolic acid were subject to catalysis by chloride and bromide salts and thiourea. The results for chloride and bromide salts are best explained in terms of formation of hydrochloric or hydrobromic acid which can then act as a general acid catalyst. For thiourea the catalysis is due to the formation of an equilibrium concentration of s-nitrosothiourea.

In acetonitrile the reactions of tertiary butyl nitrite, isopropyl nitrite, isoamyl nitrite and nitrous acid with alcohols and thioglycolic acid were found to be kinetically zero order with respect to the substrate concentration. The results have been interpreted in terms of rate limiting formation of the nitrosonium ion. With less reactive substrates, aniline, N-methylaniline, p-toluidine, acetylacetone, 1,1,1,trifluoroacetylacetone and 1,1,1,5,5,5,hexafluoroacetylacetone, the reactions are kinetically first order with respect to the substrate concentration and have been interpreted in terms of rate limiting reaction of the nitrosonium ion with the free (at low acidity) or protonated (at high acidity) form of the amine. For the ketones reaction occurs, in a rate limiting step with either the enols or enolate ions.

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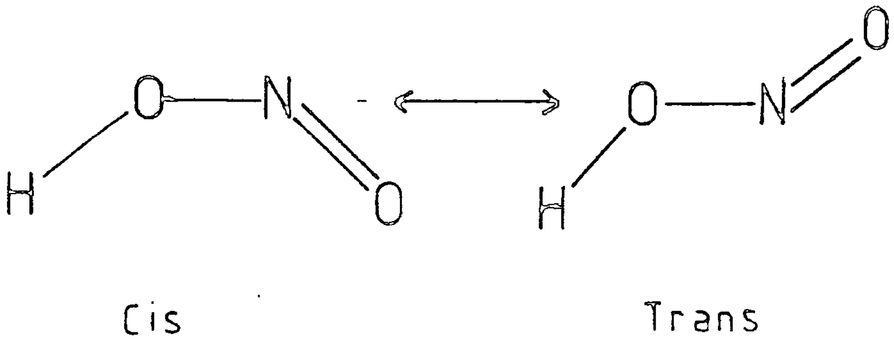
1. INTRODUCTION

1.1 Nitrosating agents

Nitrosation reactions concern the introduction of the nitroso group (-N=O) into a molecule. There are many reagents that can bring about this transformation in a wide variety of molecules, typically amines, amides, alcohols, thiols, ketones, phenols and alkenes. The products of the nitrosation reactions are sometimes unstable but frequently yield synthetically useful intermediates, for example, diazonium ions (azo dye manufacture), oximes and carbonium ions. There has also been much interest in the formation and reactions of nitrosamines since the discovery, in 1956 [1], that they are potent carcinogens.

1.1.1 Nitrous acid

Nitrous acid is the most commonly used nitrosating agent. Nitrous acid itself is unstable and is usually prepared in solution by addition of a mineral acid to an alkali metal nitrite salt. Nitrous acid is a weak acid (pK_a=3.148 at 25°C [2]). In solution it is known to exist in cis and trans forms [3], (equation 1.1), the trans form being more stable by about 2.1 kJ mol^{-1}.



(1.1)

As well as acting as a nitrosating agent, nitrous acid can also act as an oxidizing agent (equation 1.2) and a reducing agent (equation 1.3).

$$HNO_2 + H^+ + e^- = NO + H_2O \quad E^\circ = 1.0\ v \qquad (1.2)$$

$$NO_3^- + 3H^+ + 2e^- = HNO_2 + H_2O \quad E^\circ = 0.94\ v \qquad (1.3)$$

1.1.2 Nitrosyl halides

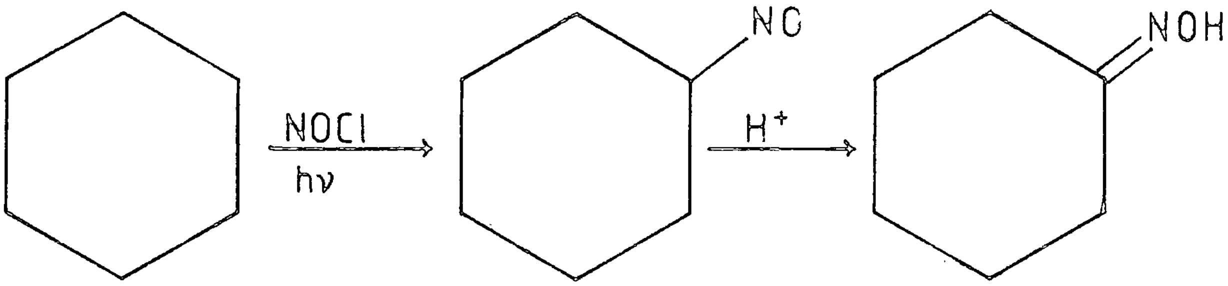
Nitrosyl halides are frequently used nitrosating agents, especially in non aqueous solvents such as chloroform [4], alcohol [5], dimethyl formamide [6] and also in aqueous alkaline solution [7]. Nitrosyl fluoride, bromide and chloride are all well known compounds, usually prepared by reacting the halogen with nitric oxide, (equation 1.4). There is also evidence for the formation of nitrosyl iodide in solution [8,9]. The physical properties of the gases are given in Table (1.1).

$$2NO + X_2 \rightleftharpoons 2XNO \tag{1.4}$$

Table 1.1
Structural and physical properties of the nitrosyl halides

Compound	Colour	Melting Point (°C)	Boiling Point (°C)	Bond lengths (A°)		Bond Angle (deg)
				N-X	N-O	
FNO	Colourless	-133	-60	1.52	1.13	110
ClNO	Orange-yellow	-62	-6	1.95	1.14	116
BrNO	Red	-56	0	2.14	1.15	114

Nitrosyl halides have been shown to act as both electrophilic and free radical nitrosating agents. The mechanism of the electrophilic process will be discussed later. The free radical reaction involves irradiation of the nitrosyl halide with U.V. light. This reaction is frequently used to produce C-nitroso compounds, as typified by the reaction of cyclohexane [10] (equation 1.5), the product from which is an intermediate in the production of nylon 6. These reactions are commonly accompanied by chlorinated products.



(1.5)

1.1.3 Nitrosyl thiocyanate

Nitrosyl thiocyanate (ONSCN) has not been isolated as a pure compound, but has been shown to exist as an unstable blood red species in solution at low temperature [11]. It is thought that the nitroso group is bound to the sulphur atom. This is to be expected from the Hard-Acid-Soft-Base (HASB) theory [12] and is predicted in an ab initio molecular orbital study [13]. Nitrosyl thiocyanate has however been identified as an electrophilic nitrosating agent in aqueous acid solutions of nitrous acid containing thiocyanate ion [14] by the observed thiocyanate ion catalysis and will be discussed later.

1.1.4 Nitrosyl acetate

Nitrosyl acetate is thought to be the effective nitrosating agent when sodium nitrite in glacial acetic acid is used as the nitrosating medium. Nitrosyl acetate has been prepared from solid silver acetate and nitrosyl chloride at low temperature [15], (equation 1.6). Nitrosyl acetate is a pale brown liquid at room temperature, a green liquid at -78°C and a green solid at -196°C.

$$CH_3COOAg + ClNO \longrightarrow CH_3COONO + AgCl \qquad (1.6)$$

It has also been identified kinetically from the catalysis by added acetate ion on the nitrosation of amines [16, 17] in the same way as nitrosyl halides and thiocyanate have been identified.

1.1.5 Nitrosonium salts

The most common example of nitrosonium salts, NO^+X^- are the tetrafluoroborate (BF_4^-), tetrachloroborate (BCl_4^-), hexafluorophosphate (PF_6^-), hydrogen sulphate (HSO_4^-), perchlorate (ClO_4^-) and hexafluoroantimonate (SbF_6^-). The salts are reasonably stable and are readily prepared from dinitrogen tetroxide, dinitrogen trioxide or nitrosyl chloride and a source of the anion [18] as exemplified by equation (1.7) for the formation of nitrosonium hydrogen sulphate, which is an important intermediate in the lead-chamber process for production of sulphuric acid.

$$N_2O_4 + H_2SO_4 \longrightarrow NO^{+}HSO_4^{-} + HNO_3 \qquad (1.7)$$

The salts are usually used under anhydrous conditions as they are readily hydrolysed to give nitrous acid. The salts are very reactive nitrosating agents, and are frequently used to bring about nitrosation of the less reactive species, for example amides [19] and sulphonamides.

1.1.6 S-Nitroso-thioureas

S-Nitrosothioureas are readily produced by the action of nitrous acid on the thiourea [20], the products are frequently unstable and react further to give the disulphide salts [21], (equation 1.8).

$$\begin{aligned} &HNO_2 + H^{+} + (NH_2)_2CS \rightleftharpoons (NH_2)_2C\overset{+}{S}\text{—}NO \\ &2(NH_2)_2C\overset{+}{S}\text{—}NO \longrightarrow (NH_2)_2C\overset{+}{S}\text{-}\overset{+}{S}\text{-}C(NH_2)_2 \end{aligned} \qquad (1.8)$$

S-Nitrosothioureas can themselves act as nitrosating agents as is frequently shown by the marked catalysis by thiourea on nitrosation kinetics [14] and will be discussed further later.

1.1.7 Nitrogen Oxides

Dinitrogen trioxide (N_2O_3) is commonly used as a nitrosating agent in organic solvents [22], and has also been shown to be effective in aqueous alkaline solution [23, 24]. It is also known to exist in equilibrium with nitrous acid in aqueous acid [25] solution, as shown in equation (1.9), and its reactions in these solutions will be discussed further later.

$$2HNO_2 \rightleftharpoons N_2O_3 + H_2O \qquad (1.9)$$

Dinitrogen trioxide exists as a blue solid or liquid at low temperatures [18] and it exhibits in absorbtion maximum at 625 nm in solution. Its nitrosation reactions can be best explained in terms of an ionic structure of the type $NO^+NO_2^-$. Reaction with dinitrogen trioxide can also yield nitro products. These probably arise from a radical addition of nitrogen dioxide which exists in equilibrium with dinitrogen trioxide (equation 1.10).

$$N_2O_3 \rightleftharpoons NO + NO_2 \qquad (1.10)$$

Dinitrogen tetroxide (N_2O_4) can also bring about both nitrosation and nitration reactions [26, 27, 28]. Dinitrogen tetroxide is known to be a pale yellow solid and is a planar molecule with a centre of symmetry and a long N-N bond [18]. In the liquid and gaseous state dinitrogen tetroxide exists in equilibrium with nitrogen dioxide, equation (1.11), and this can therefore explain its activity as a nitrating agent. Its nitrosation reactions are best explained in terms of an ionic structure $NO^+NO_3^-$.

$$N_2O_4 \rightleftharpoons 2NO_2 \qquad (1.11)$$

Dinitrogen tetroxide is a very useful synthetic reagent as it can bring about the nitrosation of compounds such as secondary amides [29], which are unreactive towards some of the other nitrosating agents.

Another commonly used nitrogen oxide in nitrosation reactions is nitric oxide (NO), [30,31]. It seems likely, however, that the nitrosating species involved is either dinitrogen trioxide or dinitrogen tetroxide, formed by oxidation of nitric oxide to nitrogen dioxide.

1.1.8 Other reagents

A wide variety of other species have been shown to be capable of acting as nitrosating agents, these include, potassium nitrosodisulphonate ($K_2[(SO_3)_2NO]$) or Fremy's salt [32], nitroalkanes [33], alkyl nitrates [34], nitroso sulphinates [35] (RSO_2NO), thionylchloronitrite (SOClONO) and thionyl dinitrite $SO(ONO)_2$ [36], nitrosothiosulphate ion [37] ($S_2O_3NO^-$), nitrososulphonium ion [38] ($(CH_3)_2\overset{+}{S}NO$), thionitrates ($RSNO_2$) [39], nitroprusside ion ($Fe(CN)_5NO^{2-}$) [40] and alkyl nitrites (RONO). The reactions of alkyl nitrites will be discussed in detail in section 1.3.

1.2 Reactions of Nitrous acid

1.2.1 Acidic Solutions

A commonly encountered rate equation in nitrosation reactions is given in equation (1.12). Here the reaction

$$\text{Rate} = k\,[HNO_2]\,[H_3O^+]\,[S] \qquad (1.12)$$

is first order in nitrous acid, substrate and hydrogen ion concentration. This equation has been found for a wide variety of substrates including thiols [41], alcohols [42], ketones [43], sulphamic acid [44], amines [45] and amides [46]. There are, however two mechanistic interpretations of such a scheme, both of which propose the formation of an equilibrium concentration of a nitrosating species which then undergoes reaction with the substrate in the rate determining step. The first scheme (scheme 1.13) involves the formation of the nitrous acidium ion ($H_2NO_2^+$) and the second involves the formation of the nitrosonium ion (NO^+), (scheme 1.14). It is known that the nitrosonium ion exists in solutions of very high acidities [47,48,49, 50], (60% H_2SO_4 or $HClO_4$), where it can be detected spectroscopically, and it is analogous

$$HNO_2 + H_3O^+ \rightleftharpoons H_2NO_2^+ + H_2O$$

$$H_2NO_2^+ + S \longrightarrow \text{Products} \qquad (1.13)$$

$$HNO_2 + H_3O^+ \rightleftharpoons H_2NO_2^+ + H_2O$$

$$H_2NO_2^+ \rightleftharpoons NO^+ + H_2O \qquad (1.14)$$

$$NO^+ + S \longrightarrow \text{Products}$$

to the formation of the nitronium ion (NO_2^+) in nitration reactions [51,59]. The nitronium ion has been identified kinetically as the nitrating agent with very reactive substrates as the reaction becomes zero order in substrate, indicating rate limiting formation of the nitrating species. This has also been reported for two cases in nitrosation reactions at low acidities. In the nitrosation of hydrogen peroxide [52] a plot of the observed first order rate constant against $[H_2O_2]$ was curved, but the concentration of hydrogen peroxide used was very high and so the curvature could be attributed to a medium effect. A similar effect was also found in the nitrosation of alcohols [53]. In this case the limiting value of the first order rate constant was different for different alcohols and a similar curvature could be brought about by the addition of an inert solvent, clearly indicating a medium effect. In the nitrosation of thiosulphate ion [54] a zero order term in $[S_2O_3^{=}]$ was found, but this could also be due to rate-limiting dinitrogen trioxide formation, as is sometimes found in the nitrosation of amines (see later).

The major argument against the involvement of the nitrosonium ion as the reactive intermediate in dilute acid solution comes from the ^{18}O exchange reaction between nitrous acid and water [55]. The exchange occurs according to equation (1.15), where k = 230 l $mol^{-1}s^{-1}$ at 0°C. If the reaction occurs via the nitrosonium ion, then this represents the fastest rate attainable in water. However for

$$\text{Rate} = k\ [HNO_2][H^+] \qquad (1.15)$$

a range of anions which obey equation (1.12) such as azide and acetate ion a limiting value of k is obtained of $\simeq 2500\ l^2\ mol^{-2}\ s^{-1}$ also at 0°C. This implies that at $[N_3^-] > 0.1\ mol\ l^{-1}$ the rate limiting step should become the formation of the nitrosonium ion, which is not observed experimentally.

The alternative interpretation of equation (1.12) is that the reactive species is the nitrous acidium ion [58], but there is no spectrophotometric evidence for its formation in dilute acid solution. This problem has also been probed theoretically. Using ab initio molecular orbital calculations [57] the most favourable conformation of the nitrous acidium ion can be considered a complex of the nitrosonium ion and water, with an unusually long N-O bond between the two. Another study using a frontier orbital treatment [58] predicts a nitrosonium water complex rather than the free nitrosonium cation.

The value of the third order rate constant, k, defined by equation (1.12), tends towards a limiting value for very reactive species such as amines and thioureas [20] of ca 7000 $l^2\ mol^{-2}\ s^{-1}$ at 25°C. This value does not change very much on increasing the basicity of the amine and is considered to be the diffusion controlled limit for nitrosation reactions. For negatively charged species such as thiocyanate ion [60], benzenesulphinate ion [61] the limit is ca 12000 $l^2\ mol^{-2}\ s^{-1}$ which is as expected, higher than that for neutral species.

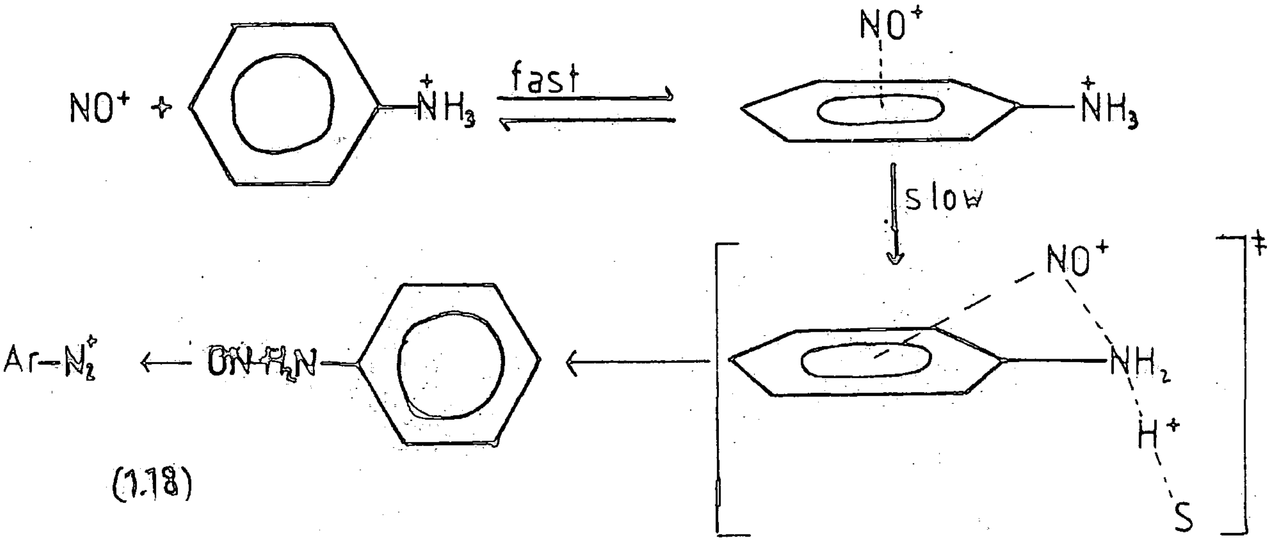
In the case of the nitrosation of basic species such as anilines equation (1.12) takes a slightly different form, as the amines are significantly protonated in these weakly acidic solutions and it is the free base form of the amine that is the reactive species at low acidity [45]. The rate equation therefore becomes equation (1.16),

$$\text{Rate} = \frac{k\,Ka[\text{Amine}]_T\,[HNO_2][H^+]}{Ka + [H^+]} \qquad (1.16)$$

where $[\text{Amine}]_T$ is the total stoichiometric concentration of amine, and Ka is the dissociation constant of the protonated amine. For weakly basic amines [62], Ka can be greater or of the order of $[H^+]$ and so acid catalysis is expected. For the highly basic amines $[H^+] \gg Ka$ and so no acid catalysis is observed at low acidities. At moderately high acidities another acid catalysed pathway occurs for aromatic amines with pKa $>$ 3 [63, 64]. Here the rate is defined by equation (1.17), where $[Ar\overset{+}{N}H_3]$ is the concentration of protonated amine and ho is the Hammett acidity function. These observations have been

$$\text{Rate} = k[ArNH_3^+][HNO_2]\,ho \qquad (1.17)$$

explained in terms of a mechanism where a rapid and reversible formation of a π complex between the protonated amine and nitrosonium ion occurs, the rate limiting step being rearrangement of the nitroso group to the amino nitrogen group, as shown in scheme (1.18).



(1.18)

In very acidic solutions (60% perchloric or sulphuric acid), the rate of nitrosation of anilines decreases with increasing acidity as shown in equation (1.19). This has been explained by the rapid and reversible formation of the protonated primary nitrosamine, the rate limiting step being proton transfer to the solvent [65] as shown in scheme (1.20).

$$\text{Rate} = k\,[\text{Ar}\overset{+}{\text{N}}\text{H}_3]\,[\text{HNO}_2]\,h_0^{-2} \qquad (1.19)$$

$$\text{Ar–NH}_3^+ + \text{NO}^+ \underset{}{\overset{\text{fast}}{\rightleftharpoons}} \text{Ar—}\overset{+}{\text{N}}\text{H}_2\text{NO} + \text{H}^+$$

$$\text{Ar—}\overset{+}{\text{N}}\text{H}_2\text{NO} + \text{S} \xrightarrow{\text{slow}} \text{ArNHNO} + \text{SH}^+ \qquad (1.20)$$

$$\text{ArNHNO} \xrightarrow{\text{fast}} \text{ArN}_2^+$$

At low acidities and high total nitrous acid concentrations, where the concentration of free nitrite ion is significantly high, another mechanism occurs in the nitrosation of amines, and for a wide range of substrates generally. In this case a second order dependence on the concentration of nitrous acid is observed. This has been explained in terms of formation of an equilibrium concentration of dinitrogen trioxide from nitrous acid, which can effect nitrosation [45]. This is shown in scheme (1.21) and the derived rate equation is equation (1.22).

$$2HNO_2 \underset{}{\overset{K}{\rightleftharpoons}} N_2O_3 + H_2O$$

$$N_2O_3 + S \xrightarrow{k} \overset{+}{S} - NO + NO_2^- \qquad (1.21)$$

$$\text{Rate} = k\,[N_2O_3][S] = k\,K\,[HNO_2]^2 . [S] \qquad (1.22)$$

The value of K for the formation of dinitrogen trioxide is known [66] to be 3.0 x 10^{-3} l mol^{-1} and so the value of the bimolecular rate constant k, for attack by N_2O_3 can be calculated. It has been found [67] that for very reactive species, such as amines with $pK > \simeq 5$ the values of k are in the range 10^8 - 10^9 l $mol^{-1}s^{-1}$, which is close to the calculated diffusion controlled limit of 7 x 10^9 l $mol^{-1}s^{-1}$ at 25°C.

For very reactive substrates the reaction with dinitrogen trioxide can be made to occur faster than the hydrolysis of dinitrogen trioxide, thus changing the rate limiting step to one of formation of dinitrogen trioxide, as shown in scheme (1.23).

$$2\ HNO_2 \xrightarrow{k'} N_2O_3 + H_2O$$

$$\text{Rate} = k'[\ HNO_2]^2 \qquad (1.23)$$

This has been found for several species including aniline [68], N-methylaniline [69] ascorbic acid [70] and azide ion [71]. The values of k' obtained are approximately constant at ca. 91 l $mol^{-1}s^{-1}$ at 25°C.

1.2.2 Nucleophile catalysed reactions

Nitrosation reactions of nitrous acid are frequently catalysed by the addition of non-basic nucleophiles, commonly chloride ion [45], bromide ion [45], iodide ion [45], thiocyanate ion [72], thiosulphate ion [37], thiourea [72], alkyl thioureas [73] and dimethyl sulphide [38]. In all cases the reactions have been explained by the equilibrium formation of a nitrosyl species XNO or $X\overset{+}{N}O$ (depending on the charge on X), which can then act as a nitrosating species. This is shown in scheme (1.24).

$$\begin{gathered} HNO_2 + H^+ + X^- \underset{}{\overset{K_{XNO}}{\rightleftharpoons}} XNO + H_2O \\ XNO + S \xrightarrow{k} \text{Products} \end{gathered} \qquad (1.24)$$

The rate equation obtained from this scheme is equation (1.25)

$$\text{Rate} = k\,[XNO][S] = k\,K_{XNO}\,[HNO_2][H^+][X^-][S] \qquad (1.25)$$

Since the values of K_{XNO} are known, the value of the bimolecular rate constant, k, can be obtained for attack of the nitrosyl species on the substrate. The values of K_{XNO} are given in Table (1.2), and some selected values of k are given in Table (1.3)

Table 1.2

Values of K_{XNO} for the equilibrium

$$X + HNO_2 + H^+ \rightleftharpoons XNO + H_2O$$

X	K_{XNO} l^2 mol^{-2} at 25°C
Cl^-	1.1×10^{-3}
Br^-	5.1×10^{-2}
SCN^-	30
Thiourea	5000
Thiosulphate ion	1.66×10^7

Table 1.3:

Values of k ($l\ mol^{-1}\ s^{-1}$), the rate constant for nitrosation by XNO at 25°C

Substrate	ClNO	BrNO	ONSCN	$(NH_2)_2CSNO$	$S_2O_3NO^-$
Methanol	2.1×10^6 (a)	2×10^4 (a)			
Thioglycolic acid	1.4×10^7 (b)	1.1×10^4 (b)			
4-Nitroaniline	2.1×10^6 (c)	4.3×10^7 (c)			
4-Chloroaniline	1.8×10^9 (c)	2.5×10^9 (c)	8.2×10^7 (d)		
Aniline	2.6×10^9 (c)	1.7×10^9 (c)	1.9×10^8 (d)	1.3×10^4 (d)	
N-Methylaniline		5×10^9 (e)	3.1×10^6 (e)		1.2×10^4 (e)
4-Methylaniline	3.4×10^9 (c)	2.5×10^9 (c)	4×10^6 (d)		
4-Ethylaniline	5.1×10^9 (c)	2.8×10^9 (c)	7.5×10^0 (d)		

a) from reference 74
b) from reference 41
c) from reference 75
d) from reference 72
e) from reference 37

As is to be expected from electronegativity considerations, the order of reactivity of the XNO species is: ClNO > BrNO > ONSCN > $(NH_2)_2C\overset{+}{S}NO$ > $S_2O_3NO^-$ but due to the size of the equilibrium constants the observed order of catalysis is $Cl^- \sim Br^- < SCN^- < (NH_2)_2CS$. The values of k in table 1.3 also tend to the diffusion controlled limit of 7 x 10^9 l $mol^{-1}s^{-1}$ with the very reactive amines with Cl^- and Br^-; the values with SCN^- are usually an order of magnitude below this value and that for thiourea is usually several orders of magnitude below this. It has, however, been shown very recently that with a very reactive species such as malononitrile [76] even these species react at the diffusion controlled limit for the reaction, as shown in scheme (1.26).

$$CH_2(CN)_2 \overset{Ka}{\rightleftharpoons} {}^-CH(CN)_2$$

$$NOX + {}^-CH(CN)_2 \xrightarrow{k} ON - CH(CN)_2 + X^- \qquad (1.26)$$

NOX	k l $mol^{-1}s^{-1}$
NOBr	1.1 x 10^{10}
NOSCN	4.2 x 10^9
$(NH_2)_2C\overset{+}{S}NO$	5.0 x 10^9

1.3 O-Nitrosation

The reaction of nitrous acid with an alcohol results in the formation of an alkyl nitrite (equation 1.27).

$$ROH + H^+ + HNO_2 \overset{K}{\rightleftharpoons} RONO + H^+ + H_2O \qquad (1.27)$$

The reaction is known to be reversible. The forward reaction [77], ie. the nitrosation of the alcohol, has been shown to involve O-nitrosation of the alcohol by reaction of an optically active alcohol with nitrous acid which yielded the corresponding alkyl nitrite without inversion of configuration or racemisation. Similarly the reverse reaction, the hydrolysis of the alkyl nitrite, has been shown to involve nitrogen-oxygen bond fission by the retention of configuration from an optically active alkyl nitrite and also by the absence of ^{18}O incorporation in the alcohol when the hydrolysis is carried out in ^{18}O enriched water.

The equilibrium constants for the formation of several simple alkyl nitrites in aqueous acid solution have been determined by three separate methods. One method involved direct spectrophotometric measurements [78] of the concentrations of nitrous acid and alkyl nitrite at 265 nm. A second method was based on the effect of varying amounts of alcohol on the nitrosation kinetics of morpholine [78]. A third method involved the direct measurements of the forward and reverse reactions by reacting a large excess of the alcohol with nitrous acid [74]. The results are given in Table (1.4).

It can be seen that the equilibrium constants decrease in the order primary > secondary > tertiary. This indicates that steric effects must be more important than electronic effects in the nitrosation of alcohols, as

Table 1.4

Equilibrium constants for the formation of alkyl nitrites defined by Keq = [RONO]/[ROH][HNO_2]

Alcohol	K l mol^{-1}		
	Method 1 (25°C)	Method 2 (25°C)	Method 3 (0°C)
MeOH	3.5 ± 0.1	5.1 ± 0.2	2.5 ± 0.5
EtOH	1.20 ± 0.06	1.39 ± 0.04	0.81 ± 0.02
^{n}PrOH	1.3 ± 0.1	1.42 ± 0.04	0.66 ± 0.03
^{i}PrOH	0.52 ± 0.05	0.56 ± 0.03	0.25 ± 0.03
2-BuOH	0.46 ± 0.03	0.39 ± 0.02	
^{i}BuOH	1.53 ± 0.05	1.90 ± 0.02	
^{t}BuOH			0.05

it is expected that increasing alkyl substitution would make the oxygen of the alcohol more nucleophilic and hence more susceptible to electrophilic nitrosation. Also electron donating substituents should stabilize the nitrite ester. These electronic effects have been seen in a series of transnitrosation experiments in deuteriochloroform as solvent, where para substituted benzyl alcohols were reacted with an equimolar concentration of ^{t}Butyl nitrite and the equilibrium constants determined by N.M.R [79]. The results given in Table 1.5 show that electron donating substituents enhance the nitrosyl exchange process whereas electron withdrawing groups disfavour the process.

Table 1.5

Equilibrium constants for the equimolar reaction of benzyl alcohols with ^{t}Butyl nitrite in deuteriochloroform

Alcohol	K
$pMeO-C_6H_4-CH_2-OH$	5.36
$pMe-C_6H_4-CH_2-OH$	5.19
$C_6H_5-CH_2-OH$	3.64
$pCl-C_6H_4-CH_2-OH$	2.19
$pO_2N-C_6H_4-CH_2-OH$	1.11

Rate constants have been obtained for the forward and reverse reactions for the formation of alkyl nitrites from nitrous acid in aqueous solution [74] (equation 1.28)

$$H^+ + ROH + HNO_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RONO + H^+ + H_2O$$

Rate of forward reaction = $k_1[ROH][HNO_2][H^+]$

Rate of reverse reaction = $k_{-1}[RONO][H^+]$

$$Keq = \frac{k_1}{k_{-1}} \qquad (1.28)$$

The results are given in Table (1.6) and show that the decrease in the equilibrium constant on going from a primary to secondary to tertiary alkylnitrite is due to a decrease in the forward rate constant, the k_1 step, since the rate constants for the hydrolysis of the alkyl nitrite (k_{-1} step) are very similar down the series. The order of the values of k_1 is as expected if steric factors dominate over electronic factors in the forward reaction. The rate equation for the forward reaction is identical with that found for a wide range of substrates (equation 1.12). As discussed in section 1.2.1, the value of the third order rate constant , k, tends towards a limiting value of ca. 7000 l^2 mol^{-2} s^{-1} at 25°C. For methanol the corresponding value at 25°C is 700 l^2 mol^{-2} s^{-1}, so the reaction of alcohols is an order of magnitude below this limit. The rate equation for the reverse reaction, the denitrosation of alkyl nitrites, has been interpreted as involving nucleophilic attack of the solvent on the protonated alkyl nitrite.

Table 1.6

Values for the forward and reverse rate constants for the nitrosation of alcohols at 0°C with nitrous acid

Alcohol	k_1 (l^2 mol^{-2} s^{-1})	k_{-1}(l mol^{-1} s^{-1})
MeOH	73 ± 10	31 ± 6
EtOH	38 ± 0.3	47 ± 0.2
n-PrOH	29 ± 1	44 ± 1
^{i}PrOH	11 ± 1	44 ± 2
^{t}BuOH		ca 100

Both the forward and reverse reactions have been shown to be halide ion catalysed [76]. This is interpreted as attack by the corresponding nitrosyl halide for the forward direction and nucleophilic attack by the halide ion for the reverse direction. The catalysis by chloride and bromide ion has been found to be less marked than is found for many amines. This can be seen by comparison of the second order rate constants for the reaction of NOBr and NOCl with alcohols and amines (Table 1.7).

Table 1.7

Rate constants for reaction with nitrosyl halides at 25°C

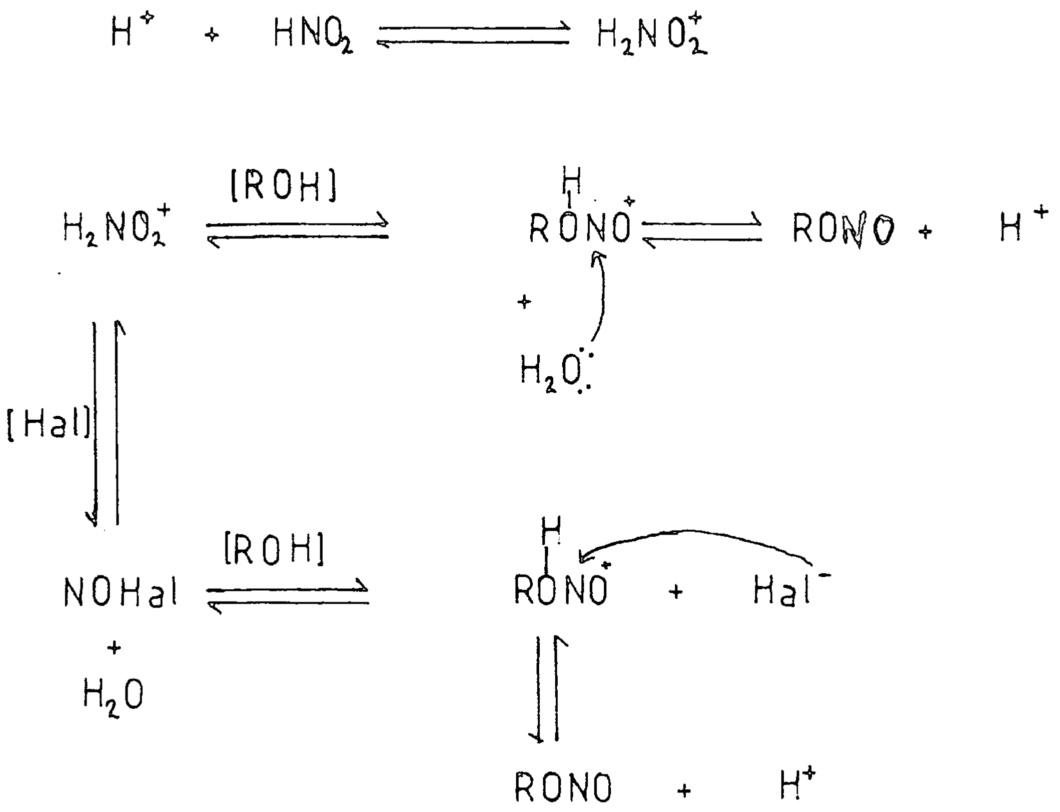
Substrate	k_{NOBr} ($l\ mol^{-1}\ s^{-1}$)	k_{NOCl} ($l\ mol^{-1}\ s^{-1}$)
MeOH	2×10^{6}	2.1×10^{5}
Aniline	1.7×10^{9}	2.2×10^{9}

The values for aniline are close to the diffusion controlled limit and the values for methanol are considerably below this. This can be rationalized in terms of the Hard and Soft Acid and Base (H.S.A.B.) theory as NOHal is expected to be a softer electrophile than the positively charged $H_2NO_2^+$ (or NO^+) ion and so will react more favourably with the softer amine species than with the harder alcohol.

The formation of alkyl nitrites in aqueous solution is summarized in scheme (1.29).

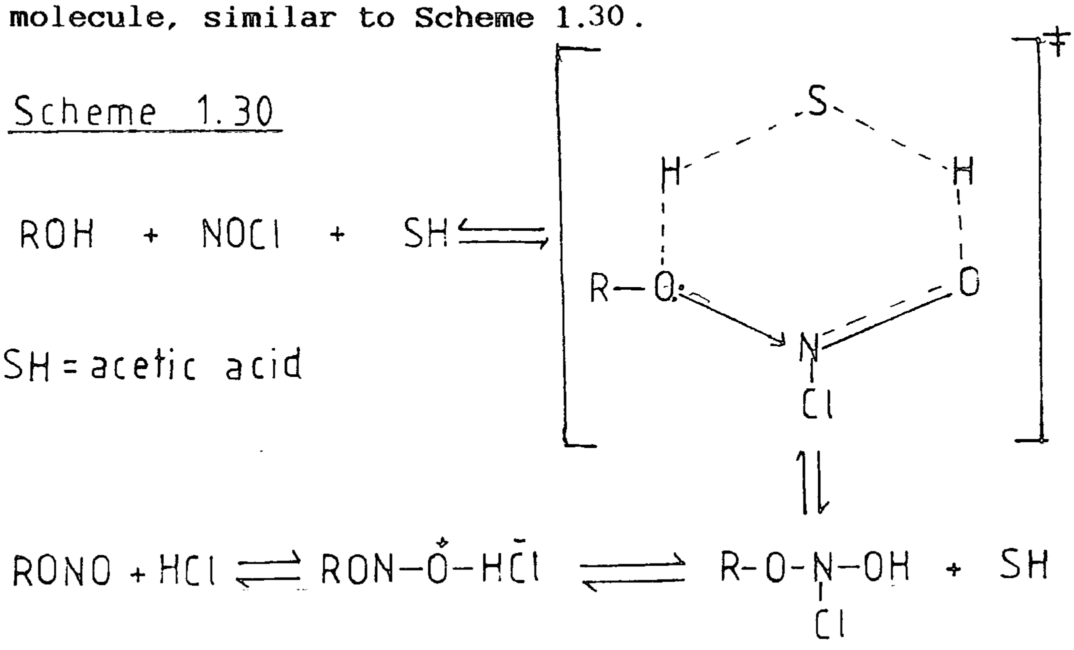
Scheme 1.29

Formation of alkyl nitrites in aqueous acid solution



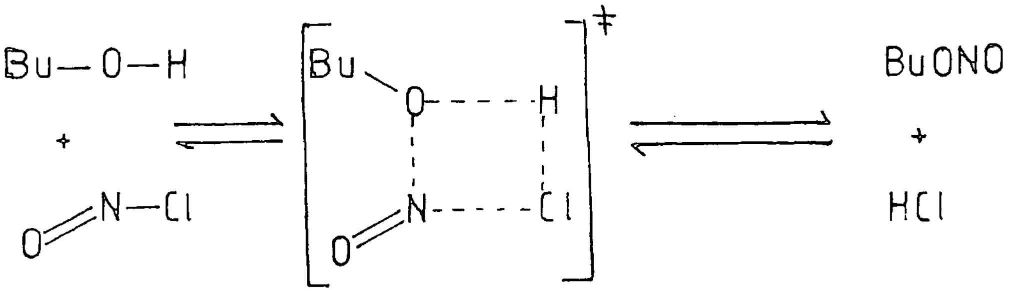
There have been two kinetic studies on the formation of alkyl nitrites from nitrosyl chloride in non aqueous solvents. In glacial acetic acid [102], the equilibrium was found to move further to the alkyl nitrite by increasing the basicity of the alcohol. The mechanism involves the attack of the alcohol on NOCl to form a six membered adduct which includes a solvent molecule. This intermediate then loses HCl to give the alkyl nitrite (Scheme 1.30). The other study was carried out in mixtures of carbon tetrachloride and acetic acid [103]. In this case the effect of varying the concentration of acetic acid on the rate of nitrosation of n-butanol was investigated. In pure CCl_4 the results were interpreted in terms of a single step formation of an activated complex by simple addition of reagents (Scheme 1.31). When acetic acid was added the reaction was believed to proceed via a six membered transition state, involving an acetic acid molecule, similar to Scheme 1.30.

Scheme 1.30



SH = acetic acid

Scheme 1.31



1.4 Reactions of Alkyl Nitrites

Alkyl nitrites are commonly used nitrosating agents, usually in non-aqueous solution, and react with a wide range of substrates such as amines [80], alcohols [79, 81], thiols [81]. Typical solvents and conditions include HCl-saturated diethyl ether, acidic alcoholic solution, basic alcoholic solution, liquid SO_2 and many aprotic solvents such as acetonitrile, chloroform, DMF, and THF without any added catalyst [107].

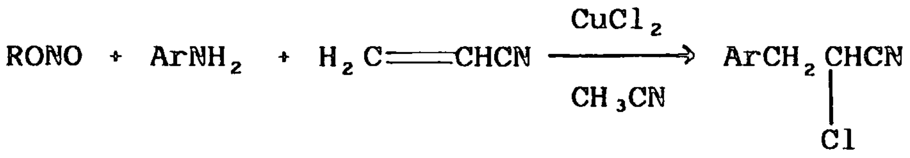
Many reactions involve the formation of diazonium ions from aromatic amines, which can then undergo similar reactions to those formed in aqueous solutions, often in better yields with fewer side reactions. Thus when the reaction is carried out in benzene solution [82] the product is the biaryl ~~product~~ (equation 1.32), probably formed by radical decomposition of the diazonium ion. When the reaction occurs in bromoform[83], the radical produced can abstract a bromine atom from the solvent to form the aryl bromide (equation 1.33). In a hydrogen radical donor solvent such as THF or DMF the main product is the deamination product [84, 85], (equation 1.34). If the reaction is carried out in acetonitrile in the presence of copper (II) halide salts the product is the aryl halide [86], (equation 1.35), and if an olefinic compound is added the reaction results in the arylation of the olefin [87] (equation 1.36).

$$RONO + ArNH_2 \xrightarrow[\text{benzene}]{\text{boiling}} ArN_2^+ \longrightarrow Ar\cdot \xrightarrow{C_6H_6} ArC_6H_5$$ (1.32)

$$RONO + ArNH_2 \xrightarrow{CHBr_3} ArN_2^+ \longrightarrow Ar\cdot \xrightarrow{CHBr_3} ArBr$$ (1.33)

$$RONO + ArNH_2 \xrightarrow[\text{or DMF}]{\text{THF}} ArH$$ (1.34)

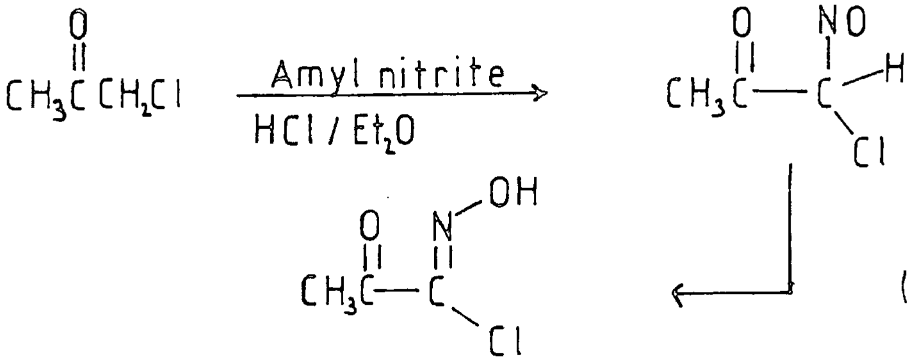
$$2RONO + 2ArNH_2 \xrightarrow[CuX_2,\ 65^\circ]{\text{Acetonitrile}} 2ArX + 2ROH + CuO + H_2O + N_2$$ (1.35)



$$RONO + ArNH_2 + H_2C{=}CHCN \xrightarrow[CH_3CN]{CuCl_2} ArCH_2\underset{\displaystyle Cl}{\underset{|}{CH}}CN + N_2$$ (1.36)

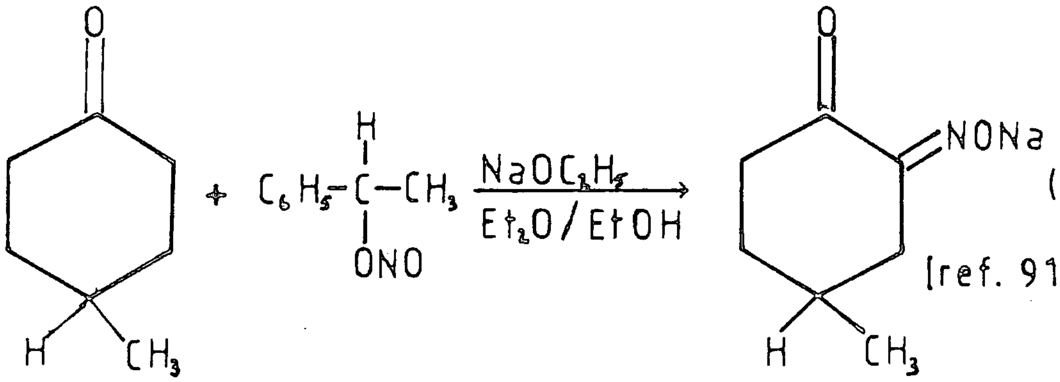
The reaction with amines in aprotic solvent is applicable to aromatic and heterocyclic amines [88, 89], but aliphatic amines appear to be unreactive under similar conditions.

Several other methods have been employed to facilitate the exchange of an amino group for a halide or thio group, these include reacting the amine with an alkyl nitrite in $CHCl_3$ [88] in the presence of bromine, iodine or dimethyl sulphide, with antimony trichloride [89] in dichloroethene and antimony tribromide [89] in dibromomethane. Alkyl nitrites have also been shown to effect nitrosation of alcohols [79, 81] and thiols [81] in non-aqueous solvents in the absence of any added catalyst. Another common synthetic procedure involves the reaction of the alkyl nitrite in diethyl ether containing HCl gas. This has been used to bring about the nitrosation of ketones [90] (equation 1.37).



(1.37)

As well as undergoing acid catalysed reactions, alkyl nitrites are also capable of affecting N, C and O nitrosation in basic media, typical procedures being sodium ethoxide in ethanol or even in aqueous alkaline solution. Examples are shown in equations (1.38 - 1.41).



(1.38)

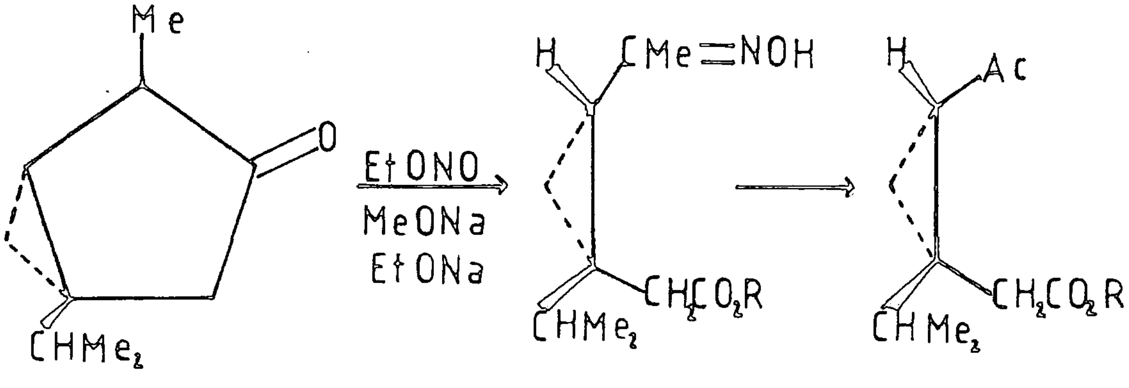
[ref. 91]

$$RONO + R_2NH \xrightarrow{OH^-} R_2NNO \qquad (1.39)$$

[ref. 92]

$$RONO + R'OH \xrightarrow{R'O^-Na} R'ONO + ROH$$

[ref. 93] (1.40)



Thujone

(1.41)

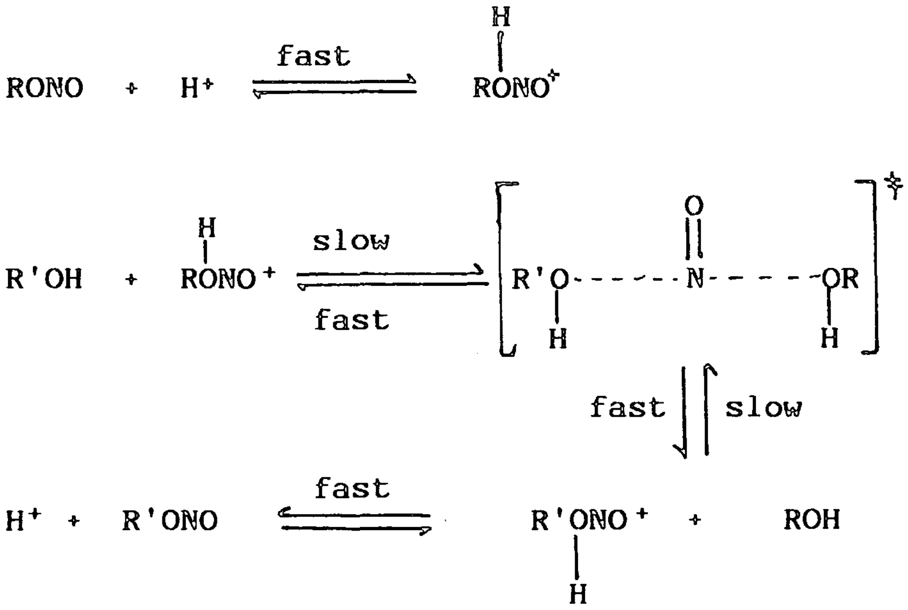
[ref. 94]

Very few kinetic studies have been carried out on the nitrosation reactions of alkyl nitrites. Due to the rapid rate of denitrosation (hydrolysis) of the alkyl nitrites [74] it seems likely that this will complicate the reaction and it has never been shown whether the reaction occurs via the nitrous acid formed or via the alkyl nitrite itself. A study of the kinetics of the N-nitrosation of sulphanilamide by cyclohexyl nitrite and by aqueous nitrous acid [95] indicated that a common nitrosating species was present in both reactions. In another study the influence of alcohols on the rate of nitrosation of morpholine in aqueous acid solution was explained in terms of an equilibrium formation of the alkyl nitrite which was itself ineffective in the nitrosation reaction [78]. The kinetics of the reaction of n-propyl nitrite in acidic n-propanol with several aromatic amines have been studied [96]. The reaction was found to be extremely slow in the absence of any nucleophilic catalyst. With added halide ion the reaction proceeded readily and the results were consistent with a mechanism involving a rapid equilibrium formation of the corresponding nitrosyl halide which attacks the free base form of the amine in the rate determining step. The acid and base catalysed transnitrosation of an alcohol has been studied in a variety of solvent systems. The reaction of 1-methyl heptyl nitrite in 1-propanol was catalysed by added acid and small amounts of water was found to inhibit strongly the reaction [97]. It was found that the reaction did not involve the asymmetric carbon centre and a mechanism was proposed involving the protonated form of the alkyl nitrite in a bimolecular reaction (scheme 1.42).

In the base catalysed reaction [93] the rate was found to be proportional to both alkyl nitrite and alkoxide ion concentration and that the asymmetric carbon centre was again not involved in the reaction. A similar scheme (1.43) was proposed involving nucleophilic attack of the alkoxide ion on the alkyl nitrite.

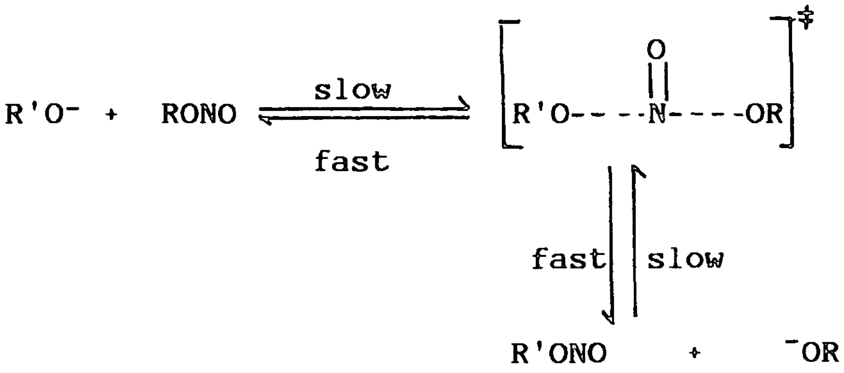
Scheme 1.42

Alcoholysis of alkyl nitrite in acidic alcohol solution



Scheme 1.43

Alcoholysis of alkyl nitrites in basic alcoholic solution

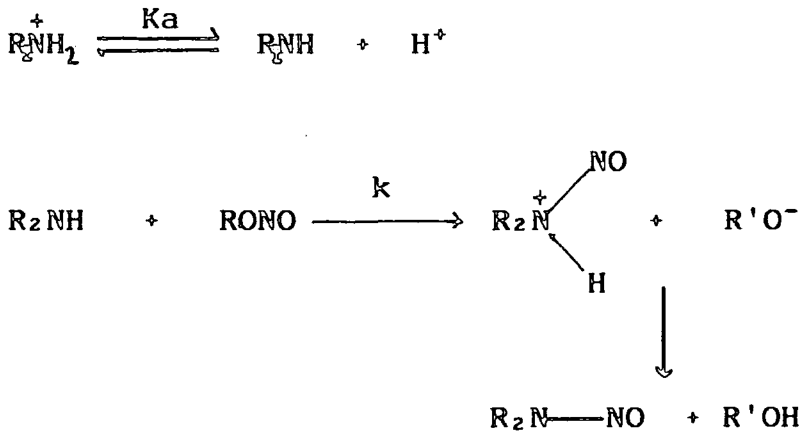


A similar reaction scheme has been found for the reactions of alkyl nitrites in basic aqueous solution with amines and cysteine. In the case of the reactions with secondary aliphatic amines to form nitrosamines [98] the reaction was interpreted as involving nucleophilic attack by the free base form of the amine on the nitrogen centre of the alkyl nitrite (Scheme 1.44). As expected the second order rate constant for attack of the amine on the alkyl nitrite increases linearly with basicity of the amine for a series of structurally similar isomers [99], but a more complex dependence is found when structural features become more important. This has been explained [92, 99] in terms of the reaction being orbital controlled, the energy of the HOMO of the amine being important. This is also born out by the fact that alkyl nitrites with ß-electron withdrawing groups such as Cl, F and OH react faster than those with electron releasing groups [98, 100]. This can be explained in terms of a lowering of the LUMO energy of the alkyl nitrite by electron withdrawing substituents. A similar trend in the reactivity of alkyl nitrites with the S-nitrosation of cysteine in aqueous alkali solution has been found [101]. The reaction in this case occurs via the S^- ion of cysteine.

The reactions in aqueous basic solution are less likely to be complicated by the hydrolysis of the alkyl nitrite than those in aqueous acid solution as the rate of alkaline hydrolysis of the alkyl nitrite has been found to be much slower than the rate of the acid catalysed hydrolysis [104].

Scheme 1.44

Reaction of alkyl nitrites with amines in basic solution



As well as being able to undergo heterolytic reactions, alkyl nitrites can also undergo homolytic reactions. This results from the weakness of the RO—NO bond. The activation energies of the radical forming reactions are given in Table 1.8.

The majority of the reactions are those of the alkoxide radical and have been discussed in a review article [105]. The most important of these reactions

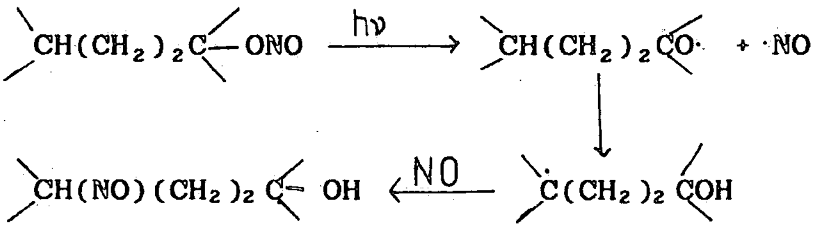
Table 1.8

Activation energy for $RO—NO \longrightarrow RO\cdot + NO\cdot$

Alkyl nitrite	Activation energy K J.mol
CH_3ONO	152.9
C_2H_5ONO	158.3
$n\ C_3H_7ONO$	155.4
$n\ C_4H_9ONO$	155.4

is the Barton reaction, whereby a 1,5 rearangement of the nitroso group in an alkyl nitrite occurs from oxygen to carbon to yield a 4-nitroso alcohol [106]. The reaction has been shown to occur via homolysis of the alkyl nitrite, photochemically, to give the alkoxy radical which then effects an intramolecular hydrogen atom abstraction to give the carbon radical. This then reacts with nitric oxide to give the C-nitroso compound which can then dimerize or isomerise to the oxime. This is outlined in Scheme (1.45).

Scheme 1.45: Mechanism of the Barton reaction



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CHAPTER 2

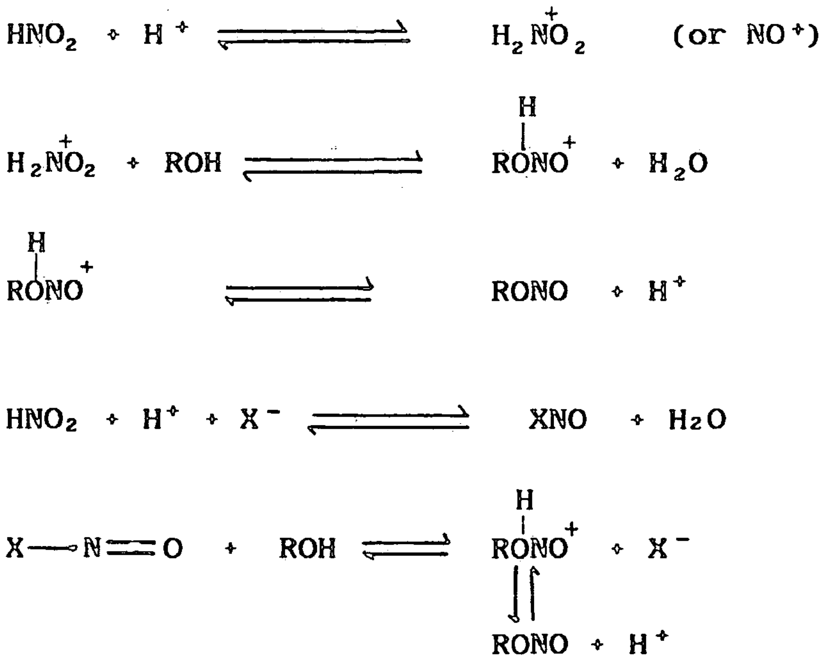
NITROSATION OF ISOPROPANOL AND TERTIARY BUTANOL IN AQUEOUS SOLUTION

The reaction of nitrous acid with various aliphatic alcohols to form alkyl nitrites has been studied previously [1] at 0°C. There the reaction was found to be reversible and both the forward and reverse reactions were catalysed by acid and halide ions. The mechanism of the reaction was explained in terms of attack of the nitrous acidium ion (or nitrosonium ion) on the oxygen centre of the alcohol in the forward reaction and nucleophilic attack of solvent (water) on the protonated alkyl nitrite in the reverse direction. In the presence of halide ion the forward reaction also involves a component due to the attack of the nitrosyl halide on the alcohol and similarly the reverse reaction includes a component due to nucleophilic attack of the halide ion on the protonated alkyl nitrite. The mechanism is summarised in Scheme (2.1).

In the previous study no information on the halide ion catalysis or on the rate constants at 25°C was obtained for the formation of isopropyl nitrite and tertiary butyl nitrite. These reactions were therefore studied using techniques developed previously [1].

Scheme 2.1

Mechanism of formation of alkyl nitrites in aqueous acid solution



$$HNO_2 + H^+ \rightleftharpoons H_2\overset{+}{N}O_2 \quad (\text{or } NO^+)$$

$$H_2\overset{+}{N}O_2 + ROH \rightleftharpoons R\overset{H}{\overset{|}{O}}NO^+ + H_2O$$

$$R\overset{H}{\overset{|}{O}}NO^+ \rightleftharpoons RONO + H^+$$

$$HNO_2 + H^+ + X^- \rightleftharpoons XNO + H_2O$$

$$X{\rightarrow}N{=}O + ROH \rightleftharpoons R\overset{H}{\overset{|}{O}}NO^+ + X^-$$

$$R\overset{H}{\overset{|}{O}}NO^+ \rightleftharpoons RONO + H^+$$

2.1 Nitrosation of tertiary butanol

2.1.1 Acid catalysis

The formation of tertiary butyl nitrite (^tBuONO) from tertiary butyl alcohol (^tBuOH) is known to be acid catalysed [1] (equation 2.2) but the equilibrium is well over to the nitrous acid side and so it has not proved possible to obtain values for the third order rate constant for the nitrosation of the tertiary butanol or its equilibrium constant for the formation of tertiary butyl nitrite with any precision by the kinetic technique employed. If the reaction is carried out under conditions where $[{}^{t}\mathrm{BuOH}] \gg [\mathrm{HNO_2}]$, the reaction can be conveniently followed by monitoring the formation of an equilibrium concentration of the alkyl nitrite in the 280 nm region by a stopped flow technique. The derived rate equation is shown in equation (2.3). On integration equation (2.3) leads to equation (2.4), hence a plot of $-\ln([\mathrm{RONO}]_{eq} - [\mathrm{RONO}]_t)$ against time leads to the observed first order rate constant, ko (equation 2.5).

$$H^+ + HNO_2 + {}^{t}BuOH \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} {}^{t}BuONO + H^+ + H_2O \qquad (2.2)$$

$$\text{Rate} = \frac{d[{}^{t}BuONO]}{dt} =$$

$$= (k_1[{}^{t}BuOH] + k_{-1})([{}^{t}BuONO]_{eq} - [{}^{t}BuONO]_t)[H^+]$$

where $[{}^{t}BuONO]_{eq}$ = equilibrium concentration of alkyl nitrite

$[{}^{t}BuONO]_t$ = concentration of alkyl nitrite at time t.

(2.3)

$$\ln \frac{[{}^{t}\text{BuONO}]_{eq} - [{}^{t}\text{BuONO}]_{o}}{[{}^{t}\text{BuONO}]_{eq} - [{}^{t}\text{BuONO}]_{t}} = k_o t \qquad (2.4)$$

$$k_o = (k_1[{}^{t}\text{BuOH}] + k_{-1})[\text{H}^+] \qquad (2.5)$$

The values of k_1 and k_{-1} can be obtained from experiments where the value of k_o is measured at different concentrations of tertiary butanol and a plot of k_o against $[{}^{t}\text{BuOH}]$ constructed. The slope yields the value of k_1 and the intercept yields the values of k_{-1}. Such experiments were carried out at 0°C and 25°C and the results are shown in Tables (2.1)-(2.4) and the results at 0°C are shown graphically in figure (2.1)

Table 2.1:

Variation of k_o with $[{}^{t}\text{BuOH}]$ at 0°C

$[\text{HNO}_2] = 0.04$ mol l^{-1} $[\text{HClO}_4] = 0.06$ mol l^{-1}

$[{}^{t}\text{BuOH}]$ mol l^{-1}	k_o s^{-1}
0.493	5.62 ± 0.20
0.740	5.58 ± 0.16
0.987	5.94 ± 0.04
1.480	6.53 ± 0.19

Slope = 0.99 ± 0.21 l mol^{-1} s^{-1}

Intercept = 4.99 ± 0.21 s^{-1}

Table 2.2:

Variation of ko with [^{t}BuOH] at 0°C

[HNO_2] = 0.04 mol l^{-1} [$HClO_4$] = 0.21 mol l^{-1}

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0.498	20.3 ± 1.2
0.747	21.6 ± 0.8
0.996	23.0 ± 1.7
1.494	23.2 ± 0.9

Slope = 2.78 ± 0.99 l mol^{-1} s^{-1}

Intercept = 19.4 ± 1.0 s^{-1}

Table 2.3:

Variation of ko with [^{t}BuOH] at 25°C

[HNO_2] = 0.02 mol l^{-1} [$HClO_4$] = 0.02 mol l^{-1}

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0.254	17.9 ± 0.7
0.508	18.0 ± 0.5
0.762	17.6 ± 0.3
1.016	17.0 ± 0.5

Slope = -1.22 ± 0.44 l mol^{-1} s^{-1}

Intercept = 18.4 ± 0.3 s^{-1}

Table 2.4:

Variation of ko with [^{t}BuOH] at 25°C

[HNO_2] = 0.02 mol l^{-1} [$HClO_4$] = 0.107 mol l^{-1}

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0.569	93.5 ± 4.2
0.758	92.1 ± 3.9
0.948	90.3 ± 1.9

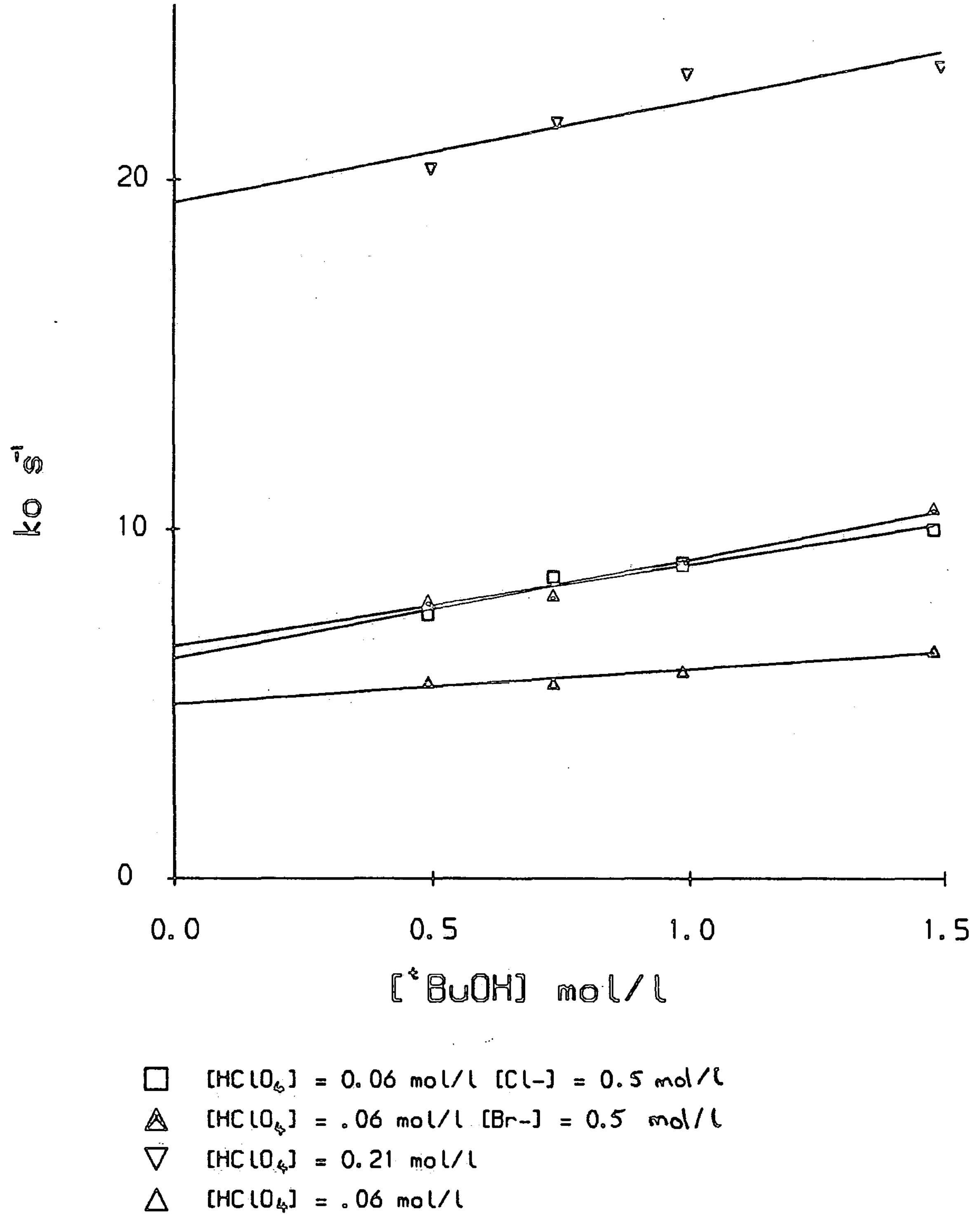
Slope = -8.44 ± 0.596 l mol^{-1} s^{-1}

Intercept = 98.4 ± 0.5 s^{-1}

The values of the slopes are subject to very large errors. The main reason is the fact that the observed change in ko on increasing [^{t}BuOH] is very small and is well within the experimental error of the measurement of the values of ko . The large error in the measurement of ko, typically ± 5%, is due to the very small absorbance change occuring in the reaction and also the reactions are very fast (especially at 25°C) and so are difficult to measure. (The plots at 25°C in fact have negative slopes but the values of ko are constant within the experimental error). It is therefore not possible to obtain meaningful values of the rate constant for nitrosation of [^{t}BuOH], k_1 , from this approach. The

Figure 2.1

Variation of ko with [^{t}BuOH] at 0°c



value of k_{-1}, the rate constant for hydrolysis of [^tBuONO], however can be obtained fairly reliably from the intercepts (or better still from the average values of k_0). The values of k_{-1} obtained are shown in Table (2.5).

Table 2.5:

Values of the second order rate constant, k_1

Temperature (°C)	[$HClO_4$] mol l^{-1}	Average k_0 s^{-1}	k_1 l mol^{-1} s^{-1}
0	0.06	5.91 ± 0.38	98.5 ± 6
0	0.21	22.0 ± 1.2	105 ± 6
25	0.02	17.6 ± 0.4	880 ± 20
25	0.107	92.0 ± 1.3	860 ± 12

The values obtained at 0°C agree well with those previously found of ca 100 l $mol^{-1}s^{-1}$, and they confirm the fact that the equilibrium constant for the formation of [^tBuONO] is indeed very small [1,2].

2.1.2 Halide ion catalysis

Halide ion catalysis of the nitrosation of alcohols and denitrosation of alkyl nitrites has been studied previously [1]. No data exist on the catalysis of the nitrosation of ^{t}BuOH . The reaction with ^{t}BuOH was found to be first order in added bromide (Table 2.6), but the effect is not very marked and there is a substantial component due to the uncatalysed reaction.

Table 2.6:

Variation of ko with [Br$^-$]

[HNO$_2$] = 0.04 mol l^{-1} [HClO$_4$] = 0.06 mol l^{-1}

[^{t}BuOH] = 0.5 mol l^{-1}

[Br$^-$] mol l^{-1}	ko s^{-1}
0	5.66 ± 0.16
0.025	5.75 ± 0.13
0.050	6.20 ± 0.47
0.075	5.91 ± 0.41
0.100	6.12 ± 0.71
0.150	7.03 ± 0.22

Slope = 8.15 ± 2.10 l mol^{-1} s^{-1}

Intercept = 5.57 ± 0.17 s^{-1}

The catalysis can be interpreted in terms of electrophilic attack of the nitrosyl halide on the alcohol for the forward reaction and nucleophilic attack of the halide ion on the protonated alkyl nitrite for the reverse reaction (Scheme 2.6). The derived rate equation also contains a term from the non nucleophile catalysed reaction, and the measured observed first order rate consant, k, is given in equation (2.7)

$$HNO_2 + H^+ + X^- \overset{K_{XNO}}{\rightleftharpoons} H_2O + XNO$$

$$XNO + {}^tBuOH \underset{k_{-X}}{\overset{k_X}{\rightleftharpoons}} {}^tBuONO + H^+ + X^- \qquad (2.6)$$

$$k_0 = (k_1[{}^tBuOH] + k_{-1})[H^+] + (k_X K_{XNO}[{}^tBuOH] + k_{-X})[H^+][X^-] \qquad (2.7)$$

The values of k_X and k_{-X} can be obtained from experiments where k_0 is measured at different concentrations of [^{t}BuOH] in the presence of added halide ion. Results from such experiments at 0°C are shown in Tables (2.7) and (2.8) and are displayed in figure (2.1)

Using the literature values for K_{XNO} of 2.2 x 10^{-2} l^2 mol^{-2} for NOBr [3] at 0°C and 5.5 x 10^{-4} l^2 mol^{-2} for NOCl [3] at 0°C allows the second order rate constant, k_X , for attack of the nitrosyl halide on ^{t}BuOH to be determined. The results are shown in Table (2.9)

Table 2.7:

Variation of k_0 with [^{t}BuOH] in presence of bromide ion

[HNO_2] = 0.04 mol l^{-1} [$HClO_4$] = 0.06 mol l^{-1}

[NaBr] = 0.50 mol l^{-1}

[^{t}BuOH] mol l^{-1}	k_0 s^{-1}
0.493	7.97 ± 0.29
0.740	8.12 ± 0.22
0.987	8.97 ± 0.29
1.480	10.61 ± 0.24

Slope = 2.82 ± 0.41 l $mol^{-1}s^{-1}$

Intercept = 6.31 ± 0.41 s^{-1}

Table 2.8:

Variation of k_0 with [^{t}BuOH] in the presence of chloride ion at 0°C

[HNO_2] = 0.04 mol l^{-1} [$HClO_4$] = 0.06 mol l^{-1}

[NaCl] = 0.50 mol l^{-1}

[^{t}BuOH] mol l^{-1}	k_0 s^{-1}
0.493	7.57 ± 0.24
0.740	8.63 ± 0.17
0.987	9.04 ± 0.14
1.480	10.0 ± 0.3

Slope = 2.33 ± 0.36 l $mol^{-1}s^{-1}$ Intercept = 6.66 ± 0.36 s^{-1}

Table 2.9:

Rate constants for chloride and bromide ion catalysis on the nitrosation of tertiary butanol at 0°C

Halide	k_X (l $mol^{-1}s^{-1}$)	k_{-X} l^2mol^{-2} s^{-1}
Cl^-	$8.72 \times 10^4 \pm 2.42 \times 10^4$	49.5 ± 13.3
Br^-	$2.74 \times 10^3 \pm 6.77 \times 10^2$	40.5 ± 14.9

$$\text{Rate of forward reaction} = k_X[NOX][{}^tBuOH]$$

$$\text{Rate of reverse reaction} = k_{-X}[{}^tBuONO][H^+][X^-]$$

The values of the rate constants for halide ion catalysis are subject to large errors as they require knowledge of the uncatalysed rate constants for their calculation. This will be especially true for k_X as this is obtained from a very small slope. The results for both the acid catalysis and halide catalysed reactions will be discussed further later.

2.2 Nitrosation of isopropanol

2.2.1 Acid Catalysis

A similar approach to that used for tertiary butanol was used to obtain the rate constants for the nitrosation of isopropanol (^{i}PrOH) and the hydrolysis of isopropyl nitrite (^{i}PrONO) at 25°C. The results are shown in Tables (2.10) - (2.12) and graphically in Figure (2.2). The values of k_1, the third order rate constant for nitrosation of ^{i}PrOH and k_{-1}, the second order rate constant for the hydrolysis of the alkyl nitrite, together with the equilibrium constant, K for the formation of ^{i}PrONO are shown in Table (2.13).

Table 2.10:

Variation of ko with [^{i}PrOH] at 25°C

$[HNO_2]$ = 0.02 mol l^{-1} $[HClO_4]$ = 0.02 mol l^{-1}

[^{i}PrOH] mol l^{-1}	ko s^{-1}
0.246	12.2 ± 0.1
0.394	12.4 ± 0.2
0.591	12.9 ± 0.4
0.739	13.3 ± 0.6
0.985	13.2 ± 0.1

Slope = 1.54 ± 0.37 l mol^{-1} s^{-1}

Intercept = 11.89 ± 0.24 s^{-1}

Table 2.11:

Variation of k_o with $[{}^{i}PrOH]$ at 25°C

$[HNO_2] = 0.02$ mol l^{-1} $[HClO_4] = 0.04$ mol l^{-1}

$[{}^{i}PrOH]$ mol l^{-1}	k_o s^{-1}
0.249	23.7 ± 0.1
0.597	25.0 ± 0.1
0.747	25.7 ± 0.2
0.896	26.4 ± 0.2
0.996	26.6 ± 0.4

Slope = 4.02 ± 0.17 l mol^{-1} s^{-1}

Intercept = 22.68 ± 0.12 s^{-1}

Table 2.12:

Variation of k_o with $[{}^{i}PrOH]$ at 25°C

$[HNO_2] = 0.02$ mol l^{-1} $[HClO_4] = 0.107$ mol l^{-1}

$[{}^{i}PrOH]$ mol l^{-1}	k_o s^{-1}
0.189	62.2 ± 1.6
0.379	67.0 ± 1.1
0.569	69.4 ± 0.9
0.758	71.3 ± 0.8
0.948	73.0 ± 0.9

Slope = 13.65 ± 1.85 l $mol^{-1}s^{-1}$ Intercept = 60.8 ± 1.17 s^{-1}

Figure 2.2

Variation of ko with ^{i}PrOH at 25°c

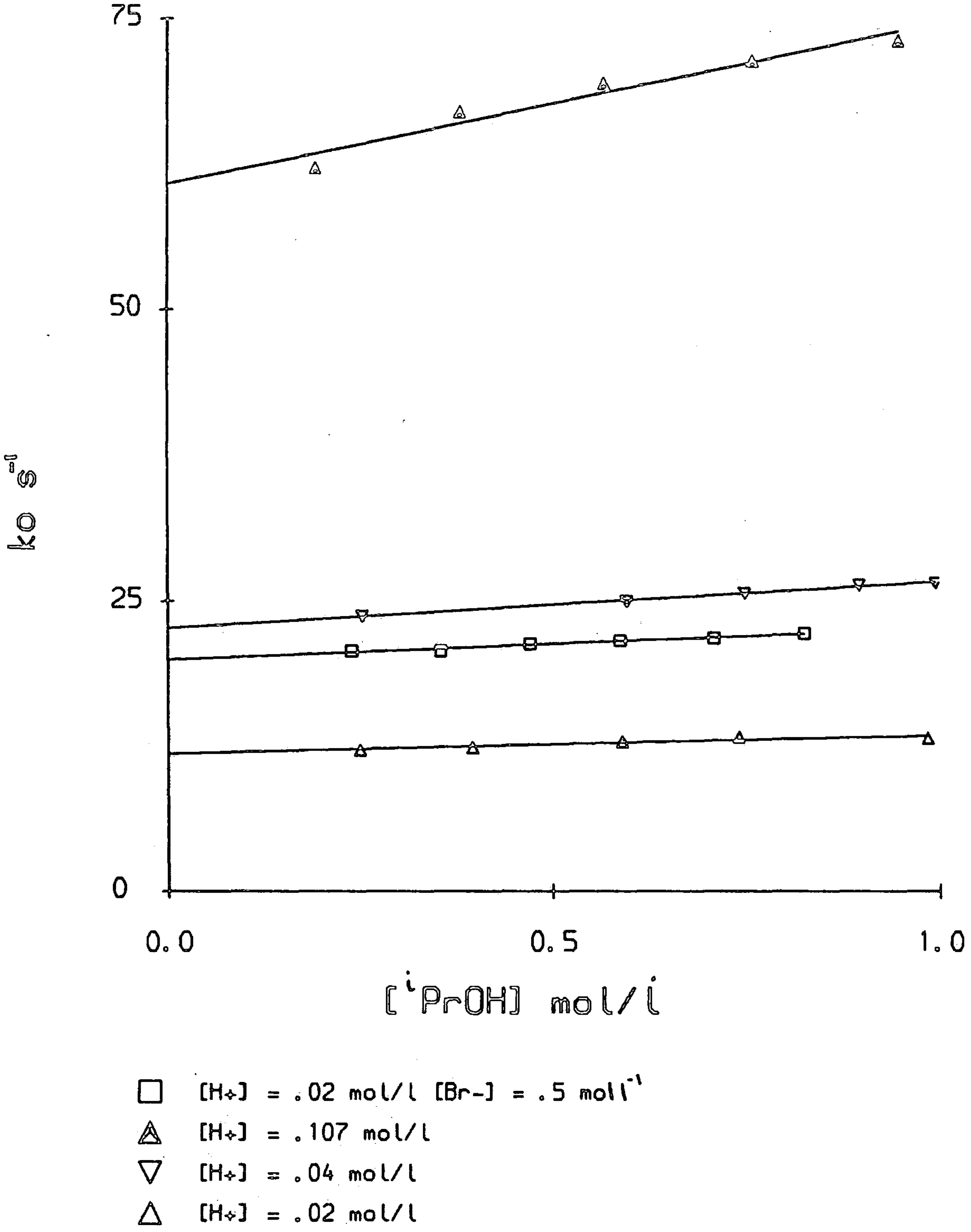


Table 2.13

Values of k_1 and k_{-1} for reaction of HNO_2 with $^{i}PrOH$ at 25°C and values of the equilibrium constant, K, for formation of $^{i}PrONO$.

$[HClO_4]$	k_1 l^2 mol^{-2} s^{-1}	k_{-1} l mol^{-1} s^{-1}	K l mol^{-1}
0.02	79.3 ± 18.2	594 ± 12	0.13 ± 0.03
0.04	100.6 ± 4.3	567 ± 3	0.18 ± 0.01
0.107	128 ± 17	568 ± 11	0.23 ± 0.03

The change in k_o with $[^{i}PrOH]$ was again very small, especially at the low acid concentrations so that the values obtained at 0.1M. $HClO_4$ are probably the most reliable values.

2.2.2 Halide ion catalysis

Experiments were carried out varying the concentration of $^{i}PrOH$ in the presence of added halide ion. The results are shown in Tables (2.14) - (2.16) and in Figure (2.2). The values of the rate constants for attack of NOX on the alcohol and the halide ion catalysed denitrosation of the alkyl nitrite were obtained, using the values of K_{NOX} [3, 4] of 5.1 x 10^{-2} l^2 mol^{-2} for NOBr at 25°C and 1.136 x 10^{-3} l^2 mol^{-2} for NOCl at 25°C.

The results are shown in Table (2.17).

Table 2.14:

Variation of ko with [^{i}PrOH] in the presence of added bromide ion at 25°C

$[HNO_2] = 0.02$ mol l^{-1} $[HClO_4] = 0.02$ mol l^{-1}

$[Br^-] = 0.50$ mol l^{-1}

[^{i}PrOH] mol l^{-1}	ko s^{-1}
0.236	20.7 ± 0.3
0.353	20.7 ± 0.3
0.471	21.3 ± 0.2
0.589	21.6 ± 0.2
0.707	21.8 ± 0.5
0.825	22.2 ± 0.3

Slope = 2.69 ± 0.26 l mol^{-1} s^{-1}

Intercept = 20.0 ± 0.15 s^{-1}

Table 2.16:

Variation of k_o with $[{}^{i}\mathrm{PrOH}]$ in the presence of added chloride ion at 25 °C

$[HNO_2]$ = 0.02 mol l^{-1} $[HClO_4]$ = 0.02 mol l^{-1}

$[NaCl]$ = 0.5 mol l^{-1}

$[{}^{i}\mathrm{PrOH}]$ mol l^{-1}	k_o s^{-1}
0.236	18.4 ± 0.2
0.353	18.9 ± 0.1
0.471	19.0 ± 0.2
0.589	20.1 ± 0.8
0.707	19.4 ± 0.4
0.825	19.9 ± 0.1

Slope = 2.45 ± 0.79 l mol^{-1} s^{-1}

Intercept = 18.0 ± 0.5 s^{-1}

Table 2.15:

Variation of k_o with $[{}^{i}\mathrm{PrOH}]$ in the presence of added bromide ion at 25°C

$[HNO_2]$ = 0.02 mol l^{-1} $[HClO_4]$ = 0.04 mol l^{-1}

$[Br^-]$ = 0.50 mol l^{-1}

$[{}^{i}\mathrm{PrOH}]$ mol l^{-1}	k_o s^{-1}
0.236	41.1 ± 1.5
0.353	40.7 ± 1.9
0.471	39.4 ± 1.4
0.589	43.7 ± 0.6
0.707	42.6 ± 1.0
0.825	43.3 ± 1.9

Slope = 4.73 ± 2.89 l $mol^{-1}s^{-1}$

Intercept = 39.3 ± 1.6 s^{-1}

Table 2.17:

Values of k_x and k_{-x} for nitrosation of isopropanol at 25°C

Halide	k_x l mol^{-1} s^{-1}	k_{-x} l^2 mol^{-2} s^{-1}
Cl^-	$4.05 \pm 0.13 \times 10^4$	634 ± 116
Br^-	$1.72 \pm 0.02 \times 10^3$	836 ± 63
	$1.13 \pm 0.07 \times 10^3$	805 ± 153

2.3 Discussion

The value of the equilibrium constant obtained for the formation of ^{i}PrONO at 25°C (ca 0.23 l mol^{-1}) is in reasonable agreement with the value obtained previously by the same method at 0°C (K= 0.25 l mol^{-1}) [1]. The values obtained at 25°C [2] previously are 0.52 l mol^{-1} and 0.56 l mol^{-1}. The discrepancy here probably arises from the high concentration of ^{i}PrOH needed for this kinetic method (typically up to 7% by volume for ^{i}PrOH and 14% by volume for ^{t}BuOH). This means that in these experiments the solvent composition is being changed markedly. A solvent [5] effect has been noted previously in the nitrosation of methanol, where a curved plot of k_o against [methanol] was obtained. Similar curves could also be obtained on the addition of a non reactive solvent (tetrahydrofuran). If a similar effect is occurring here then the measured values of the slope of a plot of ko against [alcohol] probably represent a minimum value and so the derived equilibrium constants therefore also probably represent minimum values.

The values of the rate constants for the denitrosation of the alkyl nitrite (k_{-1}) can be obtained with a larger degree of certainty as they are derived from a large intercept that can be measured fairly accurately. It has been noted previously [1] that the values of k_{-1} at 0°C for a series of aliphatic alcohols does not alter much on changing the structure of the alcohol. This trend is also found at 25°C (Table 2.18) for four alkyl nitrites. The actual values for the bimolecular rate constants for the reaction of water with the protonated alkyl nitrite cannot be obtained as the pKa of the alkyl nitrite is not known. A possible explanation for the consistency of the values of k_{-1} could be that the protonated alkyl nitrite reacts with water at the diffusion controlled limit. This would require the pKa of each alkyl nitrite to be approximately equal. Further evidence for this explanation comes from the halide ion catalysed reaction. Here the reaction is assumed to occur via nucleophilic attack of the halide ion on the nitrogen centre of the alkyl nitrite. It is known that bromide ion is significantly more nucleophilic than chloride ion in aqueous solution [6] and so the rate of attack of bromide ion would be expected to be

Table 2.18:

Values of k_{-1} for hydrolysis of the alkyl nitrite at 25°C

Alkyl nitrite	k_{-1} l $mol^{-1}s^{-1}$	
MeONO	576 ± 57	ref. [1]
EtONO	282 ± 10	ref. [1]
^{i}PrONO	576 ± 13	
^{t}BuONO	870 ± 20	

markedly greater than that of chloride ion. This is found in the case of the denitrosation of both N-methyl N-nitroso aniline [7] and N-nitroso diphenylamine [8], where attack of the halide ion again occurs at the nitrogen of the nitroso group. The results for both ^{t}BuONO and ^{i}PrONO show that there is little selectivity of the protonated alkyl nitrite between the two ions. This has been found previously for the reaction of methyl nitrite [1] and is thought to represent a diffusion controlled process.

The values of k_1, for the nitrosation of the alcohol, show a marked dependence on the structure of the alcohol. The value of k_1 for ^{t}BuOH is too small to be measured by this method and the value of k_1 for ^{i}PrOH at 25°C is ca 100 l^2 mol^{-2} s^{-1}, which is several orders of magnitude below that expected for a diffusion controlled process of ca. 7000 l^2 mol^{-2} s^{-1} [9]. It appears that steric factors are important in determining the size of k_1 .

The commonly found order of halide ion catalysis of $Br^- > Cl^-$ [10] is observed in the nitrosation of ^iPrOH and ^tBuOH. In both cases the value for k_{NOCl} is approximately one order of magnitude greater than k_{NOBr} . The value of k_{NOCl} however is typically five orders of magnitude below the diffusion controlled limit of 7×10^9 l $mol^{-1}s^{-1}$.

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CHAPTER 3

REACTIONS OF ALKYL NITRITES IN AQUEOUS ACID SOLUTION

Alkyl nitrites have long been known to effect nitrosation reactions in aqueous acid solution. It has never been shown conclusively whether the alkyl nitrite or more likely its protonated form is the reactive species or whether reaction occurs via hydrolysis of the alkyl nitrite to nitrous acid. Due to the rapid rate of hydrolysis [1, 2, 3] it appears likely that at least part of the reaction will occur via the nitrous acid route in aqueous acid solution.

3.1 Reaction of isopropyl nitrite (^{i}PrONO) with various nitrous acid traps

3.1.1 Hydrazoic acid

Hydrazoic acid is known to react rapidly with an acidic solution of nitrous acid to give nitrous oxide and nitrogen (equation 3.1). The probable intermediate is nitrosyl azide [4], which has been isolated at low temperature [5], which forms in the rate determining step.

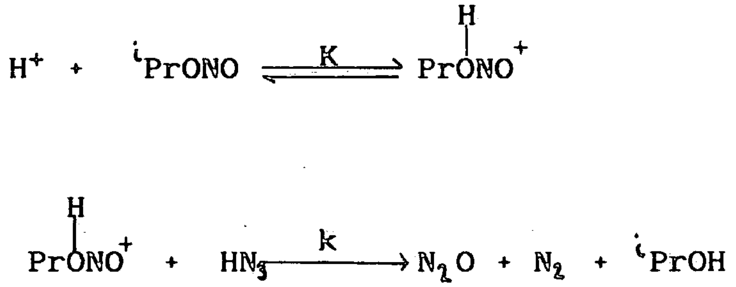
$$HNO_2 + HN_3 \longrightarrow N_3NO \longrightarrow N_2 + N_2O \qquad (3.1)$$

It has been shown that a number of reaction pathways exist in the initial nitrosation reaction. At low acidity [6], the reaction takes place via the azide ion with either the nitrous acidium ion (or nitrosonium ion) or with dinitrogen trioxide. At higher acidities, where protonation of the azide ion occurs, reaction occurs via hydrazoic acid [6,7] ($K_a = 1.8 \times 10^{-5}$ mol l^{-1} at 25°C). As expected the azide ion is more reactive to electrophilic nitrosation than hydrazoic acid, the former reacting at the diffusion controlled limit. Catalysis by acetate ion [8], chloride ion [6,9], bromide ion [6,9] and thiocyanate ion [9] has also been observed. At low acidity, where the azide ion is the reactive form the rate limiting step is usually the formation of the nitrosyl species NOX [6]. At higher acidities the rate limiting step becomes the attack of NOX [9] on hydrazoic acid.

In the present work reactions were carried out under conditions where the azide ion is fully protonated, that is the only reactive species is hydrazoic acid. The reactions were carried out with $[HN_3] \gg [{}^{i}PrONO]$

and good first order behaviour was observed in all cases by measuring the decreasing concentration of ^{i}PrONO at 370 nm. The observed first order rate constant was found to be first order in [HN_3] but was found to decrease on addition of isopropanol (^{i}PrOH). Results for two perchloric acid concentrations are shown in Tables (3.1) and (3.2) and the results for [$HClO_4$] = 0.10 mol l^{-1} are shown graphically in Figure (3.1).

There are two possibilities for the mechanism of the reaction of ^{i}PrONO, namely the alkyl nitrite or its protonated form reacts directly with hydrazoic acid (equation 3.2) or that hydrolysis of the alkyl nitrite occurs to release nitrous acid which can then effect nitrosation (equation 3.3).



$$H^+ + {}^{i}PrONO \xrightleftharpoons{K} Pr\overset{H}{\overset{|}{O}}NO^+$$

(3.2)

$$Pr\overset{H}{\overset{|}{O}}NO^+ + HN_3 \xrightarrow{k} N_2O + N_2 + {}^{i}PrOH$$

$$ {}^{i}PrONO \xrightleftharpoons{Keq} {}^{i}PrOH + HNO_2$$

(3.3)

$$HNO_2 + H^+ + HN_3 \xrightarrow{k} N_2O + N_2 + H_2O$$

Table 3.1

Variation of k_o with $[HN_3]$ at 25°C

$[{}^{i}PrONO] = 1.2 \times 10^{-3}$ mol l^{-1} $[HClO_4] = 0.10$ mol l^{-1} 370 nm

$[HN_3]$ mol l^{-1}	k_o s^{-1}		
	a	b	c
0.020	0.346 ± 0.017	0.354 ± 0.011	0.287 ± 0.005
0.040	0.731 ± 0.019	0.650 ± 0.023	0.539 ± 0.010
0.060	1.16 ± 0.03	0.992 ± 0.031	0.857 ± 0.040
0.080	1.53 ± 0.03	1.37 ± 0.03	1.21 ± 0.04
0.100	1.99 ± 0.04	1.76 ± 0.09	1.56 ± 0.07

a) $[{}^{i}PrOH] = 0.202$ mol l^{-1}
b) $[{}^{i}PrOH] = 0.402$ mol l^{-1}
c) $[{}^{i}PrOH] = 0.607$ mol l^{-1}

Table 3.2

Variation of k_o with $[HN_3]$ at 25°C

$[{}^{i}PrONO] = 1.2 \times 10^{-3}$ mol l^{-1} $[HClO_4] = 0.538$ 370 nm

$[HN_3]$ mol l^{-1}	k_o s^{-1}			
	a	b	c	d
0.020	3.07 ± 0.09	2.78 ± 0.11	2.38 ± 0.09	2.08 ± 0.06
0.040	6.13 ± 0.11	5.22 ± 0.17	4.95 ± 0.06	4.22 ± 0.04
0.060	9.31 ± 0.12	8.57 ± 0.74	7.85 ± 0.06	6.98 ± 0.11
0.080	14.3 ± 1.4	11.6 ± 0.08	10.2 ± 0.03	9.16 ± 0.11
0.100	16.6 ± 1.0	15.1 ± 0.01	13.2 ± 0.20	11.5 ± 0.14

a) $[{}^{i}PrOH] = 0$
b) $[{}^{i}PrOH] = 0.191$ mol l^{-1}
c) $[{}^{i}PrOH] = 0.402$ mol l^{-1}
d) $[{}^{i}PrOH] = 0.607$ mol l^{-1}

Figure 3.2

Plot of ko^{-1} against $[{}^{i}PrOH]$ for nitrosation of HN_3

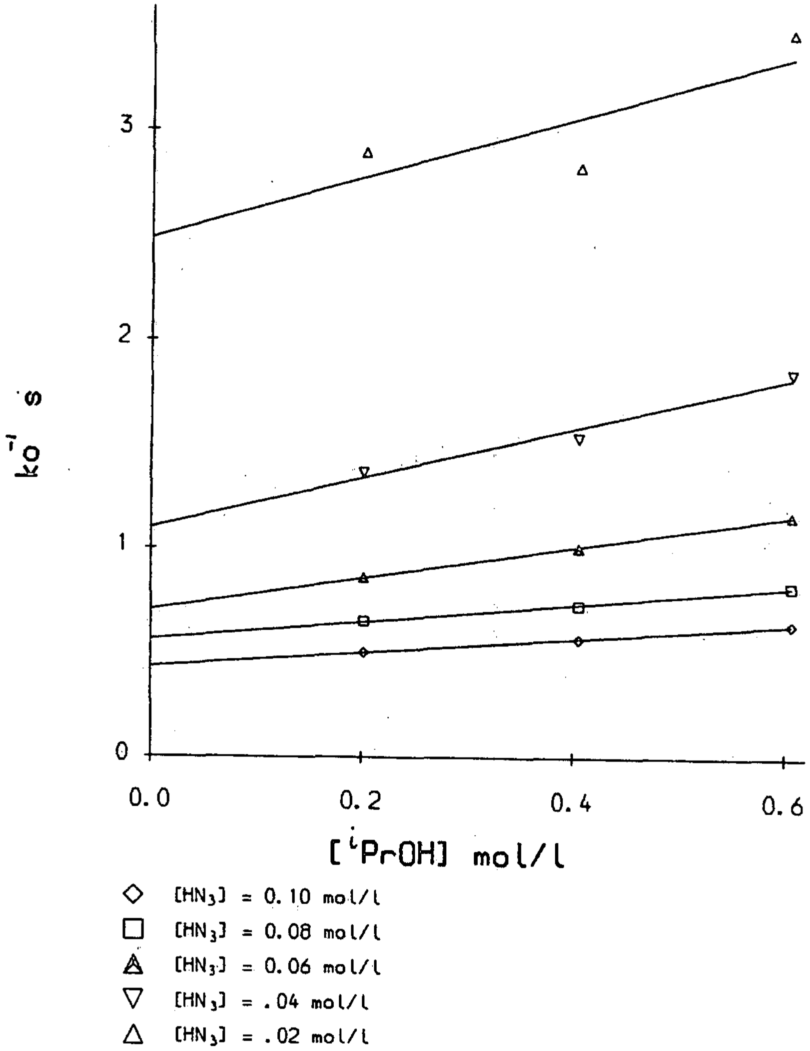
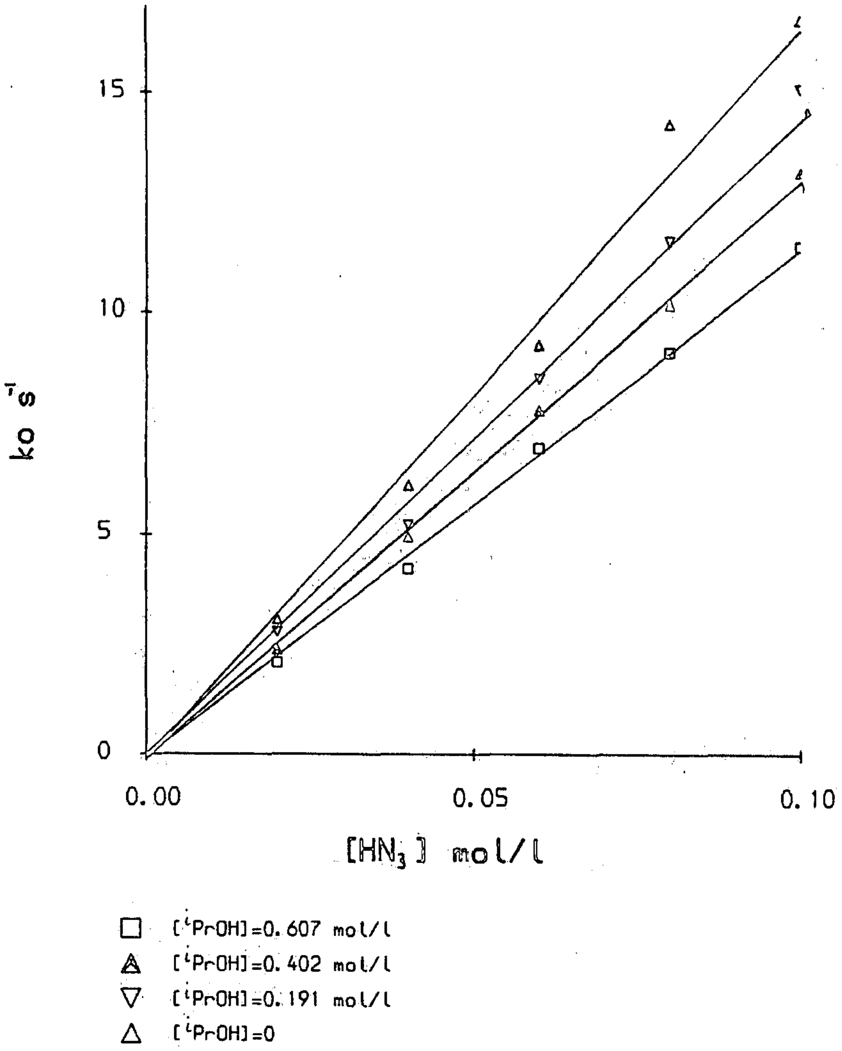


Figure 3.1

Variation of ko with $[HN_3]$ with $[H+]$ = 0.538 mol/l



Since the rate of reaction is found to decrease on addition of ^{i}PrOH the direct reaction mechanism can be ruled out as [^{i}PrOH] is not involved in any of the possible rate determining steps. The indirect reaction (equation 3.3), however, would be expected to show a dependence on [^{i}PrOH] as the initial equilibrium depends on [^{i}PrOH]. The derived rate equation for equation (3.3) is given below in equation (3.4).

$$\text{Rate} = k\,[HN_3][HNO_2][H^+]$$

$$\text{but} \quad K_{eq} = \frac{[ROH][HNO_2]}{[RONO]}$$

$$\text{and} \quad [\text{total nitrite}] = [RONO] + [HNO_2]$$

$$= \frac{[HNO_2][ROH]}{K_{eq}} + [HNO_2]$$

$$\therefore \quad [HNO_2] = \frac{[\text{Total nitrite}]\,K_{eq}}{[ROH] + K_{eq}}$$

Writing the rate in terms of [Total nitrite] gives equation (3.4).

$$\text{Rate} = \frac{k\,K_{eq}\,[HN_3][H^+]}{[ROH] + K_{eq}} \cdot [\text{Total nitrite}] \qquad (3.4)$$

Since the reaction was carried out with $[HN_3] \gg$ [Total nitrite], the observed first order rate constant, k_o, is given by equation (3.5)

$$k_o = \frac{k\ Keq\ [HN_3][H^+]}{[ROH] + Keq} \qquad (3.5)$$

Equation (3.5) predicts that the value of k_o should decrease on addition of ${}^iPrOH$, moreover the values of k, the third order rate constant for reaction of nitrous acid with HN_3, and Keq, the equilibrium constant for hydrolysis of the alkyl nitrite can be obtained since equation (3.5) can be rearranged to give equation (3.6)

$$\frac{1}{k_o} = \frac{[ROH]}{k\ Keq\ [HN_3][H^+]} + \frac{1}{k[HN_3][H^+]} \qquad (3.6)$$

A plot of k_o^{-1} against [ROH] should have a slope = $(k[HN_3][H^+]Keq)^{-1}$ and an intercept = $(k[HN_3][H^+])^{-1}$. Therefore the value of k can be obtained from the intercept and the value of Keq can be obtained from the value of intercept/slope. Such plots were obtained from the experimental results and the data for $[HClO_4]$ = 0.10 mol l^{-1} are shown graphically in Figure (3.2). The results of such an analysis for both acid concentrations are shown in Tables (3.3) and (3.4).

The average values of Keq are 1.34 ± 0.25 mol l^{-1} (for [$HClO_4$] = 0.10 mol l^{-1}) and 1.44 ± 0.19 mol l^{-1} (for [$HClO_4$]=0.538 mol l^{-1}). These values give 0.75 ± 0.14 l mol^{-1} and 0.69 ± 0.09 l mol^{-1} for the equilibrium constant for the formation isopropyl nitrite which agree reasonably well with values obtained by other methods of 0.56 [10], 0.52 [10] and 0.25 [3] l mol^{-1} at 25°C.

The value of k, the third order rate constant for attack of nitrous acid on HN_3 has also been determined previously [9] as 160 l^2 mol^{-2} s^{-1} at 25°C. This value was the extrapolated value of k as $[H^+] \rightarrow 0$ since the rate was found not to be a linear function of [H^+]. The corresponding values of k at 0.10 and 0.538 mol l^{-1} of $HClO_4$ can be interpolated from the variation of k_o with [H^+] and are 214 l^2 mol^{-2} s^{-1} and 360 l^2 mol^{-2} s^{-1}. The values obtained here are 220 ± 11 l^2 mol^{-2} s^{-1} and 300 ± 11 l^2 mol^{-2} s^{-1} which agree well with those obtained from the reaction with nitrous acid.

3.1.2 Sulphamic Acid

Sulphamic acid is a fairly strong acid (pKa = 1.1) [9] and is commonly used as a trap for nitrous acid, reacting according to equation (3.7) [11].

Table 3.3

Values of K_{eq} and k at 25°C from plots of k_o^{-1} against [^{i}PrOH]

$[KClO_4]$ = 0.10 mol l^{-1}

$[HN_3]$ mol l^{-1}	Slope l mol^{-1}s	Intercept s	Keq mol l^{-1}	k $l^2mol^{-2}s^{-1}$
0.020	1.485 ± 1.023	2.467 ± 0.446	1.66 ± 1.18	203 ± 37
0.040	1.205 ± 0.200	1.101 ± 0.087	1.49 ± 0.27	227 ± 18
0.060	0.754 ± 0.128	0.708 ± 6 x 10^{-3}	0.939 ± 0.16	235 ± 2
0.080	0.419 ± 0.026	0.568 ± 0.011	1.35 ± 0.09	220 ± 4
0.100	0.342 ± 7 x 10^{-3}	0.431 ± 3 x 10^{-3}	1.26 ± 0.03	232 ± 2

Table 3.4

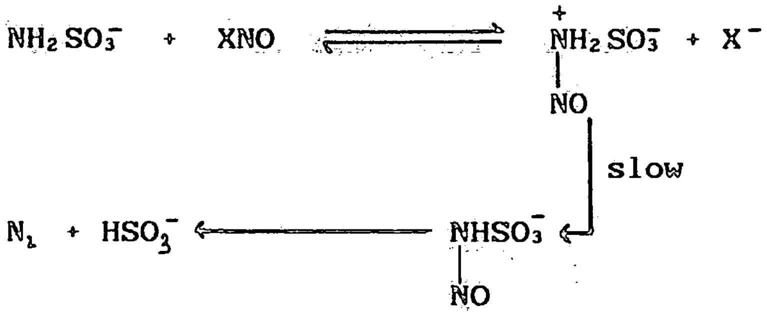
Values of Keq and k at 25°C from plots of k_o^{-1} against [^{i}PrOH]

$[KClO_4]$ = 0.538 mol l^{-1}

$[HN_3]$ mol l^{-1}	Slope l mol^{-1}s	Intercept s	Keq mol l^{-1}	k $l^2mol^{-2}s^{-1}$
0.020	0.261 ± 0.019	0.318 ± 7 x 10^{-3}	1.22 ± 0.09	292 ± 7
0.040	0.114 ± 0.017	0.164 ± 6 x 10^{-3}	1.44 ± 0.22	284 ± 10
0.060	0.0596 ± 4.5 x 10^{-3}	0.106 ± 2 x 10^{-3}	1.77 ± 0.14	294 ± 6
0.080	0.0520 ± 1.5 x 10^{-3}	0.0772 ± 6 x 10^{-4}	1.48 ± 0.05	299 ± 3
0.100	0.0450 ± 2.9 x 10^{-3}	0.0586 ± 1.1 x 10^{-3}	1.30 ± 0.09	317 ± 6

$$NH_2SO_3H \; + \; HNO_2 \longrightarrow N_2 \; + \; HSO^- \; + \; H_2O \; + \; H^+ \qquad (3.7)$$

The reaction is believed to occur via N-nitrosation. At low acidity the reaction occurs via the sulphamate ion [9,11], $NH_2SO_3^-$, sulphamic acid being much less reactive. At high acidity (>0.25 mol l^{-1}), where the concentration of sulphamate ion is very low, there is evidence for reaction of sulphamic acid itself [11]. Interestingly [9,11], the nitrosation of sulphamic acid is not subject to catalysis by halide ion or thiocyanate ion. This is also found in the nitrosation of amides [12,13,14,15] and seems to apply generally to the nitrosation of amines with powerful electron withdrawing groups next to them. The results have been explained in terms of a rapid reversible N-nitrosation followed by a rate limiting proton transfer.



The reaction of ^{i}PrONO with sulphamic acid was carried out in a similar way to that of hydrazoic acid.

Results showing the dependence of k_o on [sulphamic acid] at various [^{i}PrOH] are given in Table (3.5) and Figure (3.3).

The value of k_o again was found to decrease with increasing [^{i}PrOH]. The reaction is therefore similar to that of HN_3 but in this case as the sulphamate ion is the likely reactive species, the protonation of the sulphamate ion must be taken into account. The reaction is shown in Scheme (3.8).

$$^{i}PrONO \xrightleftharpoons{Keq} {}^{i}PrOH + HNO_2$$

$$\begin{tikzcd} HNO_2 + H^+ + NH_2SO_3^- \arrow[r, "k"] \arrow[d, shift right, "{[H^+]}"'] & N_2 + HSO_4^- + 2H_2O + 2H^+ \\ NH_2SO_3H \arrow[u, shift right, "Ka"'] & \end{tikzcd}$$

(3.8)

The observed first order rate constant derived for such a scheme is given in equation (3.9). This can be rearranged to give equation (3.10) which predicts that plotting k_o^{-1} against [^{i}PrOH] should be a straight line with slope = $(Ka + [H^+])/k\ Keq\ Ka$ [sulphamic acid]$[H^+]$ and intercept = $(Ka + [H^+])/\ k\ Ka$ [sulphamic acid]$[H^+]$.

The value of Keq can be readily obtained from the ratio of slope / intercept and the value of k, the third order rate constant for attack of nitrous acid on the sulphamate ion can be calculated assuming that the pKa of sulphamic acid is 1.1 at 25°C [9]. The results of such an analysis are shown in Table (3.6).

$$ko = \frac{k\ Keq\ Ka\ [\text{sulphamic acid}][H^+]}{(Ka + [H^+])(Keq + [ROH])} \qquad (3.9)$$

Where [sulphamic acid] = total stoichiometric concentration of sulphamic acid

$$ko^{-1} = \frac{(Ka + [H^+])[ROH]}{k\ Keq\ Ka \left[\begin{matrix}\text{sulphamic}\\ \text{acid}\end{matrix}\right][H^+]} + \frac{(Ka + [H^+])}{k\ Ka \left[\begin{matrix}\text{sulphamic}\\ \text{acid}\end{matrix}\right][H^+]} \qquad (3.10)$$

The average value of Keq is 1.46 ± 0.16 mol l^{-1} which agrees well with the values found for the reaction with HN_3 . The value of k, the third order rate constant for reaction of nitrous acid with sulphamate ion is known to be 1.13 x 10^3 l^2 mol^{-2} s^{-1} at 25°C. The average value obtained in this work is 2.55 x 10^3 ± 90 l^2 $mol^{-2}s^{-1}$. The small discrepancy could arise from the fact that the analysis assumes that the reaction occurs via the sulphamate ion but the possibility remains that there is a component of the reaction here via the acid form.

Table 3.5

Values of ko against [sulphamic acid] at 25°C

[^{i}PrONO] = 1.2 x 10^{-3} mol l^{-1} [$HClO_4$] = 0.522 mol l^{-1}

[sulphamic acid]	ko s^{-1}			
mol l^{-1}	a	b	c	d
0.020	3.52 ± 0.04	3.03 ± 0.14	2.87 ± 0.05	2.63 ± 0.16
0.030	5.29 ± 0.06	4.64 ± 0.05	4.14 ± 0.23	3.83 ± 0.12
0.040	6.94 ± 0.20	6.34 ± 0.05	5.52 ± 0.11	4.89 ± 0.17
0.050	8.54 ± 0.13	7.55 ± 0.12	6.52 ± 0.16	6.18 ± 0.14
0.060	11.0 ± 0.3	9.54 ± 0.15	8.63 ± 0.15	8.01 ± 0.15
0.070		11.0 ± 0.4	9.85 ± 0.03	8.70 ± 0.18

a) [^{i}PrOH] = 0.040 mol l^{-1} b) [^{i}PrOH] = 0.200 mol l^{-1}

c) [^{i}PrOH] = 0.402 mol l^{-1} d) [^{i}PrOH] = 0.602 mol l^{-1}

Table 3.6:

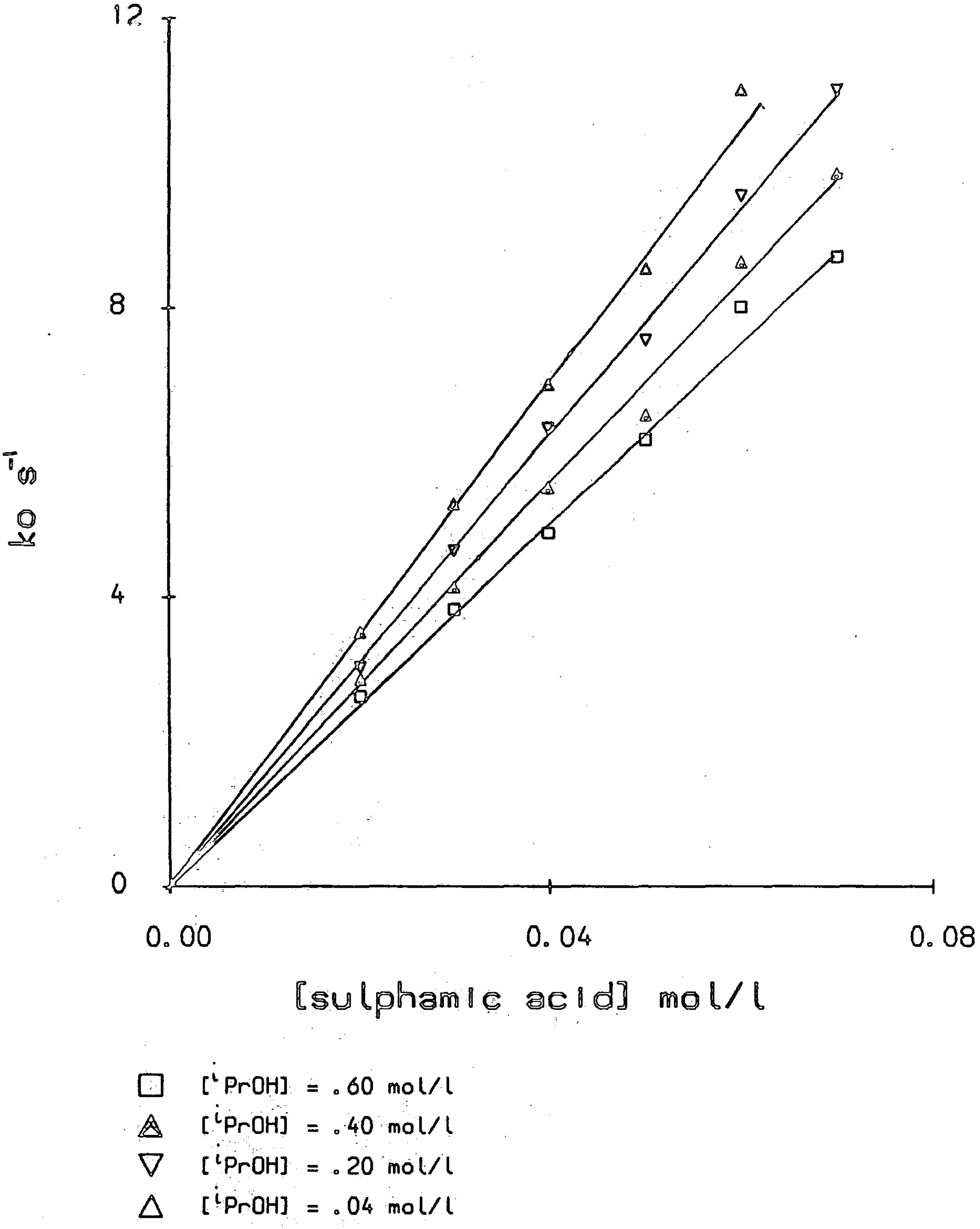
Values of Keq and k at 25°C from plots of ko^{-1} against [^{i}PrOH]

[$HClO_4$] = 0.522 mol l^{-1}

[sulphamic acid] mol l^{-1}	Slope l mol^{-1} s	Intercept s	K mol l^{-1}	k l^{2} mol^{-2} s^{-1}
0.020	0.161 ± 0.025	0.286 ± 9 x 10^{-3}	1.77 ± 0.28	2534 ± 80
0.030	0.128 ± 9 x 10^{-3}	0.187 ± 4 x 10^{-3}	1.46 ± 0.11	2584 ± 55
0.040	0.109 ± 5 x 10^{-3}	0.138 ± 2 x 10^{-3}	1.27 ± 0.06	2626 ± 39
0.050	0.082 ± 0.010	0.116 ± 4 x 10^{-3}	1.41 ± 0.18	2499 ± 86
0.060	0.059 ± 6 x 10^{-3}	0.091 ± 3 x 10^{-3}	1.54 ± 0.16	2655 ± 88
0.070	0.060 ± 4 x 10^{-3}	0.079 ± 2 x 10^{-3}	1.32 ± 0.09	2383 ± 60

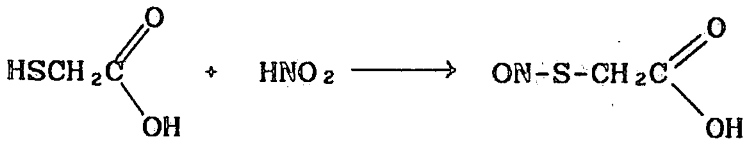
Figure 3.3

Plot of ko against [sulphamic acid]



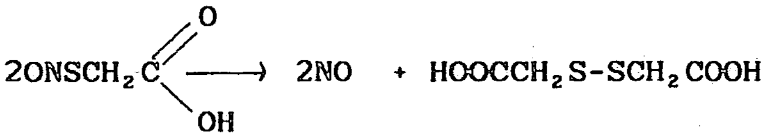
3.1.3 Thioglycolic acid

Thioglycolic acid (TGA) is known to undergo S-nitrosation [16] in acidic solution of nitrous acid, as shown in equation (3.11). The product thionitrite



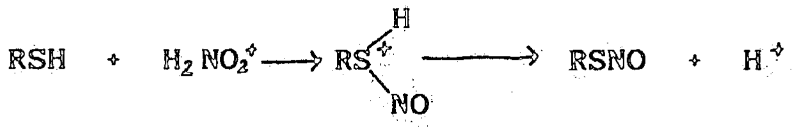
$$HSCH_2C(=O)OH + HNO_2 \longrightarrow ON{-}S{-}CH_2C(=O)OH \qquad (3.11)$$

is unstable as are almost all thionitrites, decomposing to the disulphide [17] (equation 3.12), but has been identified in solution by the appearance of a broad absorption band at 330 nm in the UV/visible spectrum.

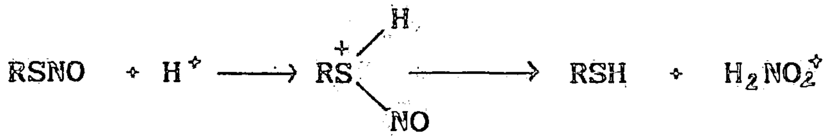


$$2ONSCH_2C(=O)OH \longrightarrow 2NO + HOOCCH_2S{-}SCH_2COOH \qquad (3.12)$$

The formation of thionitrites from thiols has been shown to be effectively irreversible [18], which contrasts markedly with the reactions of alcohols to form alkyl nitrites [3]. This can be rationalized by considering the effect of changing from an oxygen centre to a sulphur centre on the rates of the forward reaction (equation 3.13) and reverse reaction (3.14). The forward rate



$$RSH + H_2NO_2^+ \longrightarrow R\overset{H}{\underset{NO}{S^+}} \longrightarrow RSNO + H^+ \qquad (3.13)$$



$$RSNO + H^+ \longrightarrow R\overset{H}{\underset{NO}{S^+}} \longrightarrow RSH + H_2NO_2^+ \qquad (3.14)$$

of reaction is expected to depend on the nucleophilicity of the sulphur or oxygen centre, with the sulphur site being the more nucleophilic. The reverse reaction depends on the basicity of the oxygen or sulphur site, oxygen being the more basic site. Therefore an oxygen centre (alkyl nitrite) favours the reverse reaction whereas a sulphur centre (thionitrite) favours the forward reaction.

The nitrosation of thioglycolic acid with nitrous acid has been shown to follow the commonly found rate law [16] (equation 3.15) in the absence of any added nucleophilic catalyst and the value of k, the third order rate constant is known to be 2630 l^2 mol^{-2} s^{-1} at 25°C. Under the conditions used in the study TGA exists mainly as the free acid.

$$\text{Rate} = k\,[TGA][HNO_2][H^+] \qquad (3.15)$$

It is likely that the ionized form is also reactive, but at pH $<$ 2 any contribution from this form can be ignored (pKa of TGA [19] = 3.42). The reaction is also known to be catalysed by added nucleophiles [16], the reactivity sequence of the corresponding nitrosyl species being the commonly encountered one of nitrosyl chloride $>$ nitrosyl bromide $>$ nitrosyl thiocyanate. In the presence of either bromide ion or thiocyanate ion and with high [TGA] it has been possible to achieve rate limiting formation of nitrosyl bromide or nitrosyl thiocyanate and the rate constants obtained agree well with values obtained by other methods.

The reaction of ^{i}PrONO with TGA were carried out at 330 nm, following the formation of the thionitrite. Experiments were carried out with [TGA]$\gg$[^{i}PrONO] and good first order behaviour was found in all cases. Results were obtained showing the dependence of the observed first order rate constant, k_o , on [TGA] at various [^{i}PrOH]. The results are shown in Table (3.7) and Figure (3.4)

The reaction is first order in [TGA] and the kinetic pattern is similar to that found for the reactions of hydrazoic acid and sulphamic acid on the addition of isopropanol. The reaction is therefore taking place via hydrolysis of the alkyl nitrite, the nitrous acid formed effecting nitrosation of TGA (Scheme 3.16)

Table 3.7:

Variation of ko with [TGA] at 25°C

[^{i}PrONO] = 1.2 x 10^{-4} mol l^{-1} [$HClO_4$] = 0.203 mol l^{-1}

330 nm

[TGA] mol l^{-1}	ko s^{-1} a	 b	 c
0.0297	13.2 ± 0.3	12.0 ± 0.2	10.7 ± 0.2
0.0396	17.6 ± 0.7	15.6 ± 0.3	14.4 ± 0.3
0.0494	21.4 ± 0.3	18.6 ± 0.1	17.0 ± 0.2
0.0593	26.2 ± 0.3	22.5 ± 1.0	20.6 ± 0.3
0.0692	28.7 ± 0.2	27.2 ± 0.7	24.0 ± 0.2
0.0791	32.1 ± 0.6	31.3 ± 0.1	26.0 ± 0.6

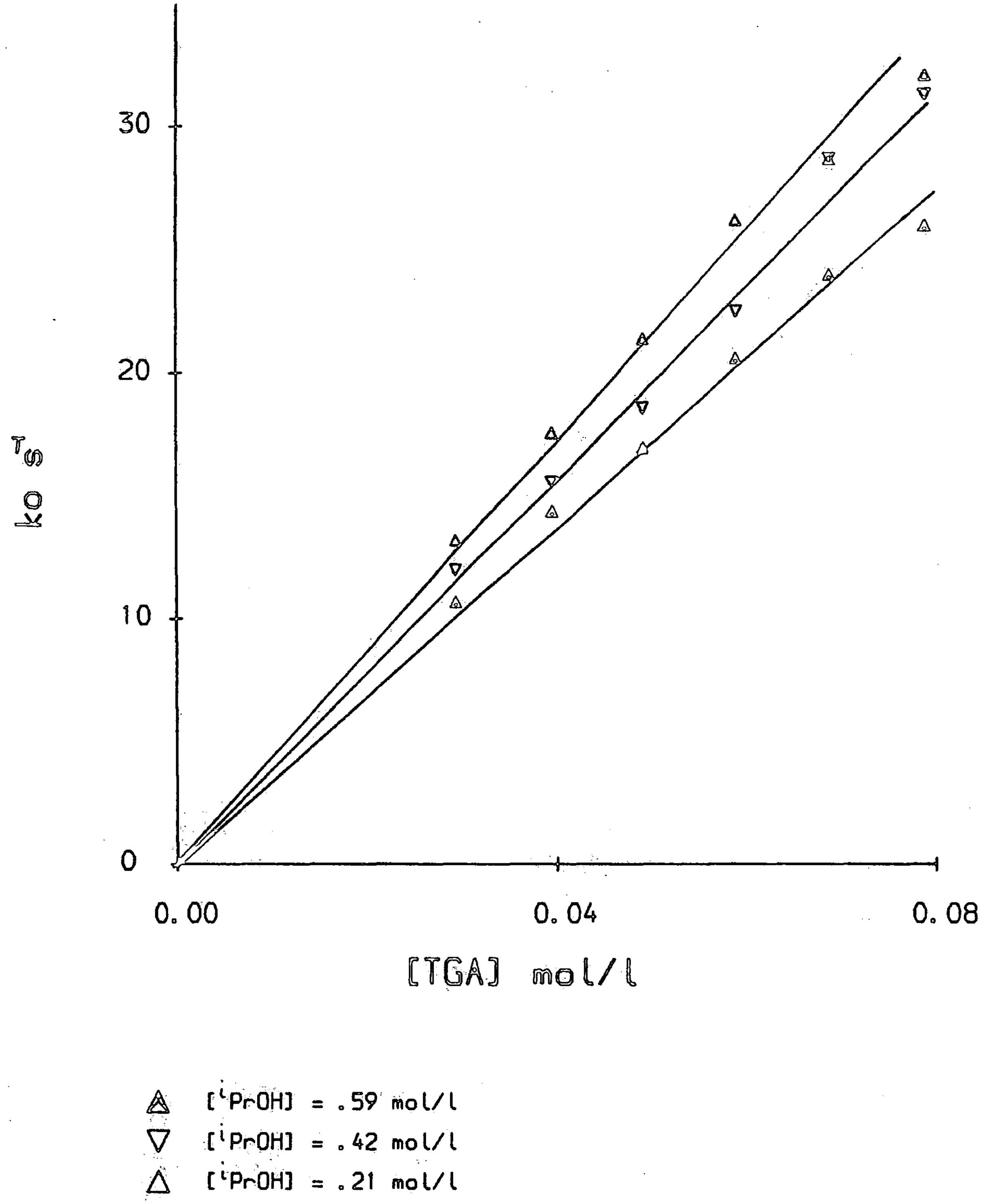
a) [^{i}PrOH] = 0.207 mol l^{-1}

b) [^{i}PrOH] = 0.415 mol l^{-1}

c) [^{i}PrOH] = 0.592 mol l^{-1}

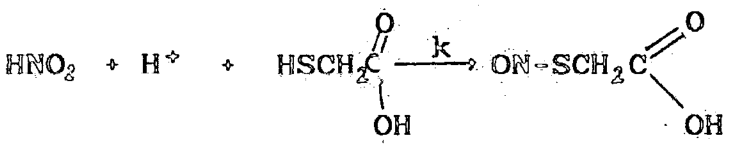
Figure 3.4

Plot of ko
against [TGA]



$$ {}^{i}\mathrm{PrONO} \xrightleftharpoons{K_{eq}} \mathrm{HNO_2} + {}^{i}\mathrm{PrOH} $$

(3.16)



$$ \mathrm{HNO_2} + \mathrm{H^+} + \mathrm{HSCH_2C(=O)OH} \xrightarrow{k} \mathrm{ON{-}SCH_2C(=O)OH} $$

The observed first order rate constant for such a scheme is given in equation (3.17) which can be rearranged as before to give equation (3.18)

$$ k_o = \frac{k\ K_{eq}\ [\mathrm{TGA}][\mathrm{H^+}]}{[{}^{i}\mathrm{PrOH}] + K_{eq}} \qquad (3.17) $$

$$ k_o^{-1} = \frac{[{}^{i}\mathrm{PrOH}]}{k\ K_{eq}\ [\mathrm{TGA}][\mathrm{H^+}]} + \frac{1}{k[\mathrm{TGA}][\mathrm{H^+}]} $$

(3.18)

A plot of k_o^{-1} against $[{}^{i}\mathrm{PrOH}]$ should have a slope = $(k\ [\mathrm{TGA}][\mathrm{H^+}]K_{eq})^{-1}$ and intercept = $(k\ [\mathrm{TGA}][\mathrm{H^+}])^{-1}$, from which the values of k, the third order rate constant for attack of nitrous acid on thioglycolic acid can be obtained. The results of such an analysis are shown in Table (3.8)

Table 3.8:

Values of Keq and k at 25°C from plots of ko^{-1} against [$^{n}PrOH$]

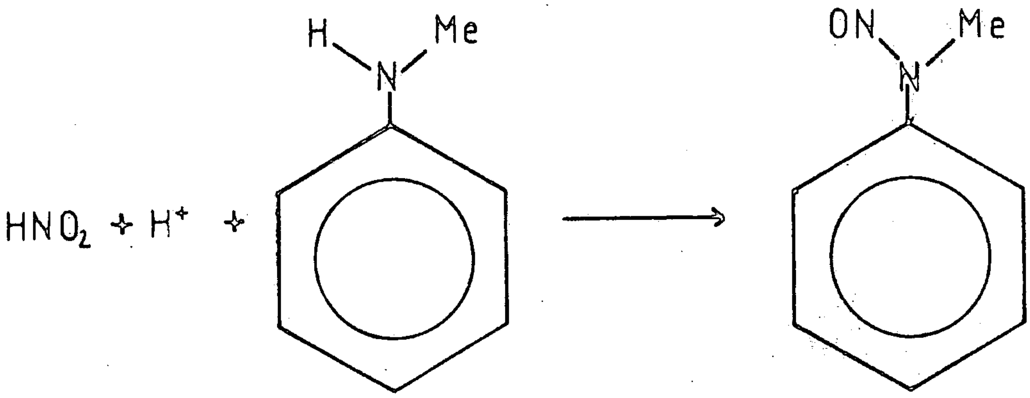
[$HClO_4$] = 0.203 mol l^{-1}

[TGA] mol l^{-1}	Slope l mol^{-1} s	Intercept s	Keq mol l^{-1}	k l^2 mol^{-2} s^{-1}
0.0297	0.445 ± 5.9 x 10^{-3}	0.0661 ± 2.6 x 10^{-3}	1.49 ± 0.21	2512 ± 99
0.0396	0.0336 ± 1.4 x 10^{-3}	0.0498 ± 6 x 10^{-4}	1.48 ± 0.06	2500 ± 30
0.0494	0.0318 ± 1.5 x 10^{-3}	0.0403 ± 7 x 10^{-4}	1.26 ± 0.07	2476 ± 43
0.0593	0.0273 ± 2.2 x 10^{-3}	0.0327 ± 1.0 x 10^{-3}	1.20 ± 0.11	2543 ± 78
0.0692	0.0175 ± 5.3 x 10^{-3}	0.0306 ± 2.3 x 10^{-3}	1.75 ± 0.55	2329 ± 175
0.0791	0.0186 ± 9.4 x 10^{-3}	0.0263 ± 4.1 x 10^{-3}	1.41 ± 0.39	2371 ± 370

The average value of Keq obtained = 1.43 ± 0.18 mol l^{-1} which agrees well with the earlier values. The value of k, 2455 ± 78 l^2 mol^{-2} s^{-1} agrees well with the value measured directly [16] (2630 l^2 mol^{-2} s^{-1} at 25°C).

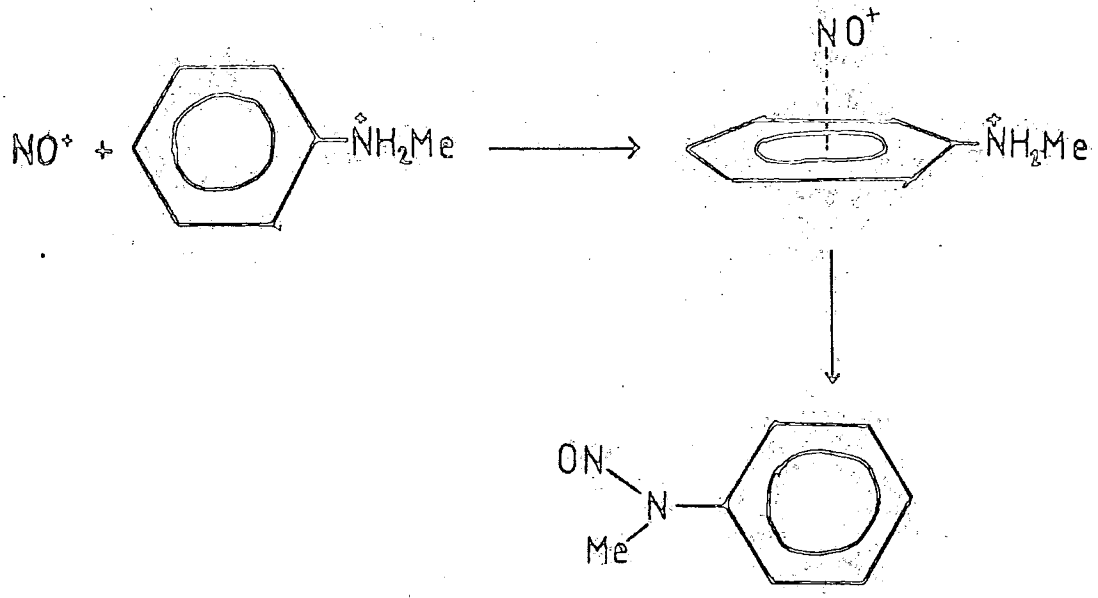
3.1.4 N-Methylaniline

Nitrosation of N-methylaniline (NMA) is an example of nitrosamine formation (equation 3.19).



(3.19)

At low and moderate acidities [20] the free base form of the amine is the reactive species, reacting at or near to the diffusion controlled limit [21] with the nitrous acidium ion (or nitrosonium ion), dinitrogen trioxide, nitrosyl chloride and nitrosyl bromide. At higher acidities [22] reaction can also occur via the protonated form of the amine, possibly by a π complex intermediate (equation 3.20)



(3.20)

The reaction of ^{i}PrONO with NMA was studied at 280 nm, following the appearance of the nitrosamine. The reaction was carried out with [NMA] $\gg$ [^{i}PrONO] and good first order behaviour was found in each case. Experiments were carried out to investigate the effect of acidity on the observed first order rate constant k_o, (Table 3.9) and also the effect of [NMA] at various [^{i}PrOH] on k_o, (Table 3.10).

Table 3.9:

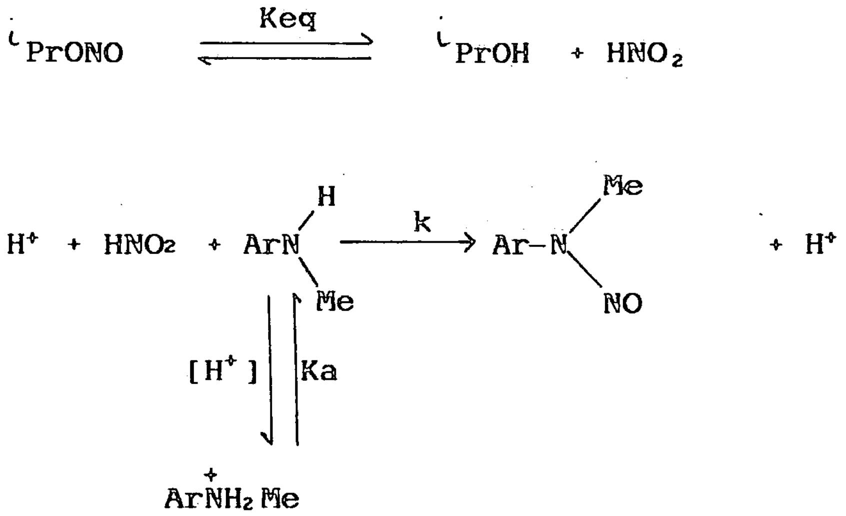
Effect of acidity on the nitrosation of NMA at 25°C

[^{i}PrONO] = 1 x 10^{-4} mol l^{-1} [NMA] = 5.34 x 10^{-3} mol l^{-1}

[^{i}PrOH] = 0.20 mol l^{-1} 280 nm

[$HClO_4$] mol l^{-1}	10^4 k_o s^{-1}
0.067	6.40
0.083	6.24
0.100	6.29

The value of k_o is independent of the acidity, is first order in [NMA] and is decreased on the addition of ^{i}PrOH. These observations are consistent with reaction occurring by denitrosation (or hydrolysis) of the alkyl nitrite to give nitrous acid which can then react with the free base form of the amine, as is shown in Scheme (3.21).



(3.21)

Since the pKa of protonated NMA is known to be 4.85 [23], at the acidities used in these experiments the total stoichiometric concentration of the amine is effectively equal to the concentration of the protonated form, i.e., $[\mathrm{NMA}]_T \simeq [\mathrm{Ar\overset{+}{N}H_2Me}]$. The derived value of k_o for this scheme is therefore equation (3.22). A plot of k_o^{-1} against [^{i}PrOH] can therefore be used to obtain values for Keq and k, the third order rate constant for attack of nitrous acid on the free base form of

Table 3.10:

Variation of ko with [NMA] at 25°C

$[{}^{i}PrONO] = 1 \times 10^{-4}$ mol l^{-1} $[HClO_4] = 0.0667$ mol l^{-1} 280 nm

[NMA] mol l^{-1}	10^4 ko s^{-1} a	b	c
1.22×10^{-3}	1.99 ± 0.07	1.92 ± 0.26	1.88 ± 0.06
2.45×10^{-3}	3.88 ± 0.38	3.43 ± 0.23	2.84 ± 0.05
3.67×10^{-3}	5.20 ± 0.17	4.70 ± 0.06	3.81 ± 0.01
4.89×10^{-3}	6.19	5.77	5.42
5.72×10^{-3}	8.53 ± 0.18	7.79 ± 0.14	7.05 ± 0.32
7.15×10^{-3}	9.80 ± 0.09	8.89 ± 0.20	8.56 ± 0.04

a) $[{}^{i}PrOH] = 0.200$ mol l^{-1} b) $[{}^{i}PrOH] = 0.337$ mol l^{-1}

c) $[{}^{i}PrOH] = 0.596$ mol l^{-1}

the amine. The results of such an analysis are shown in Table (3.11)

$$k = \frac{k \; Keq \; [NMA] \; Ka}{[\;PrOH] + Keq} \qquad (3.22)$$

The values of Keq obtained in this case are much more scattered than those previously found. This arises from the large errors in the reproducibility of the values of k and the small size of the decrease in k on addition of ^{i}PrOH. The average value of k, the third order rate constant for attack of nitrous acid on the free amine is 11513 ± 1379 l^2 mol^{-2} s^{-1}. This is somewhat larger than the literature value of 4600 l^2 mol^{-2} s^{-1} [21], but is of the right order of magnitude.

3.1.5 Conclusion

All the results obtained for nitrosation of hydrazoic acid, sulphamic acid, thioglycolic acid and N-methylaniline with isopropyl nitrite are consistent with a mechanism involving a fast hydrolysis of the alkyl nitrite to give an equilibrium concentration of nitrous acid which then effects nitrosation of the substrate. There is no evidence for a direct reaction between the alkyl nitrite and any of these substrates.

Table 3.11:

Values of Keq and k at 25°C from plots of k_o^{-1} against [^{n}PrOH]

$[NMA]_T$ mol l^{-1}	slope l mol^{-1} s	intercept s	Keq mol l^{-1}	k l^2 mol^{-2} s^{-1}
1.22×10^{-3}	702 ± 230	4919 ± 95	7.01 ± 2.30	11723 ± 226
2.45×10^{-3}	2377 ± 33	2107 ± 14	0.89 ± 0.02	13680 ± 91
3.67×10^{-3}	1791 ± 108	1548 ± 45	0.87 ± 0.16	12408 ± 361
4.89×10^{-3}	560 ± 108	1519 ± 45	2.71 ± 0.53	9531 ± 282
5.72×10^{-3}	608 ± 75	1062 ± 31	1.75 ± 0.22	11611 ± 339
7.15×10^{-3}	346 ± 151	974 ± 62	2.81 ± 0.54	10122 ± 644

3.2 Reaction of tertiary butyl nitrite with various nitrous acid traps

3.2.1 Reaction with sulphamic acid

The reaction of tertiary butyl nitrite (^{t}BuONO) with sulphamic acid was carried out in a similar way to the same reaction with ^{i}PrONO. Thus under conditions where [^{t}BuONO] $\ll$ [sulphamic acid], good first order behaviour was obtained, following the disappearance of the alkyl nitrite at 370 nm. The effect of added tertiary butyl alcohol (^{t}BuOH) on the value of k_o, the observed first order rate constant, was determined and the results are shown in Table (3.12).

The results show that under these conditions the reaction is first order in [sulphamic acid] and the values of k_o are independent of the concentration of added ^{t}BuOH within the experimental error. A possible explanation of this effect is due to the fact that the equilibrium constant for the hydrolysis of the alkyl nitrite is much larger for ^{t}BuONO than ^{i}PrONO [3, 10]. Assuming that the reaction occurs by a similar route to that of ^{i}PrONO a similar rate equation should apply in the case of ^{t}BuONO (equation 3.23). The value of the equilibrium constant for formation of ^{t}BuONO from nitrous acid has been estimated [3] to be < 0.05 l mol^{-1} at 0°C. This means that Keq, the

Table 3.12:

Effect of [^{t}BuOH] and [sulphamic acid] on ko at 25°C

[^{t}BuONO] = 1.2×10^{-3} mol l^{-1} [$HClO_4$] = 0.522 mol l^{-1}

370 nm

Sulphamic acid mol l^{-1}	ko s^{-1} a	 b
0.020	3.51 ± 0.06	3.51 ± 0.14
0.030	5.45 ± 0.29	5.53 ± 0.13
0.040	6.94 ± 0.18	6.81 ± 0.24
0.050	8.61 ± 0.13	8.81 ± 0.36
0.060	10.5 ± 0.35	9.97 ± 0.11
0.070	12.0 ± 0.2	11.6 ± 0.51

a) [^{t}BuOH] = 0.201 mol l^{-1}

slope = 169 ± 3 l mol^{-1} s^{-1}

b) [^{t}BuOH] = 0.603 mol l^{-1}

slope = 159 ± 6 l mol^{-1} s^{-1}

$$k_{o} = \frac{k\ Keq\ Ka\ [\text{sulphamic acid}]\ [H^{+}]}{(Ka + [H^{+}])\ (Keq + [{}^{t}BuOH])} \qquad (3.23)$$

equilibrium constant for hydrolysis of the alkyl nitrite will be > 20 mol l^{-1} . This means that under the conditions used Keq $\gg [{}^{t}BuOH]$ and so equation (3.23) reduces to equation (3.24), which predicts that the

$$k_{o} = \frac{k\ Ka\ [\text{sulphamic acid}]\ [H^{+}]}{(Ka + [H^{+}])} \qquad (3.24)$$

reaction should be first order in [sulphamic acid] and independent of $[{}^{t}BuOH]$. In the case of ${}^{i}PrONO$, the equilibrium constant for formation of ${}^{i}PrONO$ is ca 0.56 l mol^{-1} [10], which corresponds to a Keq of ca 1.8 mol l^{-1} , therefore under the conditions used ($[{}^{i}PrOH]$ = 0.2 - 0.6 mol l^{-1}) the value of Keq is comparable in size with $[{}^{i}PrOH]$ and so there is a measurable decrease in rate on addition of ${}^{i}PrOH$. Equation (3.24) predicts that the value of k, the third order rate constant for nitrosation of the sulphamate anion can be obtained from a plot of k_{o} against [sulphamic acid], assuming that pKa = 1.1 . From the data in Table 3.12 the value of k is 2379 ± 73 l^{2} mol^{-2} s^{-1} which is in good agreement with those obtained from analysis of the data for the reaction of ^{i}PrONO.

Experiments were carried out to investigate the effect of [sulphamic acid] at different acidities on the reaction rate. The results at four different acidities are shown in Tables (3.13) - (3.16).

Table 3.13:

Effect of [sulphamic acid] on k_o at 25°C

[^{t}BuONO] = 1.2×10^{-3} mol l^{-1} [^{t}BuOH] = 0.1 mol l^{-1}

[$HClO_4$] = 7.74×10^{-3} mol l^{-1} 370 nm

[sulphamic acid]mol l^{-1}	k_o s^{-1}
0.025	0.34 ± 0.01
0.050	0.72 ± 0.02
0.100	1.12 ± 0.05
0.150	1.60 ± 0.02
0.301	3.20 ± 0.20
0.677	6.05 ± 0.22
0.803	5.98 ± 0.33

Table 3.14:

Effect of [sulphamic acid] on ko at 25°C

[^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1} [^{t}Bu OH] = 0.1 mol l^{-1}

[HClO$_4$] = 0.050 mol l^{-1} 370 nm

[sulphamic acid]mol l^{-1}	ko s^{-1}
0.025	1.68 ± 0.07
0.050	3.36 ± 0.15
0.150	9.47 ± 0.61
0.301	16.2 ± 0.5
0.462	23.1 ± 1.4
0.679	31.7 ± 2.1
0.803	33.3 ± 1.6

Table 3.15:

Effect of [sulphamic acid] on ko at 25°C

[^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1} [^{t}BuOH] = 0.1 mol l^{-1}

[HClO$_4$] = 0.19 mol l^{-1} 370 nm

[sulphamic acid] mol l^{-1}	ko s^{-1}
0.025	2.82 ± 0.09
0.050	6.69 ± 0.24
0.075	9.57 ± 0.45
0.150	18.3 ± 0.5
0.300	32.6 ± 1.2
0.450	46.6 ± 4.0
0.600	78.4 ± 4.6
0.803	93.0 ± 9.0

Table 3.16:

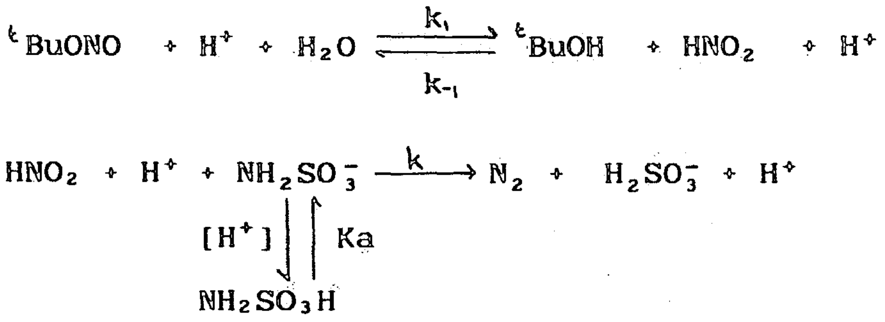
Effect of [sulphamic acid] on ko at 25°C

[^{t}BuONO] = 1.2×10^{-3} mol l^{-1} [^{t}BuOH] = 0.1 mol l^{-1}

[$HClO_4$] = 0.50 mol l^{-1} 370nm

[sulphamic acid] mol l^{-1}	ko s^{-1}
0.025	4.32 ± 0.05
0.050	8.65 ± 0.28
0.075	12.2 ± 0.3
0.100	16.4 ± 0.4
0.150	23.9 ± 0.8
0.300	54.8 ± 3.7
0.525	90.4 ± 3.2

The results for the four acidities are shown in Figure (3.5). It can be seen that in each case, ko is first order in [sulphamic acid] at low [sulphamic acid], but the plots curve at high [sulphamic acid], tending to a limit value of ko . The effect is much more marked at the lower acidities, where the concentration of the sulphamate anion is the greatest. Since the reaction order changes from a first order to a zero order dependence on [sulphamic acid], this means that the rate determining step must have changed from being attack of the nitrous acidium (or nitrosonium ion) on the sulphamate anion to an earlier step, ie. hydrolysis of the alkyl nitrite. The reaction scheme is shown in equation (3.25).



$$
\begin{tikzcd}[column sep=small]
{}^{t}BuONO + H^{+} + H_2O \arrow[r, shift left, "k_1"] & {}^{t}BuOH + HNO_2 + H^{+} \arrow[l, shift left, "k_{-1}"]
\end{tikzcd}
$$

(3.25)

$$
\begin{tikzcd}[column sep=small]
HNO_2 + H^{+} + {} & NH_2SO_3^{-} \arrow[r, "k"] \arrow[d, shift right, "{[H^{+}]}"'] & N_2 + H_2SO_3^{-} + H^{+} \\
& NH_2SO_3H \arrow[u, shift right, "Ka"'] &
\end{tikzcd}
$$

From the reaction scheme it can be seen that if $k\ [H^{+}][NH_2SO_3^{-}] \gg k_{-1}\ [{}^{t}BuOH]$ then the slow step will become the hydrolysis of the alkyl nitrite, the k_1 step. The derived rate equation for scheme (3.25) is equation (3.26)

$$
k_o = \frac{k\ k_1\,[\text{sulphamic acid}][H^{+}]Ka}{k_{-1}\,[{}^{t}BuOH](Ka + [H^{+}]) + k\ Ka[\text{sulphamic acid}]}
$$

(3.26)

Equation (3.26) predicts that at high [sulphamic acid], if

$$
\frac{k\ Ka\ [\text{sulphamic acid}]}{(Ka + [H^{+}])} \gg k_{-1}\,[{}^{t}BuOH]
$$

then the equation reduces to equation (3.27), ie. the value of ko should be zero order in [sulphamic acid], and the limiting value of ko should yield the value of k_1 , the second order rate constant for hydrolysis of the alkyl nitrite. Estimating the limiting values of

$$ko = k_1 [H^+] \qquad (3.27)$$

ko from the data at $[HClO_4]$ = 7.74 x 10^{-3} (ko ≃ 6 s^{-1}) and 0.05 mol l^{-1} (ko ≃ 35 s^{-1}) yield values of ca 780 l^2 mol $^{-2}$ s^{-1} and 700 l^2 mol $^{-2}$ s^{-1} for the values of k_1, which are in reasonable agreement with the values measured directly of 880 and 890 l^2 mol^{-2} s^{-1}.

A more detailed kinetic analysis of the data show that plots of ko^{-1} against [sulphamic acid]$^{-1}$give reasonable straight lines with slopes and intercepts that are $\propto [H^+]^{-1}$ (Table 3.17 and Figure 3.6).
Equation (3.26) predicts that a plot of ko^{-1} against [sulphamic acid]$^{-1}$ should be a straight line with slope = k_{-1} [ROH](Ka + $[H^+]$)/k_1k Ka $[H^+]$ and intercept = $(k_1 [H^+])^{-1}$. The average value of k_1 obtained from the intercept = 1492 ± 290 l^2 mol^{-1}s^{-1}, which is in fair agreement with those previously found. Also, by plotting the slope against $[H^+]^{-1}$, the value of Ka for sulphamic acid can be obtained from the ratio of slope /intercept of this graph. The value obtained = 0.0997 mol l^{-1} , which

Figure 3.6

Plot of ko^{-1} against [sulphamic acid]$^{-1}$

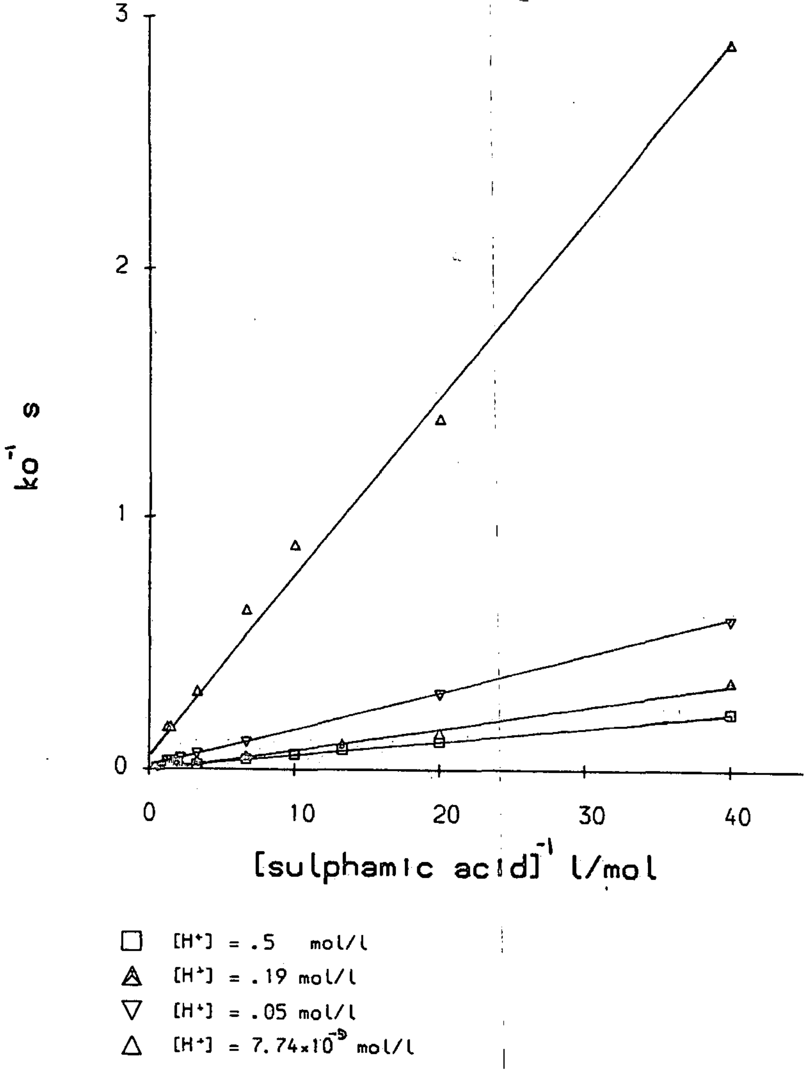


Figure 3.5

Plot of ko against [sulphamic acid] at different acidities

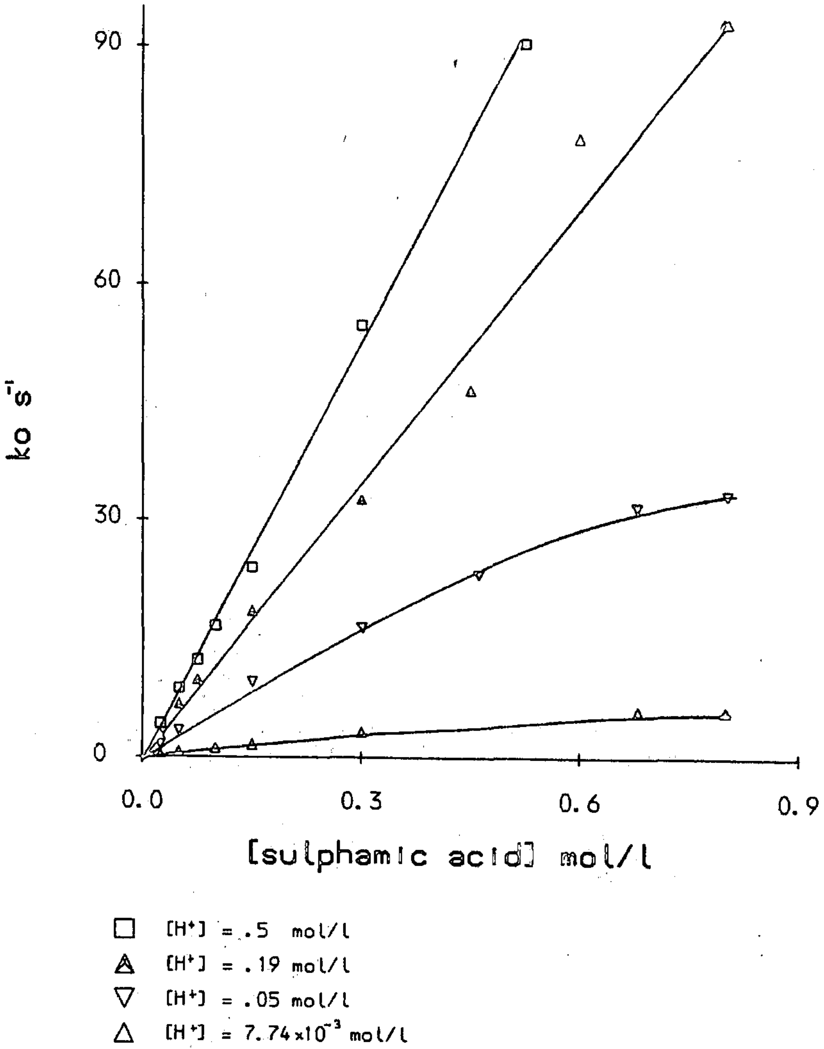


Table 3.17:

Values of slope and intercept from plots of k_o^{-1} against [sulphamic acid]$^{-1}$

$[H^+]$ mol l^{-1}	slope mol l^{-1}s	intercept s
7.74×10^{-3}	$0.0704 \pm 2.2 \times 10^{-3}$	0.0951 ± 0.0383
0.050	$0.0145 \pm 7.6 \times 10^{-5}$	$0.0107 \pm 1.29 \times 10^{-3}$
0.19	7.43×10^{-3}	3.23×10^{-3}
0.50	$5.76 \times 10^{-3} \pm 7.7 \times 10^{-5}$	$1.79 \times 10^{-3} \pm 1.4 \times 10^{-4}$

corresponds to a pKa of 1.0 which is in good agreement with the literature values of 1.1 [9] at 25°C and 0.98 [11] at 0°C.

All the data obtained are consistent with a reaction mechanism where the alkyl nitrite undergoes hydrolysis to nitrous acid which is then responsible for nitrosation. It is possible for the hydrolysis step or the subsequent reaction of nitrous acid to be the rate limiting step under the appropriate conditions.

Further confirmation of this mechanism comes from the effect of added nucleophiles. It is known that the nitrosation of sulphamic acid by nitrous acid is not subject to catalysis by added nucleophiles [9, 11].

Results showing the effect of added chloride ion on ko are shown in Table (3.18). Clearly no catalysis is observed, indicating that the reaction behaves kinetically similarly to that using nitrous acid itself.

Table 3.18:

Effect of added chloride ion on ko at 25°C

[sulphamic acid] = 0.017 mol l^{-1} [$HClO_4$] = 0.507 mol l^{-1}

[^{t}BuOH] = 0.096 mol l^{-1} [^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1}

[NaCl] mol l^{-1}	ko s^{-1}
0	2.83 ± 0.02
0.041	2.89 ± 0.02
0.082	2.86 ± 0.03
0.123	2.83 ± 0.04
0.204	2.87 ± 0.03

At high concentrations of sulphamic acid and at low acidity, under conditions where hydrolysis of the alkyl nitrite is rate limiting, catalysis by added nucleophiles would be expected as the hydrolysis of the alkyl nitrite is known to be catalysed by added nucleophiles [1,2,3]. Results under these conditions are shown in Tables (3.19) and (3.20) for both chloride and bromide ions.

Table 3.19:

Effect of chloride ion at high [sulphamic acid] at 25°C

[^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1} [HClO$_4$] = 7.74 x 10^{-3} mol l^{-1}

[sulphamic acid] = 0.80 mol l^{-1} 370 nm

[NaCl] mol l^{-1}	ko s^{-1}
0.050	6.63 ± 0.19
0.100	5.15 ± 0.26
0.150	5.52 ± 0.15
0.200	5.65 ± 0.14

Table 3.20:

Effect of bromide ion at high [sulphamic acid] at 25°C

[^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1} [HClO$_4$] = 7.74 x 10^{-3} mol l^{-1}

[sulphamic acid] = 0.80 mol l^{-1}

[NaBr] mol l^{-1}	ko s^{-1}
0.050	6.20 ± 0.24
0.100	5.55 ± 0.32
0.150	5.40 ± 0.22
0.200	5.27 ± 0.25

For both anions, k_o decreases slightly on addition of the anion. This is possible due to a salt effect. The effect of added nucleophiles on the denitrosation rate of alkyl nitrites is known to be small [3], much less than that found in the denitrosation of nitrosamines [24,25], but it is a catalytic effect. Catalysis by added chloride and bromide salts in this case may possibly not be observed due to the large errors involved in the values of k_o (due to gas formation) and also due to a salt effect that causes a reduction in the rate.

3.2.2 Reaction with hydrazoic acid

The reaction of ^{t}BuONO with hydrazoic acid (HN_3) was studied at 370 nm, following the disappearance of the alkyl nitrite. The reactions were carried out under conditions where [^{t}BuONO]$\lll$[HN_3] and good first order behaviour was observed in each case. The value of the observed first order rate constant, k_o , was found to decrease slightly on the addition of ^{t}BuOH (Table 3.21), but the effect is within the experimental error. These results are again consistent with the fact that the equilibrium constant for formation of ^{t}BuONO is considerably smaller than it is for ^{i}PrONO.

The reaction was also found to be first order in [HN_3], as shown by the dependence of k_o on [HN_3] at two different acidities (Tables 3.22 and 3.23). The results for $[HClO_4]$ = 0.10 mol l^{-1} are shown in Figure (3.7)

Table 3.21:

Effect of ^{t}BuOH on the rate of nitrosation of HN_3 at 25°C

$[^{t}BuONO] = 1.2 \times 10^{-3}$ mol l^{-1} $[HClO_4] = 0.477$ mol l^{-1}

$[HN_3] = 0.025$ mol l^{-1} 370 nm

$[^{t}BuOH]$ mol l^{-1}	ko s^{-1}
0	3.07 ± 0.05
0.0238	3.04 ± 0.05
0.0477	3.01 ± 0.04
0.0953	2.91 ± 0.05
0.238	2.88 ± 0.04

The first order dependence on $[HN_3]$ means that the rate limiting step must be reaction of nitrous acid with HN_3, although at high $[HN_3]$ there is a slight curvature on the plots of ko against $[HN_3]$, indicating that the hydrolysis of the alkyl nitrite has become partly rate-limiting. By comparison with the reaction of ^{i}PrONO with HN_3 the rate equation (equation 3.28) can be written for this reaction. Again, since the equilibrium constant

Table 3.22

Dependence of ko on $[HN_3]$ at 25°C

$[{}^{t}BuONO] = 1.2 \times 10^{-3}$ mol l^{-1} $[HClO_4] = 0.10$ mol l^{-1}

370 nm

$[HN_3]$ mol l^{-1}	ko s^{-1}
0.020	0.411 ± 0.021
0.040	0.822 ± 0.025
0.060	1.22 ± 0.06
0.080	1.68 ± 0.05
0.100	2.05 ± 0.08

Slope = 20.68 ± 0.34 l $mol^{-1}s^{-1}$

Intercept = $4 \times 10^{-3} \pm 2 \times 10^{-2}$ s^{-1}

Table 3.23:

Dependence of ko on $[HN_3]$ at 25°C

$[{}^{t}BuONO] = 1.2 \times 10^{-3}$ mol l^{-1} $[HClO_4] = 0.50$ mol l^{-1}

370 nm

$[HN_3]$ mol l^{-1}	ko s^{-1}
0.0125	1.77 ± 0.04
0.025	3.26 ± 0.08
0.050	6.19 ± 0.23
0.075	8.62 ± 0.15
0.125	13.2 ± 0.6

$$k_o = \frac{k\ K_{eq}\ [HN_3][H^+]}{(K_{eq} + [{}^tBuOH])} \tag{3.28}$$

for the formation of the alkyl nitrite is very small ($<$ 0.05), the equilibrium constant for hydrolysis of the alkyl nitrite, Keq, will be large so that the inequality Keq $\gg [{}^tBuOH]$ will hold. Therefore equation (3.28) can be simplified to equation (3.29). This predicts

$$k_o = k\,[HN_3][H^+] \tag{3.29}$$

that a plot of ko against $[HN_3]$ will have slope = $k[H^+]$ and so k, the third order rate constant for attack of nitrous acid on hydrazoic acid can be obtained. The values obtained for k from these results are 205 l^2 $mol^{-2}s^{-1}$ at $[HClO_4]$ = 0.10 $mol\,l^{-1}$ and 250 l^2 mol^{-2} s^{-1} at $[HClO_4]$ = 0.50 mol l^{-1} . These are in good agreement with the values found from analysis of the data from the reaction of ${}^iPrONO$ with HN_3 (k = 220 l^2 mol^{-2} s^{-1} at $[HClO_4]$ = 0.10 mol l^{-1} and 300 l^2 mol^{-2} s^{-1} at $[HClO_4]$ = 0.538 mol l^{-1}). Equation (3.29) also predicts that ko should be linear in $[H^+]$. Results showing the dependence of ko on $[H^+]$ are shown in Table (3.24). The results are shown graphically in Figure (3.8).

Figure 3.8

Plot of ko against $[H^+]$ for $[HN_3]$ = .025 mol/l

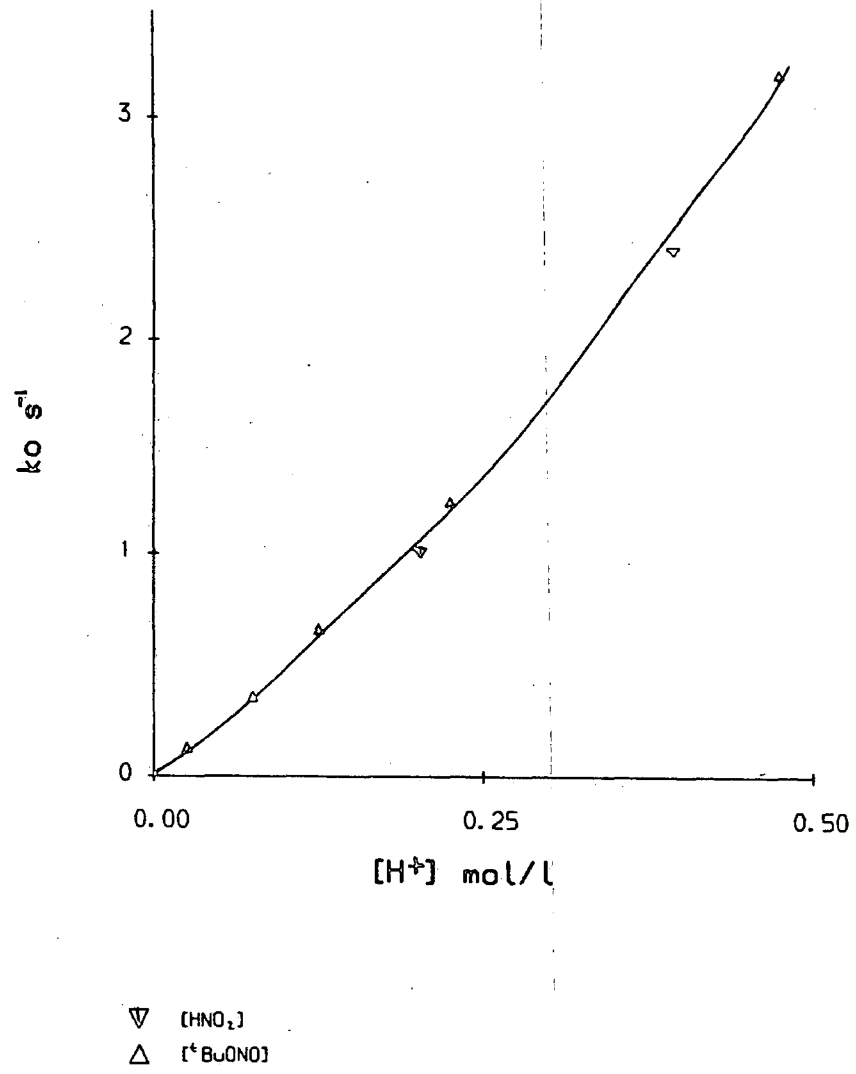


Figure 3.7

Plot of ko against $[HN_3]$ for $[HClO_4]$ =.10 mol/l

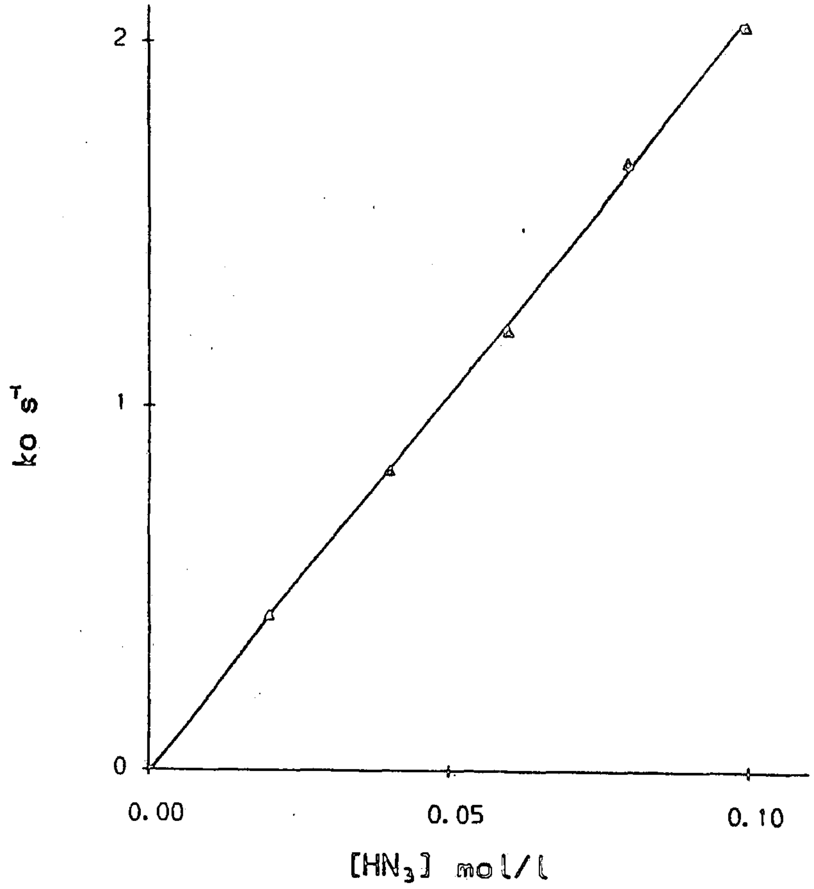


Table 3.24:

Effect of [$HClO_4$] on the rate of nitrosation of HN_3 at 25°C

[^tBuONO] = 1.2×10^{-3} mol l^{-1} [HN_3] = 0.025 mol l^{-1}

370 nm

[$HClO_4$] mol l^{-1}	ko s^{-1}
0.025	0.133 ± 0.004
0.075	0.359 ± 0.009
0.125	0.648 ± 0.013
0.225	1.25 ± 0.05
0.475	3.21 ± 0.04

The dependence of ko on [H^+] is not linear, a plot of ko against [H^+] shows an upward curve. This is exactly the same acid dependence as is found in the nitrosation of HN_3 with nitrous acid [9]. Further, when these results are compared with those obtained from the reaction of nitrous acid with HN_3 (Figure 3.8) there is no difference between them. This is predicted by equation (3.29), which is identical to the rate equation for nitrous acid nitrosation of HN_3. In other words, this means that ^tBuONO is virtually completely hydrolysed to nitrous acid and ^tBuOH before any significant reaction of nitrous acid with the substrate occurs. Indeed, if K, the equilibrium constant for formation of alkyl nitrite is taken to be 0.05 l mol^{-1} and [^{t}BuOH] is typically 0.2 mol l^{-1} the calculated extent of hydrolysis is 95%.

The reaction of ^{t}BuONO with HN_3 (contrasting with the reaction of NH_2SO_3H) was found to be markedly catalysed by added bromide ions. The results are shown in Table (3.25)

Table 3.25:

Catalysis by bromide ions at 25°C

[^{t}BuONO] = 1.2×10^{-3} mol l^{-1} [HN_3] = 0.025 mol l^{-1}

[$HClO_4$] = 0.50 mol l^{-1} 370 nm

[NaBr] mol l^{-1}	k_o s^{-1}
0	3.26 ± 0.08
0.025	16.9 ± 0.6
0.050	31.2 ± 1.3
0.075	44.5 ± 10
0.125	78.9 ± 4.35

Catalysis by halide ions has also been observed in the nitrosation of HN_3 by nitrous acid [9]. If the reaction is assumed to be occurring via attack of nitrosyl bromide on HN_3 and that the alkyl nitrite is almost completely hydrolysed before any reaction with HN_3 occurs then the value of the second order rate constant for attack of NOBr on HN_3 can be obtained as $9.5 \times 10^5 \pm 3 \times 10^4$ $l\ mol^{-1}s^{-1}$. This value compares reasonably well with the two published values [9] of 1.3×10^6 and 2.0×10^6 $l\ mol^{-1}s^{-1}$.

At very low acidity, where there is a substantial concentration of the azide ion (N_3^-), present in solution (pKa of HN_3 = 5), the reaction is zero order in $[N_3^-]$. The results at pH = 6.02 are shown in Table (3.26).

Table 3.26:

Nitrosation of HN_3 in dihydrogen orthophosphate buffer at pH = 6.02 and 25°C

$[{}^tBuONO] = 2 \times 10^{-3}$ mol l^{-1} $[{}^tBuOH] = 0.084$ mol l^{-1}

$[KH_2PO_4] = 0.104$ mol l^{-1} 370 nm

$[N_3^-]$	k_o s^{-1}
0	$2.45 \times 10^{-3} \pm 4.9 \times 10^{-4}$
0.0191	$2.46 \times 10^{-3} \pm 1.8 \times 10^{-4}$
0.0381	3.45×10^{-3}
0.0572	3.39×10^{-3}
0.0762	2.82×10^{-3}
0.0953	2.63×10^{-3}

The value of ko at $[N_3^-] = 0$ represents the rate of hydrolysis of the alkyl nitrite in the buffer to give the nitrite ion. The values of ko quoted are subject to quite large errors (typically ± 5-10%) due to the fact that there was excessive bubble formation occurring during the reaction which caused difficulties in obtaining accurate absorbance values, but even so the value of ko can be seen to be independent of $[N_3^-]$. This means that the rate of reaction under these conditions is governed by the hydrolysis of the alkyl nitrite. There was also an effect on the rate due to the buffer as shown in Table (3.27). The effect is relatively small

Table 3.27

Effect of buffer concentration on the rate of nitrosation of N_3^- at 25°C

$[{}^tBuONO] = 2 \times 10^{-3}$ mol l^{-1} $[N_3^-] = 0.0191$ mol l^{-1}

$[KH_2PO_4]$ mol l^{-1}	ko s^{-1}
0.0518	1.93×10^{-3}
0.0647	1.99×10^{-3}
0.0776	2.65×10^{-3}
0.0906	2.16×10^{-3}
0.104	2.46×10^{-3}

and probably arises due to a salt effect. The limiting value of k_o at $[KH_2PO_4]$ = 0.104 mol l^{-1} of ca 2.5 x 10^{-3} s^{-1} can be extrapolated to zero buffer concentration to give a value of ca 1 x 10^{-3} s^{-1}. This corresponds to a value of k_1, the second order rate constant for the acid catalysed denitrosation of the alkyl nitrite of ca 1000 l $mol^{-1}s^{-1}$ which agrees quite well with values previously obtained. There is no evidence for a direct reaction between the alkyl nitrite or its protonated form and the azide ion.

3.3 Discussion

All the data obtained for the reactions of ^{i}PrONO and ^{t}BuONO with a variety of substrates in aqueous acid solution are consistent with reactions proceeding via the hydrolysis of the alkyl nitrite to give nitrous acid which can then effect nitrosation of the substrate. In both cases the hydrolysis is rapid. In the case of ^{i}PrONO the rate of reaction is decreased on addition of ^{i}PrOH, which can be interpreted in terms of an increase in the concentration of ^{i}PrONO, which is ineffective as a nitrosating agent. In the case of ^{t}BuONO, at low substrate concentrations hydrolysis of the alkyl nitrite occurs almost completely before any reaction with the substrate occurs but at high substrate concentrations the rate depends only on the rate of denitrosation of the alkyl nitrite. There is no evidence for a direct reaction of the alkyl nitrite with any of the substrates used, but the protonated alkyl nitrite must react directly with the solvent (water) and also chloride and bromide ion, which are known to catalyse the hydrolysis [2,3] reaction. This is analogous to the situation found for the reaction of aromatic nitrosamines as nitrosating agents. These have been shown to occur by hydrolysis of the nitrosamine to nitrous acid [24], which can then react with a nitrous acid trap, eg. sulphamic acid. The equilibrium for the denitrosation in this case lies well over to the side of the nitrosamine and the rate of reaction is markedly reduced on addition of the amine. At low concentrations of sulphamic acid the rate of reaction is first order in [sulphamic acid] but at higher concentrations it becomes zero order in [sulphamic acid] indicating that rate limiting denitrosation is occurring. The major difference between the reaction of alkyl nitrites and that of nitrosamines in aqueous acid solution is that the reaction of nitrosamines is markedly catalysed by added nucleophiles [24,25] whereas the reaction of alkyl nitrites is only slightly catalysed by added nucleophiles [3] (chloride and bromide). Indeed nitrosamines have also been shown to react directly with nucleophilic species such as thiols. The difference between the two systems can be explained if the denitrosation of alkyl nitrites by water is a diffusion controlled process. The concentration of water in these solutions is always far in excess of the concentration of the added substrate and so in aqueous solution hydrolysis of the alkyl nitrite would be much faster than the reaction of the alkyl nitrite with the substrate.

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CHAPTER 4

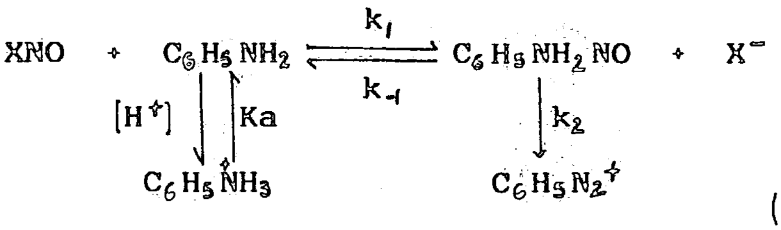
REACTIONS OF ALKYL NITRITES IN ACIDIC ALCOHOL SOLUTION

Alkyl nitrites are frequently used nitrosating agents in both acidic and basic alcohol solutions. The advantages of these procedures over the normal aqueous nitrous acid procedure for nitrosation becomes apparent when the nitrosation of substrates of limited solubility in aqueous solution is required.

In a previous study [1], the alcoholysis of (+) and (-) 1-methylheptyl nitrite was studied in 1-propanol, 1-pentanol and tertiary butanol using various strong acids as catalysts. It was found that perchloric, hydrochloric and methanesulphonic acids were all equally efficient as catalysts at very low concentrations (10^{-4} - 10^{-5} mol l^{-1}), suggesting that all three acids are virtually completely dissociated and that the hydrogen ion is the only significant catalyst. The rate constant for reaction with tertiary butanol was found to be about twice that of the two primary alcohols. This was explained in terms of their being a higher concentration of the protonated alkyl nitrite in the tertiary alcohol than in the primary alcohols, as the nucleophilic power of the alcohols is in the order 1-propanol $\sim$ 1-pentanol $>$ tertiary butanol. Catalysis by added chloride and bromide salts was also observed. In both cases the dependence of the rate constant on [Halide] was not linear but tended to a maximum value. This was explained in terms of a salt effect and a depression of the H^+ concentration due to association of H^+ with halide ion.

In another study [2] the reaction of 1-propyl nitrite in acidic 1-propanol was studied with aniline, N-methylaniline and p-nitroaniline. In the absence of any added nucleophile the reaction was very slow, indicating that the protonated alkyl nitrite was not an effective nitrosating agent of aniline derivatives under the conditions used. In the presence of chloride ion, bromide ion and thiourea the reaction proceeded readily. Here the rate constant was again found to tend towards a limiting value at high concentrations of chloride ion, bromide ion and thiourea and was explained in terms of an equilibrium formation of the nitrosyl halide or nitrosyl thiourea which reacts reversibly with the amine to form the nitrosamine intermediate which then undergoes various reactions involving proton transfer and water loss (for primary nitrosamines) to give the diazonium ion, or in the case of N-methylaniline, proton loss to give the nitrosamine (Scheme 4.1). This has also been found in the diazotization of aniline in methanol [3,4] solutions of HCl and HBr and for diazotizations involving nitrosyl halides in water solvent when electron withdrawing groups are present in the aromatic ring [5].

$$\mathrm{RONO} + \mathrm{H^+} + \mathrm{X^-} \rightleftharpoons \mathrm{ROH} + \mathrm{XNO}$$



$$\begin{tikzcd}[column sep=small] \mathrm{XNO} + & \mathrm{C_6H_5NH_2} \arrow[d, shift right, "{[H^+]}"'] \arrow[r, shift left, "k_1"] & \mathrm{C_6H_5NH_2NO} \arrow[l, shift left, "k_{-1}"] \arrow[d, "k_2"] & + \; \mathrm{X^-} \\ & \mathrm{C_6H_5\overset{+}{N}H_3} \arrow[u, shift right, "Ka"'] & \mathrm{C_6H_5N_2^+} & \end{tikzcd}$$

(4.1)

The aim of the present work is to ascertain whether or not an alkyl nitrite does react directly in acid solution as a nitrosating agent. Two alkyl nitrites were chosen for the study, tertiary butyl nitrite (^{t}BuONO), an example of a tertiary nitrite and isopropyl nitrite, an example of a secondary nitrite. The reaction of each alkyl nitrite was studied in its parent alcohol as solvent with both thiourea and thioglycolic acid.

4.1 Reaction of tertiary butyl nitrite in tertiary butanol

4.1.1 Nitrosation of thiourea

Thiourea [6], and indeed alkyl thioureas in general, are known to undergo a rapid and reversible S-nitrosation reaction in aqueous acidic solutions of nitrous acid as shown in equation (4.2).

$$\overset{K}{H^+ + (NH_2)_2C{=}S + HNO_2 \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (NH_2)_2C{=}\overset{+}{S}{-}NO + H_2O} \qquad (4.2)$$

The values of k_1, the third order rate constant for attack of nitrous acid, and k_{-1}, the first order rate constant for hydrolysis of S-nitrosothiourea and K, the equilibrium constant for formation of S-nitrosothiourea are known and are shown in table (4.1)

Table 4.1:
Values of k_1, k_{-1} and K at 25°C

$k_1 = 6960\ l^2\ mol^{-2}\ s^{-1}$

$k_{-1} = 1.39\ s^{-1}$

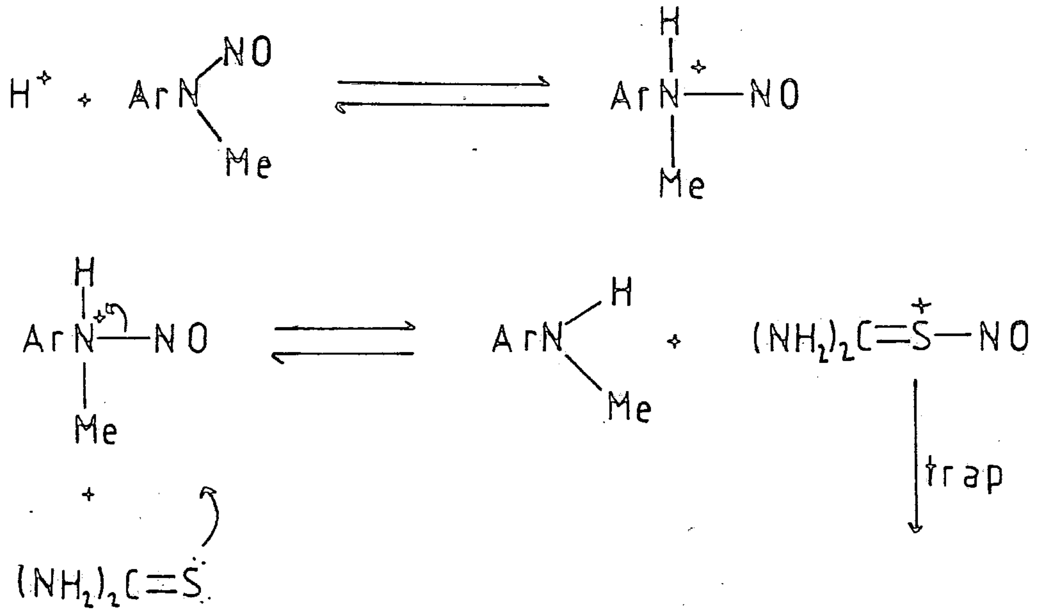
$K = 5000\ l^2\ mol^{-2}$

The product S-nitrosothiourea is unstable, decomposing according to equation (4.3) [7].

$$2(NH_2)_2C{=}\overset{+}{S}{-}NO \longrightarrow (NH_2)_2C{=}\overset{+}{S}{-}\overset{+}{S}{=}C(NH_2)_2 + 2NO \tag{4.3}$$

S-nitrosothiourea can also act as a nitrosating agent with many substrates including amines, thiols and ketones. This is usually shown by a marked catalytic effect of the addition of thiourea [8, 9, 10] in the reaction using nitrous acid. The S-nitrosothiourea ion is markedly less reactive than the nitrosyl halides, but the catalytic effect of thiourea is much more pronounced than the effect of chloride and bromide ion, due to the large equilibrium constant for its formation.

Thiourea has also been shown to catalyse the denitrosation of nitrosamines in acid solution [11, 12]. Here the reaction is believed to occur via nucleophilic attack of thiourea on the protonated nitrosamine (Scheme 4.4). The catalytic effect of thiourea is much more marked than that of Br^- and Cl^-, and there is a direct correlation between the rate of reaction with the nitrosamine and the nucleophilicity of the attacking species as defined by n, the Pearson nucleophilicity factor. This reaction is of course the reverse of that of the nitrosation of amines using thiourea as catalyst.



Scheme (4.4)

The reaction of tertiary butyl nitrite (^{t}BuONO) with thiourea was followed at 420 nm, where only the S-nitrosothiourea absorbs. All reactions were carried out at 30°C. Under the conditions used with [thiourea] $\gg$ [^{t}BuONO], good first order behaviour was observed in all cases.

The variation of the observed first order rate constant, k_o , with the concentration of thiourea was studied at two different concentrations of sulphuric acid. The results are shown in Table (4.2) and graphically in Figure (4.1).

Table 4.2:

Variation of k_o with [thiourea] at 30°C

$[{}^tBuONO] = 1 \times 10^{-3}$ mol l^{-1}

[thiourea] mol l^{-1}	k_o s^{-1} a	k_o s^{-1} b
0.012	$0.156 \pm 6 \times 10^{-3}$	$0.209 \pm 5 \times 10^{-3}$
0.024	$0.203 \pm 2 \times 10^{-3}$	$0.319 \pm 6 \times 10^{-3}$
0.036	0.301 ± 0.013	$0.406 \pm 3 \times 10^{-3}$
0.048	0.296 ± 0.014	$0.467 \pm 6 \times 10^{-3}$
0.060	0.314 ± 0.021	$0.530 \pm 9 \times 10^{-3}$

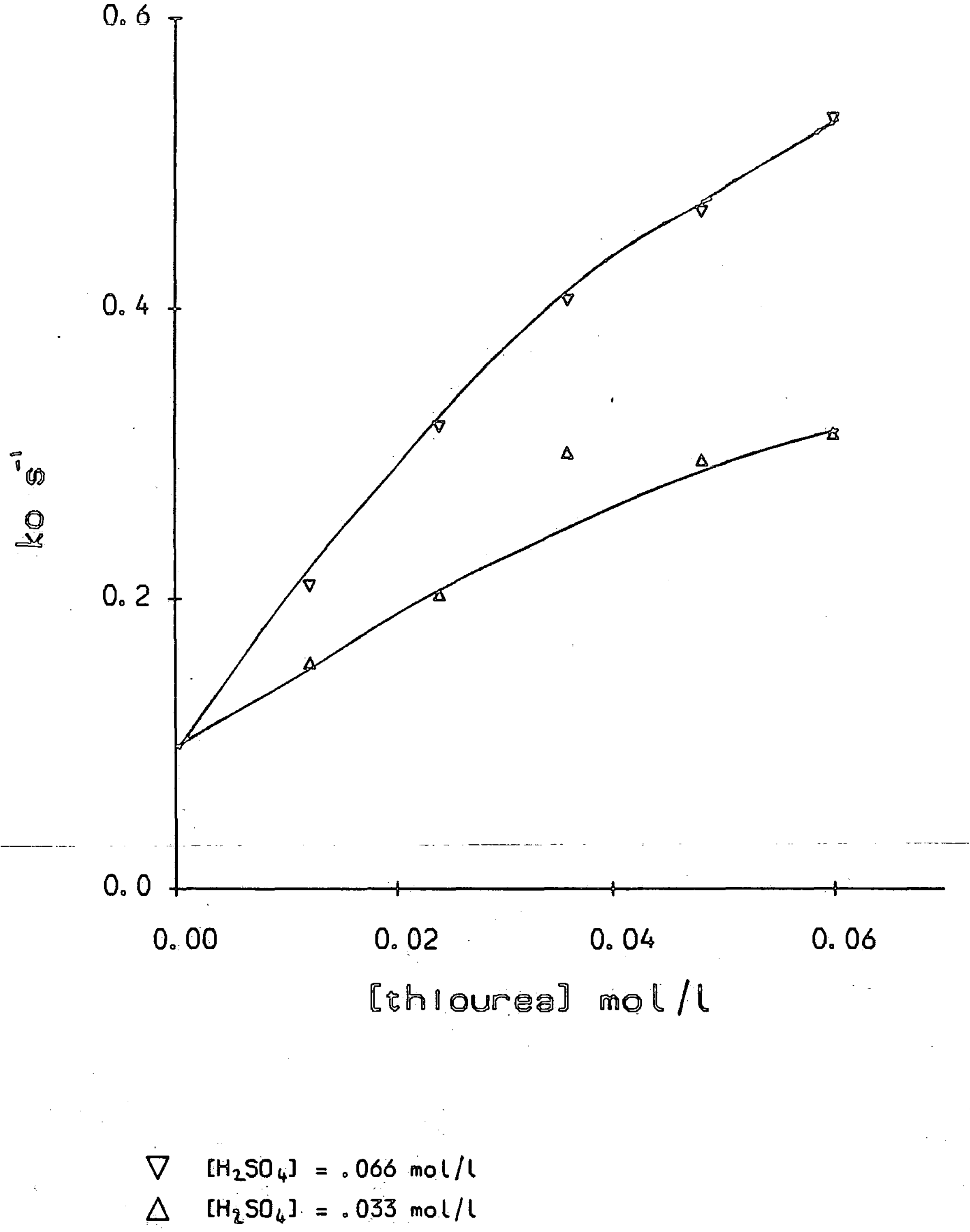
a) $[H_2SO_4] = 0.033$ mol l^{-1}

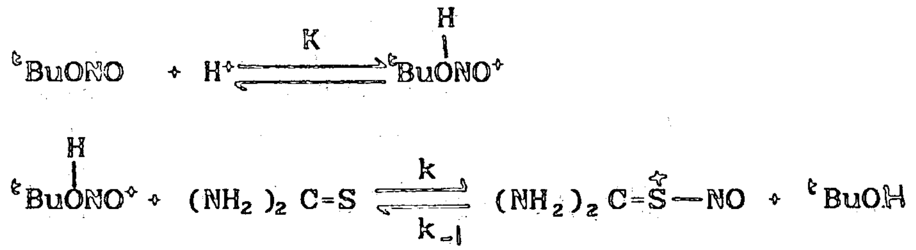
b) $[H_2SO_4] = 0.066$ mol l^{-1}

The plots of k_o against [thiourea] give curves with common positive intercepts. The common intercept at the two different acidities can be explained if there is a simple equilibrium reaction between the protonated alkyl nitrite and thiourea. This is analogous to the reaction found in aqueous solution between thiourea and nitrous acid and is shown in Scheme (4.5)

Figure 4.1

Variation of ko with [thiourea]





$$ {}^{t}BuONO + H^{+} \underset{}{\overset{K}{\rightleftharpoons}} {}^{t}Bu\overset{H}{\overset{|}{O}}NO^{+} $$

$$ {}^{t}Bu\overset{H}{\overset{|}{O}}NO^{+} + (NH_2)_2C{=}S \underset{k_{-1}}{\overset{k}{\rightleftharpoons}} (NH_2)_2C{=}\overset{+}{S}{-}NO + {}^{t}BuOH \qquad (4.5) $$

The observed first order rate constant for such a scheme is equation (4.6)

$$ k_o = k_1[H^+][(NH_2)_2CS] + k_{-1} \qquad (4.6) $$

Equation (4.6) predicts that a plot of k_o against [thiourea] should give a straight line with slope = $k_1[H^+]$ and intercept = k_{-1}. This means that the slopes of such plots should increase with increasing acidity, but the intercepts should be independent of acidity. Equation (4.6) also predicts that the plots should be linear, whereas the experimental results show a substantial curvature, tending towards a limiting value of ko . A similar curvature is also found in the variation of ko with $[H_2SO_4]$. The results are shown in Table (4.3), and graphically in Figure (4.2). Equation (4.6) also predicts that a plot of k_o against $[H^+]$ should be linear with a positive intercept corresponding to k_{-1}. The data in Table (4.3) show marked curvature in a plot of k_o against $[H_2SO_4]$, reaching a limiting value of k_o at high $[H_2SO_4]$. This ~~easy~~ can be explained if there is a

Table 4.3:

Variation of ko with $[H_2SO_4]$ at 30°C

$[{}^tBuONO] = 1$ x 10^{-3} mol l^{-1} $\quad$ [thiourea] = 0.015 mol l^{-1}

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}	$[H_2SO_4]^{-1}$ l mol^{-1}	$(ko-0.06)^{-1}$ s
0.0264	0.156 ± 0.003	37.9	10.36
0.0396	0.186 ± 0.007	25.3	7.88
0.0528	0.222 ± 0.015	18.9	6.11
0.1056	0.279 ± 0.005	9.47	4.51
0.1584	0.305 ± 0.005	6.31	4.02
0.2111	0.328 ± 0.005	4.74	3.67
0.2639	0.341 ± 0.006	3.79	3.50

Figure 4.3

Double reciprical plot for nitrosation of thiourea

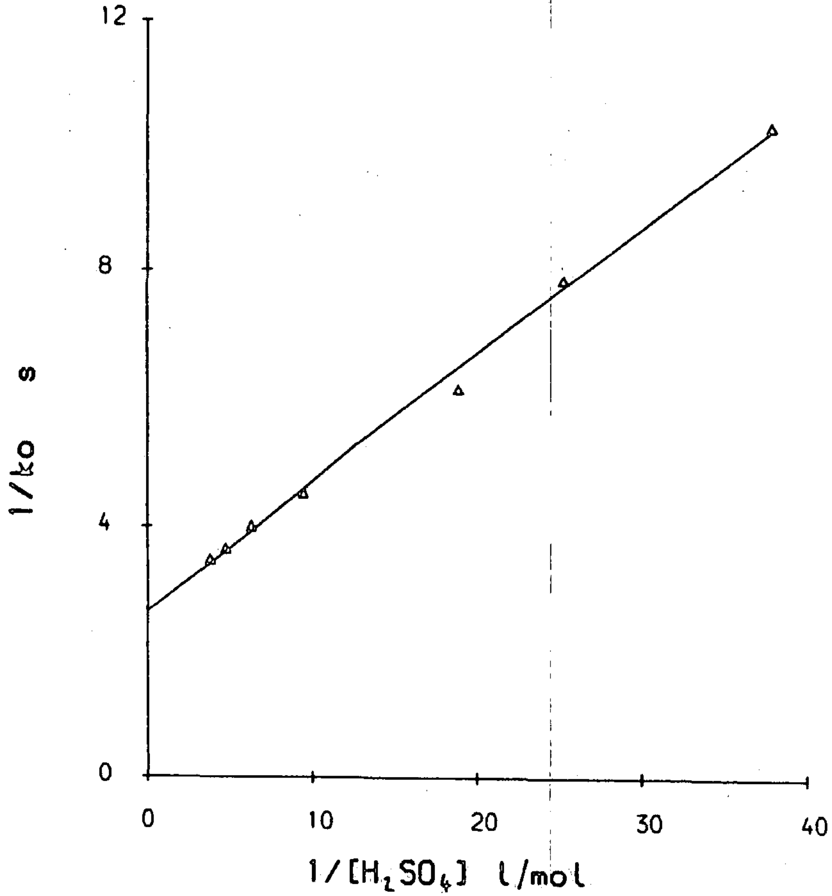
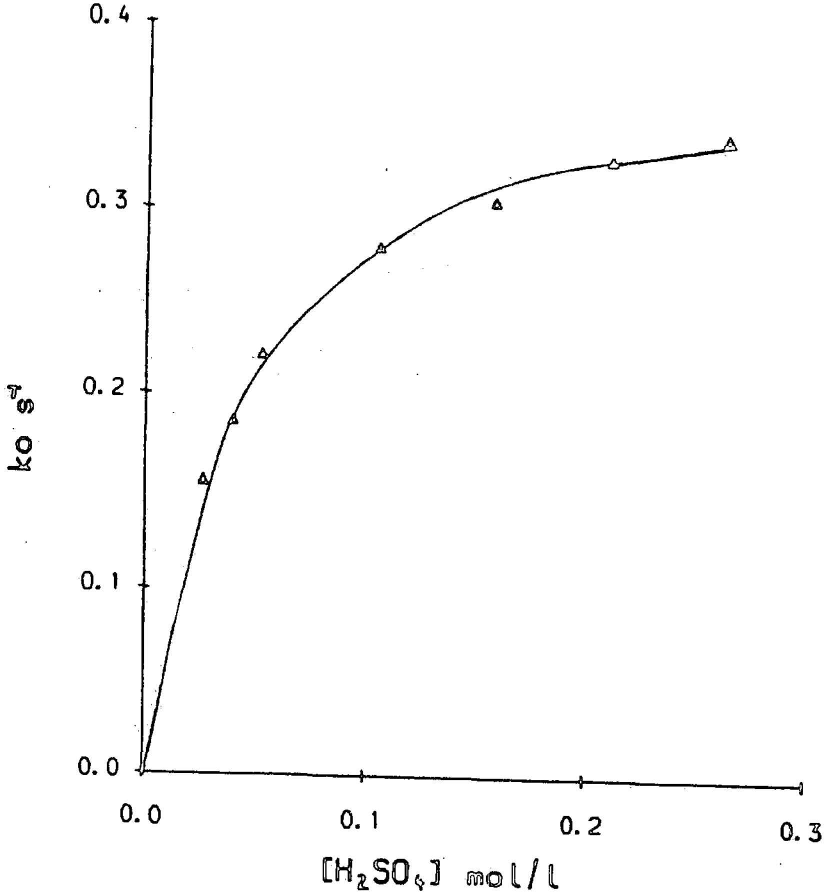
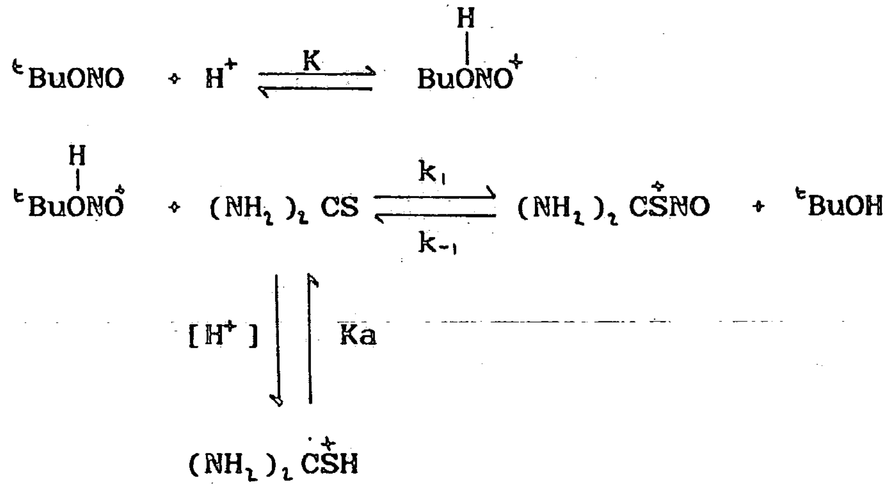


Figure 4.2

Variation of ko with [H$_2$SO$_4$]



significant degree of protonation of thiourea under these conditions which would lower the effective concentration of both H_2SO_4 and thiourea. In water the pKa of protonated thiourea is known to be -1.19 and protonation is believed to occur on sulphur [13,14,15]. The pKa values for meta and para substituted phenyl thioureas have been found to be larger in methanol [16] than those found in water by about 4 pKa units. If a similar trend occurs in this case then the pKa of thiourea in ${}^tBuOH$ will be around 3 and so a substantial amount of protonation would be expected in these solutions. The modified reaction scheme (Scheme 4.7), allowing for protonation of thiourea, allows the equation for ke to be derived (equation 4.8).



$$ {}^tBuONO + H^+ \underset{}{\overset{K}{\rightleftharpoons}} Bu\overset{H}{O}NO^+ $$

$$ {}^tBu\overset{H}{O}N\overset{+}{O} + (NH_2)_2CS \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} (NH_2)_2\overset{+}{C}SNO + {}^tBuOH $$

$$ (NH_2)_2CS \underset{Ka}{\overset{[H^+]}{\rightleftharpoons}} (NH_2)_2\overset{+}{C}SH \qquad (4.7) $$

$$ k_o = k_1[(NH_2)_2CS][H^+] + k_{-1} $$

$$ \text{but } Ka = \frac{[(NH_2)_2CS][H^+]}{[(NH_2)_2\overset{+}{C}SH]} $$

and the total thiourea concentration,

$$[(NH_2)_2CS]_T = [(NH_2)_2CS] + [(NH_2)_2C\overset{+}{S}H]$$

$$\text{so } [(NH_2)_2CS] = \frac{[(NH_2)_2CS]_T\,Ka}{Ka + [H^+]}$$

$$\text{so } k_o = \frac{k_1 Ka\,[(NH_2)_2CS]_T[H^+]}{Ka + [H^+]} + k_{-1} \qquad (4.8)$$

Equation (4.8) predicts that at high $[H^+]$ a plot of k_o against $[H^+]$ should be independent of $[H^+]$ if $[H^+] \gg Ka$, the limiting value of $k_o = k_1 Ka[(NH_2)_2CS]_T + k_{-1}$. From the plots of k_o against [thiourea] (Figure 4.1) a value of k_{-1} of ca 0.06 s^{-1} can be estimated. Equation (4.8) predicts that a plot of $(k_o - 0.06)^{-1}$ against $[H^+]^{-1}$ should give a straight line with slope = $(k_1[(NH_2)_2CS]_T)^{-1}$ and intercept = $(k_1\ Ka\ [(NH_2)_2CS]_T)^{-1}$. The actual hydrogen ion concentration is unknown for sulphuric acid in ^tBuOH, but a plot of $(k_o - 0.06)^{-1}$ against $[H_2SO_4]^{-1}$ gave a reasonable straight line (Figure 4.3) with slope = 0.201 ± 0.006 mol l^{-1} s and intercept = 2.61 ± 0.12s The ratio of slope / intercept gives Ka for thiourea. The value of Ka obtained = 0.075 ± 0.004 mol l^{-1}, therefore pKa = 1.12 . This value can only be considered a very approximate one as it was obtained from an estimate of the value of k_{-1} and of the hydrogen ion concentration. The value of Ka can now be used to correct the data in Table (4.2) for protonation of thiourea.

Let A = total concentration of thiourea added

B = total concentration of acid added (assumed to be equal to the total hydrogen ion concentration)

and at equilibrium we have x mol l^{-1} of $(NH_2)_2\overset{+}{C}SH$

then
$$Ka = \frac{(A - x)\ (B - x)}{x}$$

or
$$x^2 - (A + B + Ka)\ x + AB = 0 \qquad (4.9)$$

The value of A, B and Ka are known, so equation (4.9) can be solved for x, which is also equivalent to the amount of acid that is effectively removed from the solution. Equation (4.8) predicts that at a given acid concentration the values of ko at two different thiourea concentrations are related by equation (4.10). Also, from the variation of ko with $[H_2SO_4]$, the value of k_o for $[(NH_2)_2CS]_T = 0.015$ mol l^{-1} at any acid concentration can be calculated from equation (4.11).

$$\frac{(k_o' - 0.06)}{(k_o - 0.06)} = \frac{[(NH_2)_2CS]_T'}{[(NH_2)_2CS]_T} \qquad (4.10)$$

$$(k_o - 0.06) = 0.201\,[H_2SO_4]^{-1} + 2.61 \qquad (4.11)$$

writing a = $(k_o - 0.06)$ as the rate constant, corrected for a reduction in acidity at the experimental thiourea concentration.

b = $(k_o - 0.06)$ as the observed rate constant ie. the rate constant at the actual acidity of the solution

c = $(k_o - 0.06)$ as the rate constant at the apparent acid concentration (0.066 or 0.033 mol l^{-1}) as calculated from equation (4.11) for thiourea = 0.015 mol l^{-1}

d = $(k_o - 0.06)$ as the rate constant at the actual acidity of the solution calculated from equation (4.11) for thiourea = 0.015 mol l^{-1}.

From equation (4.10), $\frac{a}{c} = \frac{b}{d}$, so that the value of a, hence the corrected k_o can be calculated. The results of such analysis are shown in Table (4.4) and (4.5).

Both sets of data now give linear plots of k_o(corrected) against [thiourea]$_T$ (figure 4.4). The slopes of the plots clearly depend on the $[H_2SO_4]$ but the intercepts are independent of $[H_2SO_4]$ within the experimental error. The intercept corresponds to the value of k_{-1}, the rate constant for the alcoholysis of S-nitrosothiourea. The average value of k_{-1} is 0.107 ± 0.016 s^{-1}. Equation (4.8) predicts that the slope = $k_1 Ka[H^+]/(Ka + [H^+])$. The value of k_1 can be estimated from the slope, assuming $[H^+] \simeq [H_2SO_4]$ and Ka = 0.075 mol l^{-1}. For $[H_2SO_4]$ = 0.033 mol l^{-1}, k = 245 l^2 mol^{-2} s^{-1} and for $[H_2SO_4]$ = 0.066 mol l^{-1}, k = 259 l^2 mol^{-2} s^{-1}. The value of k_1 can also be obtained from the limiting value of k_o from the variation of k_o with $[H_2SO_4]$, since k_o(limiting) = $k_1 Ka\ [(NH_2)_2CS]_T + k_{-1}$. Using k_o(limiting) = 0.34 s^{-1} and k_{-1} = 0.107 s^{-1}, the value of k_1 obtained is 207 l^2 mol^{-2} s^{-1}, which is in reasonable agreement with the two values obtained before. The average value of k_1 is therefore 237 ± 22 l^2 mol^{-2} s^{-1}. Using these values of k_1 and k_{-1} the equilibrium constant for formation of S-nitrosothiourea can be calculated since $K = k_1/k_{-1}$ = 2215 ± 390 l^2 mol^{-2}. This appears to be a reasonable

Table 4.4:

Corrected values of ko for [H_2SO_4] = 0.033 mol l^{-1}

[thiourea] mol l^{-1}	x mol l^{-1}	[H_2SO_4]actual mol l^{-1}	b s^{-1}	c s^{-1}	d s^{-1}	a s^{-1}	ko corrected s^{-1}
0.012	3.4×10^{-3}	0.0296	0.096	0.115	0.106	0.105	0.164
0.024	6.3×10^{-3}	0.0267	0.143	0.115	0.0986	0.167	0.227
0.036	8.8×10^{-3}	0.0242	0.241	0.115	0.0916	0.303	0.363
0.048	0.0109	0.0221	0.236	0.115	0.0854	0.318	0.378
0.060	0.0128	0.0202	0.254	0.115	0.0796	0.327	0.427

slope = 5.62 + 0.26 l mol^{-1} s^{-1}

intercept = 0.0956 ± 0.0105 s^{-1}

Table 4.5:

Corrected values of ko for [H_2SO_4] = 0.066 mol l^{-1}

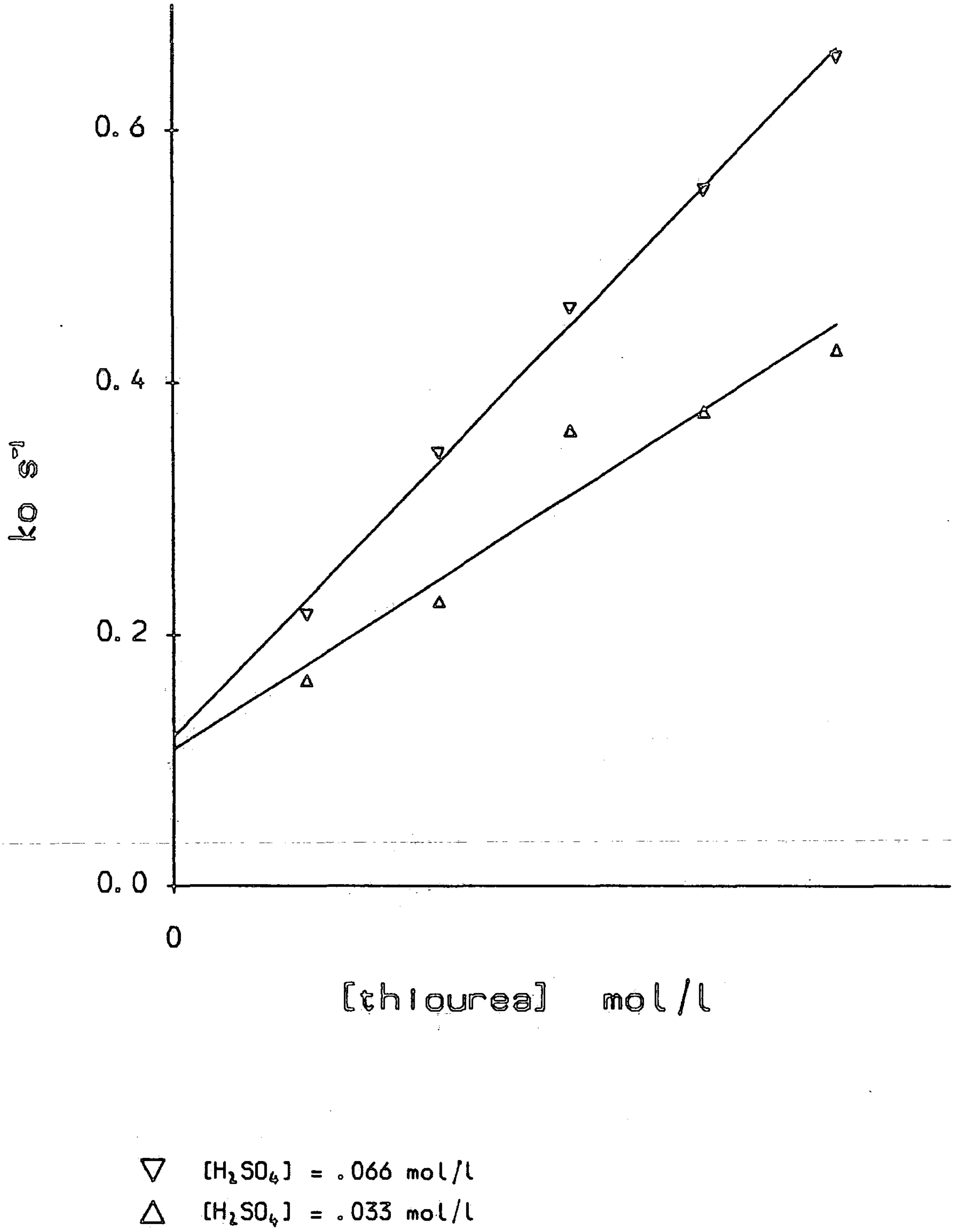
[thiourea] mol l^{-1}	x mol l^{-1}	[H_2SO_4]actual mol l^{-1}	b s^{-1}	c s^{-1}	d s^{-1}	a s^{-1}	ko corrected s^{-1}
0.012	5.4×10^{-3}	0.0606	0.149	0.177	0.169	0.156	0.216
0.024	0.0102	0.0558	0.259	0.177	0.161	0.285	0.345
0.036	0.0146	0.0514	0.346	0.177	0.153	0.400	0.460
0.048	0.0186	0.0474	0.407	0.177	0.146	0.493	0.553
0.060	0.0221	0.0439	0.470	0.177	0.139	0.598	0.658

slope = 9.10 ± 0.32 l mol^{-1} s^{-1}

intercept = 0.118 ± 0.012 s^{-1}

Figure 4.4

Plot of corrected ko against [thiourea]



value as the corresponding value in aqueous solution between nitrous acid and thiourea is 5000 l^2 mol^{-2} [6]. This means that the approximation used of $[H^+] \simeq [H_2SO_4]$ must be valid since the equilibrium involves the acid concentration term. The dissociation constants of hydrochloric and hydrobromic acid in tertiary butanol have been measured previously [17]. The overall acid-base equilibrium in ^{t}BuOH, and indeed in non-aqueous solvents in general, is complicated by ion-pairing and ion association. This arises due to the poor solvation of certain ions by solvents of low polarity. Some of the important species found in dilute solution of HCl or HBr in ^{t}BuOH are shown in Scheme (4.12), and the various equilibrium constants are shown in Table (4.6).

$$
\begin{aligned}
HX &\xrightleftharpoons{K_d} H^+ + X^- \\
HX + X^- &\xrightleftharpoons{K^f(HX_2^-)} HX_2^- \\
HX + H^+ &\xrightleftharpoons{K^f(H_2X^+)} H_2X^+ \\
3HX &\xrightleftharpoons{K^d(3HX)} H_2X^+ + HX_2^-
\end{aligned}
\qquad (4.12)
$$

It can be seen that the minor species in these solutions is going to be the H^+ ion or more correctly the H^+ ion

Table 4.6:

Values of equilibrium constants of hydrogen halides in BuOH at 25°C

		HCl	
^{i}PrOH	pKd = 3.10		K^f (HX_2^-) 0
^{t}BuOH	pKd = 5.5	K^f (HX_2^-) = 7	K^f (H_2X^+) = 8
		HBr	
^{i}PrOH	pKd = 2.0		
^{t}BuOH	pKd = 5.0	K^f (HX_2^-)=2.0	K^f (H_2X^+)=1.6

solvated by ^{t}BuOH, in fact the major species will be the free undissociated acid. By analogy with results in other solvents [18], it can be expected that H_2SO_4 will behave similarly in ^{t}BuOH to the hydrogen halides and so the major species present will be undissociated H_2SO_4. The acid catalysis could be explained if general acid catalysis is occuring, ie. H_2SO_4 is the actual acid catalyst rather than the solvated proton. This point will be discussed further in section 4.5.

4.1.2 Nitrosation of thioglycolic acid by tertiary butyl nitrite in tertiary butanol at 30°C

The nitrosation of thioglycolic acid is known to occur on sulphur in aqueous acid solution to form S-nitrosothioglycolic acid [19]. The sulphur atom of thioglycolic acid, and of thiols generally, is expected to be much less nucleophilic than the sulphur atom of thiourea [20], and so it is of interest to see if a direct reaction between the thiol and alkyl nitrite occurs in tertiary butanol.

The reactions were carried out at 30°C. Under the conditions used, with $[\mathrm{TGA}] \gg [{}^{t}\mathrm{BuONO}]$ good first order behaviour was obtained in all cases by following the appearance of the thionitrite at 330 nm. The observed first order rate constant, k_o, was found to be first order in [TGA] (Table 4.7) and also was strictly first order in $[H_2SO_4]$ over the acid range studied (Table 4.8 and Figure 4.5).

The results are consistent with a direct reaction between the protonated alkyl nitrite and the sulphur atom of TGA (Scheme 4.13). The derived rate equation is given in equation (4.14). The strict first order behaviour of k_o upon $[H_2SO_4]$ indicates that there is no significant protonation of the sulphur atom occuring in these solutions.

Table 4.7:

Variation of k_o with [TGA] at 30°C

[^{t}BuONO] = 2.5×10^{-4} mol l^{-1} [H_2SO_4] = 0.1014 mol l^{-1}

330 nm

[TGA] mol l^{-1}	k_o s^{-1}
0.010	$8.02\times10^{-3} \pm 3.3\times10^{-4}$
0.020	$0.0153 \pm 9 \times 10^{-4}$
0.030	$0.0209 \pm 9 \times 10^{-4}$
0.040	$0.0283 \pm 1.0 \times 10^{-3}$
0.050	$0.0367 \pm 9 \times 10^{-4}$
0.060	$0.0434 \pm 3 \times 10^{-4}$

slope = 0.710 ± 0.018 l $mol^{-1}s^{-1}$

intercept = $6 \times 10^{-4} \pm 7 \times 10^{-4}$ s^{-1}

Table 4.8:

Variation of k_o with [H_2SO_4] at 30°C

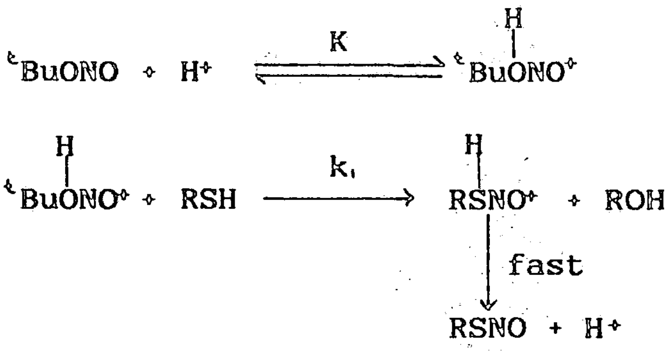
[^{t}BuONO] = 2.5×10^{-4} mol l^{-1} [TGA] = 0.020 mol l^{-1} 330 nm

[H_2SO_4] mol l^{-1}	k_o s^{-1}
0.0203	$3.43 \times 10^{-3} \pm 7 \times 10^{-5}$
0.0406	$6.41 \times 10^{-3} \pm 2.4 \times 10^{-4}$
0.0608	$0.0100 \pm 3.9 \times 10^{3}$
0.0811	$0.0136 \pm 1 \times 10^{-4}$
0.1014	$0.0153 \pm 9 \times 10^{-4}$
0.1217	$0.0201 \pm 9 \times 10^{-4}$

(Table 4.8 cont.)

slope = 0.160 ± 8 x 10^{-3} l $mol^{-1}s^{-1}$

intercept = 1 x 10^{-4} ± 6 x 10^{-4} s^{-1}



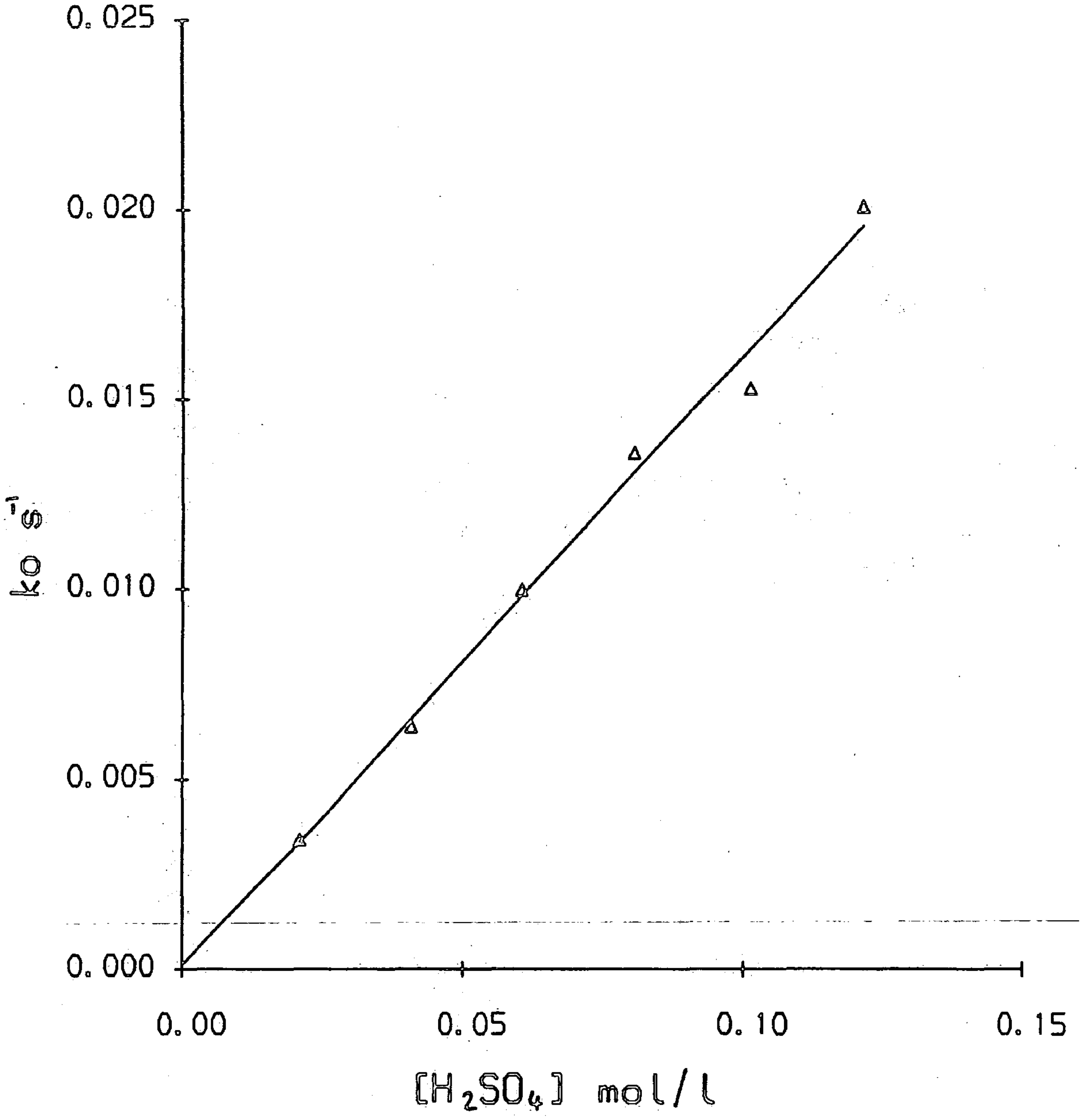
$$\begin{aligned} &{}^{t}\mathrm{BuONO} + \mathrm{H}^{+} \overset{K}{\rightleftharpoons} {}^{t}\mathrm{Bu}\overset{\mathrm{H}}{\mathrm{O}}\mathrm{NO}^{+} \\ &{}^{t}\mathrm{Bu}\overset{\mathrm{H}}{\mathrm{O}}\mathrm{NO}^{+} + \mathrm{RSH} \xrightarrow{k_1} \mathrm{R}\overset{\mathrm{H}}{\mathrm{S}}\mathrm{NO}^{+} + \mathrm{ROH} \\ &\qquad\qquad\qquad\qquad \downarrow \text{fast} \\ &\qquad\qquad\qquad\qquad \mathrm{RSNO} + \mathrm{H}^{+} \end{aligned} \tag{4.13}$$

$$k_o = k_1 [TGA][H^+] \tag{4.14}$$

Equation (4.14) predicts that a plot of k_o against $[H^+]$ should have slope = k_1 [RSH] and a plot of k_o against [RSH] should have slope = k_1 $[H^+]$. Assuming that $[H^+] \simeq [H_2SO_4]$ then the values of k_1 can be obtained of 7 and 8 $l^2\,mol^{-1}\,s^{-1}$ respectively. These values of k_1 are considerably smaller than the value found for thiourea, as expected from the relative nucleophilicities of the two substrates.

Figure 4.5

Plot of ko against $[H_2SO_4]$ for nitrosation of TGA



4.2 Reactions of isopropyl nitrite in isopropanol

4.2.1 Nitrosation of thiourea

The reaction of isopropyl nitrite (^{i}PrONO) with thiourea was followed at 420 nm, where only the S-nitrosothiourea absorbs. All reactions were carried out at 30°C. Under the conditions used with [thiourea] $\gg$ [^{i}PrONO], good first order behaviour was observed in all cases. Results showing the variation of the observed first order rate constant, k_o , with [thiourea] are shown in Table (4.9) and Figure (4.6). The plot of k_o against

Table 4.9:

Variation of k_o with [thiourea] at 30°C

[^{i}PrONO] = 1.2×10^{-3} mol l^{-1} [H_2SO_4] = 0.117 mol l^{-1}

[thiourea] mol l^{-1}	k_o s^{-1}
0.0162	$0.249 \pm 7 \times 10^{-3}$
0.0323	$0.368 \pm 6 \times 10^{-3}$
0.0485	0.484 ± 0.012
0.0647	0.585 ± 0.012
0.0809	0.653 ± 0.026
0.0970	0.723 ± 0.011

[thiourea] was slightly curved with a positive intercept. The value of k_o was also found to be independent of $[H_2SO_4]$ at high $[H_2SO_4]$ (Table 4.10 and Figure 4.7), indicating that under these conditions a significant amount of protonation of thiourea is occuring. From the plot of k_o against [thiourea] (Figure 4.6), the value of k_{-1}, the rate constant for the reaction of S-nitrosothiourea with the solvent, can be estimated as ca. 0.13 s^{-1}. The value of pKa of protonated thiourea

Table 4.10:

Variation of k_o with $[H_2SO_4]$ at 30°C

[thiourea] = 0.0186 mol l^{-1} $[{}^iPrONO]$ = 1.2×10^{-3} mol l^{-1}

$[H_2SO_4]$mol l^{-1}	k_o s^{-1}	$[H_2SO_4]^{-1}$ l mol^{-1}	$(k - 0.13)^{-1}$s
0.0140	0.192 ± 0.017	71.4	16.1
0.0234	0.228 ± 0.019	42.7	10.2
0.0468	0.274 ± 6×10^{-3}	21.4	6.9
0.0936	0.330 ± 5×10^{-3}	10.7	5.0
0.1404	0.317 ± 3×10^{-3}	7.12	5.4
0.1872	0.330 ± 5×10^{-3}	5.34	5.0
0.2340	0.323 ± 0.012	4.27	5.2

Figure 4.7

Plot of ko against $[H_2SO_4]$

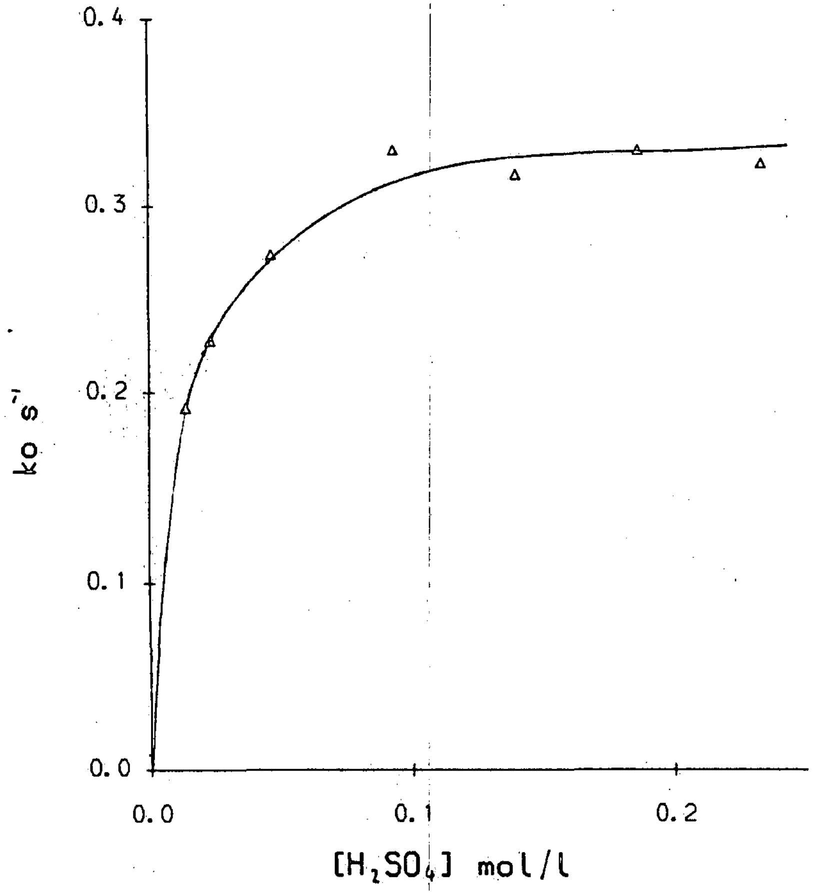
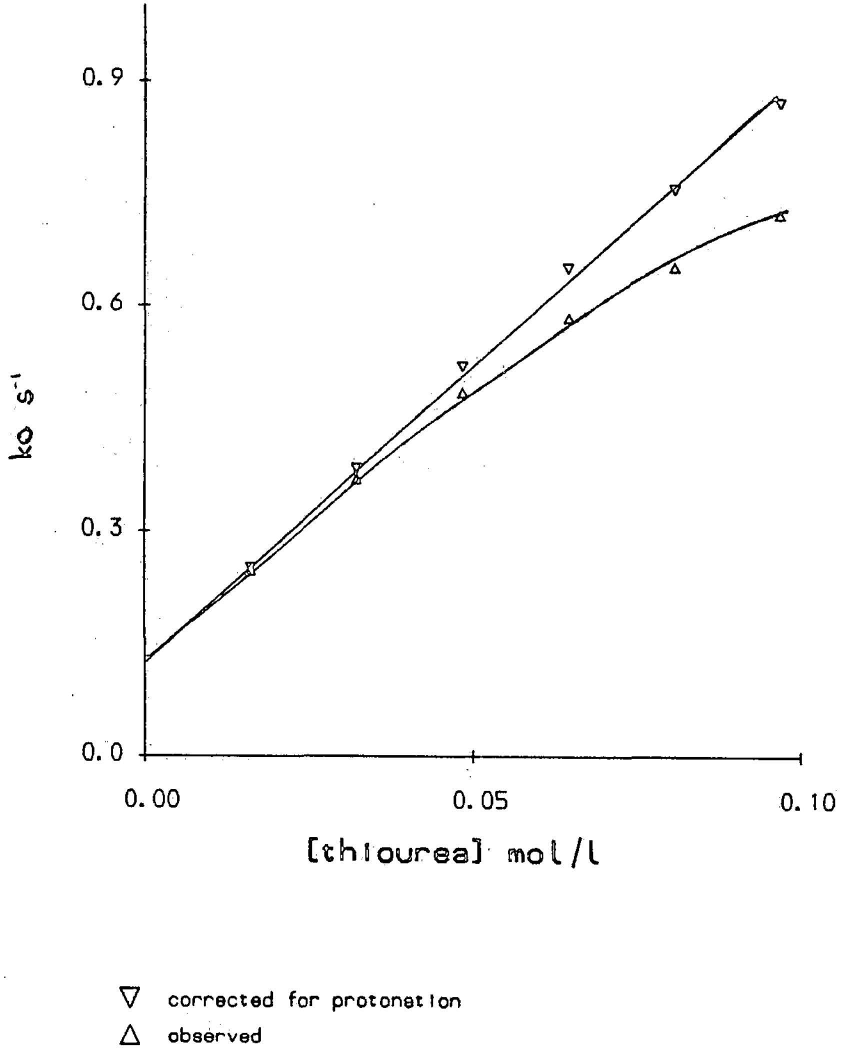


Figure 4.6

Plot of ko against [thiourea] for reaction with $^{i}PrONO$



in this solvent can then be calculated from a plot of $(k - 0.13)^{-1}$ against $[H_2SO_4]^{-1}$. The plot has slope = 0.164 ± 0.010 mol l^{-1} s and intercept = 3.88 ± 0.33 s. The value of Ka can be calculated as 0.0422 ± 0.0044 mol l^{-1} (pKa = 1.38). The value of Ka can then be used to 'correct' the values of k_o in a similar way to before. The corrected values of k_o are shown in Table (4.11).

A plot of k_o corrected against [thiourea] (Figure 4.6) gave a good straight line with slope = 7.69 ± 0.18 l $mol^{-1}s^{-1}$ and intercept = 0.13 ± 0.011 s^{-1}. The value of k_1 obtained from the slope = 248 l^2 mol^{-2} s^{-1}. The value of k_{-1} = 0.130 ± 9 x 10^{-3} s^{-1}, so the equilibrium constant for formation of S-nitrosothiourea = 1823 l^2 mol^{-2}. All these values are reasonably similar to those found for the reaction with ^{t}BuONO in ^{t}BuOH.

4.2.2 Nitrosation of thioglycolic acid

The reactions were again carried out at 30°C. In all cases good first order behaviour was observed under the conditions used ($[TGA] \gg [^iPrONO]$), by following the appearance of S-nitrosothioglycolic acid at 330 nm. The reaction was found to be first order in [TGA] (Table 4.12), with slope = 1.42 ± 0.07 l mol^{-1} s^{-1} and zero intercept. Assuming that the reaction is analogous to

Table 4.11:

Corrected values of ko for $[H_2SO_4]$ = 0.117 mol l^{-1}

$[thiourea]_T$ mol l^{-1}	x mol l^{-1}	$[H_2SO_4]$actual mol l^{-1}	b s^{-1}	c s^{-1}	d s^{-1}	a s^{-1}	ko corrected s^{-1}
0.0162	0.0116	0.1054	0.119	0.189	0.184	0.122	0.252
0.0323	0.0223	0.0947	0.238	0.189	0.178	0.253	0.382
0.0485	0.0323	0.0847	0.354	0.189	0.172	0.389	0.519
0.0647	0.0421	0.0749	0.455	0.189	0.165	0.521	0.651
0.0809	0.0498	0.0672	0.523	0.189	0.158	0.626	0.756
0.0970	0.0570	0.0600	0.593	0.189	0.151	0.742	0.872

Table 4.12:

Variation of k_o with [TGA] at 30°C

[^iPrONO] = 2.5 x 10^{-4} mol l^{-1} [H_2SO_4] = 0.234 mol l^{-1}

[TGA] mol l^{-1}	k_o s^{-1}
0.0143	0.0226 ± 9 x 10^{-4}
0.0199	0.0307 ± 1.9 x 10^{-3}
0.0257	0.0411 ± 1.6 x 10^{-3}
0.0314	0.0502 ± 2.5 x 10^{-3}
0.0371	0.0564 ± 5 x 10^{-4}
0.0428	0.0630 ± 3 x 10^{-4}

slope = 1.42 ± 0.07 l mol^{-1} s^{-1}

intercept = 3 x 10^{-3} ± 2 x 10^{-3} s^{-1}

that found for ^tBuONO, then slope = k_1 [H+], so k_1 = 6.1 ± 0.3 l^2 mol^{-2} s^{-1}. This value is very similar to that found for reaction of TGA with ^tBuONO. The value of k_o was also found to decrease markedly on addition of small amounts of water (Table 4.13 and Figure 4.8). The value of k_o drops off steeply at first but as more water is added the value of k_o levels off. This has been found previously for the reaction of alkyl nitrites with alcohols [1] as solvent and was interpreted in terms of water being a stronger base than the alcohol and so lowers the effective acidity of the solution.

Table 4.13:

Effect of water on k_o at 30°C

$[TGA] = 0.0517$ mol l^{-1} $[H_2SO_4] = 0.0594$ mol l^{-1}

$[{}^{i}PrONO] = 1.5 \times 10^{-3}$ mol l^{-1}

Volume % H_2O	k_o s^{-1}
0	$0.0177 \pm 1.0 \times 10^{-3}$
0.5	$8.85 \times 10^{-3} \pm 4.3 \times 10^{-4}$
1	$6.38 \times 10^{-3} \pm 2.65 \times 10^{-4}$
1.5	$4.69 \times 10^{-3} \pm 4 \times 10^{-5}$
2	$3.64 \times 10^{-3} \pm 7.3 \times 10^{-4}$
2.5	$3.44 \times 10^{-3} \pm 1.1 \times 10^{-4}$
5	$2.74 \times 10^{-3} \pm 3.5 \times 10^{-5}$

4.3 Nucleophilic catalysis of the nitrosation of thioglycolic acid by tertiary butyl nitrite in tertiary butanol at 30°C

4.3.1 Catalysis by chloride and bromide salts

The reaction was carried out in a similar way as described in section 4.1.2, but tetraethylammonium

Figure 4.9

Variation of ko with [Et_4NCl]

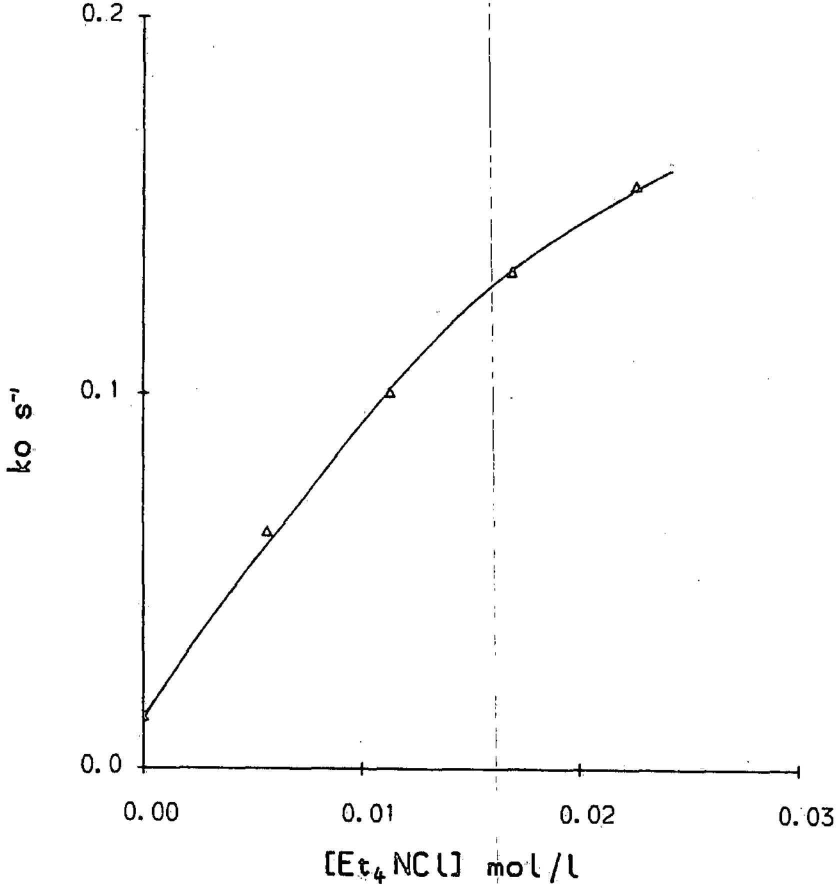
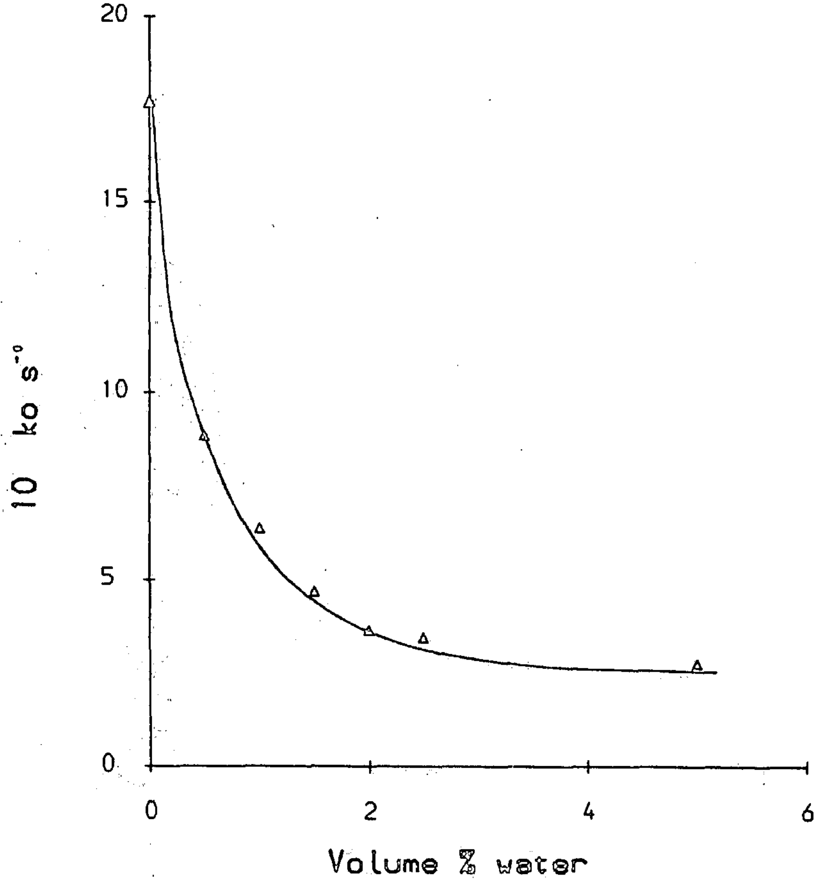


Figure 4.8

Effect of water



chloride (Et_4NCl) or bromide (Et_4NBr) was used as a source of halide ions. The effect of [Et_4NCl] on the observed first order rate constant, k_o, at two different acidities was investigated (Tables 4.14 and 4.15) and the effect of acidity (Table 4.16) and [TGA] (Table 4.17) on k_o in the presence of Et_4NCl was also investigated.

Table 4.14:

Effect of Et_4NCl on k at 30°C

[H_2SO_4] = 0.0811 mol l^{-1} [^tBuONO] = 2.5×10^{-4} mol l^{-1}

[TGA] = 0.0144 mol l^{-1} 330 nm

[Et_4NCl] mol l^{-1}	k_o s^{-1}
0	$0.0136 \pm 1 \times 10^{-4}$
5.66×10^{-3}	$0.0633 \pm 2.7 \times 10^{-3}$
0.0113	$0.1005 \pm 1.45 \times 10^{-3}$
0.0169	$0.1325 \pm 3.7 \times 10^{-3}$
0.0226	$0.1547 \pm 1.7 \times 10^{-3}$

The data in Table (4.14) show that the reaction is catalysed by added Et_4NCl. A plot of k_o against [Et_4NCl] (Figure 4.9) is curved, tending towards a maximum value of k_o , with a positive intercept. The intercept

Table 4.15:

Effect of Et_4NCl at low acidity at 30°C

$[H_2SO_4]$ = 6.59 x 10^{-4} mol l^{-1} $[^tBuONO]$ = 2.5 x 10^{-4} mol l^{-1}

[TGA] = 0.0144 mol l^{-1} 330 nm

$[Et_4NCl]$ mol l^{-1}	k s^{-1}
7.08 x 10^{-3}	5.15 x 10^{-3} ± 1.1 x 10^{-4}
9.44 x 10^{-3}	5.13 x 10^{-3} ± 2 x 10^{-5}
0.0189	4.64 x 10^{-3} ± 1.6 x 10^{-4}
0.0283	5.10 x 10^{-3} ± 3 x 10^{-5}
0.0472	5.31 x 10^{-3} ± 6 x 10^{-5}

Table 4.16:

Effect of $[H_2SO_4]$ on ko in presence of Et_4NCl

$[^tBuONO]$ = 2.5 x 10^{-4} mol l^{-1} [TGA] = 0.0144 mol l^{-1}

[Et NCl] = 9.44 x 10^{-3} mol l^{-1} 330 nm

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
5.28 x 10^{-3}	0.0271 ± 1.0 x 10^{-3}
0.0106	0.0475 ± 1.2 x 10^{-3}
0.01581	0.0501 ± 7 x 10^{-4}
0.0211	0.0585 ± 9 x 10^{-4}
0.0264	0.0585 ± 2.6 x 10^{-3}

Table 4.17:

Effect of [TGA] on k_o in presence of Et_4NCl

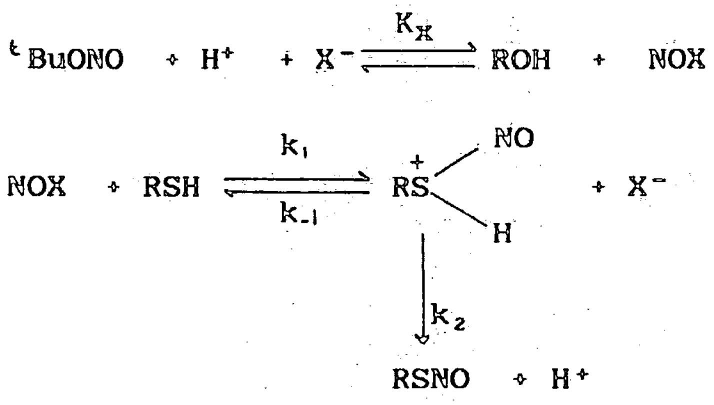
[^tBuONO] = 2.5×10^{-4} mol l^{-1} [H_2SO_4] = 0.0496 mol l^{-1}

[Et_4NCl] = 8.26×10^{-3} mol l^{-1} 330 nm

[TGA] mol l^{-1}	k s^{-1}
0.0259	$0.0433 \pm 7 \times 10^{-4}$
0.0518	$0.0885 \pm 7 \times 10^{-4}$
0.0777	$0.124 \pm 2 \times 10^{-3}$
0.103	$0.138 \pm 1 \times 10^{-3}$
0.129	$0.141 \pm 3 \times 10^{-3}$
0.156	$0.147 \pm 2 \times 10^{-3}$

corresponds to the uncatalysed rate of reaction. Under conditions where [Et_4NCl] $\gg$ [H_2SO_4] (Table 4.15) the reaction rate was found to be independent of the concentration of Et_4NCl, even at concentrations of Et_4NCl that produced an increase in rate under the conditions used in Table (4.14).

The leveling off of k_o at high concentrations of added chloride ion has been found for the reaction of n-propyl nitrite in n-propanol [2] with three aromatic amines. It was explained in terms of a reversible nitrosation of the amine by nitrosyl chloride followed by a slow proton transfer step. If a similar explanation exists in the present case then reaction scheme (4.15) will apply.



(4.15)

Applying a steady state treatment to [RSHNO$^+$] equation (4.16) can be derived. This predicts that at high [X$^-$] the value of k_o should become independent of [X$^-$] ie. $k_{-1}[X^-] \gg k_2$, but this should not depend on

$$k_o = \frac{k_1 k_2 K_X [H^+][TGA][X^-]}{k_{-1}[X^-] + k_2} \qquad (4.16)$$

the acidity. This scheme also assumes that the initial nitrosation step is reversible and can compete with the loss of a proton from the $\overset{+}{RS}\!<\!\genfrac{}{}{0pt}{}{NO}{H}$ species. The relative values of k_2/k_{-1} can be found from a plot of

k_o^{-1} against $[X^-]^{-1}$. This has slope = $1/(k_1 K_X [H^+][TGA])$ and intercept = $k_{-1} / (k_1 k_2 K_X [H^+] [TGA])$ and so slope / intercept = k_2 / k_{-1}. Such a plot was carried out in this case, making an allowance for the uncatalysed rate and gave a reasonable straight line with slope = 0.070 ± 2 x 10^{-3} mol l^{-1}s and intercept = 3.47 ± 0.23 s. The value of k_2 / k_{-1} = 0.020 ± 0.002 mol l^{-1}. The values reported for the reaction of n-propyl nitrite in n-propanol [2] with three aromatic amines are shown in Table (4.18).

Table 4.18:

Values of k_2/k_{-1} (mol l^{-1}) for the reaction of n-propyl nitrite with aromatic amines at 30°C

Nucleophile	aniline	N-methylaniline	p-nitro aniline
Cl^-	0.037	0.025	0.037
Br^-	0.033	0.021	0.032
thiourea	0.013	0.010	/

The value obtained in this work is in reasonable agreement with those shown in Table (4.18), but it seems unlikely that the value should be the same since one set of data is concerned with S-nitrosation and the

Figure 4.11

Plot of ko against [TGA] in the presence of Et_4NCl

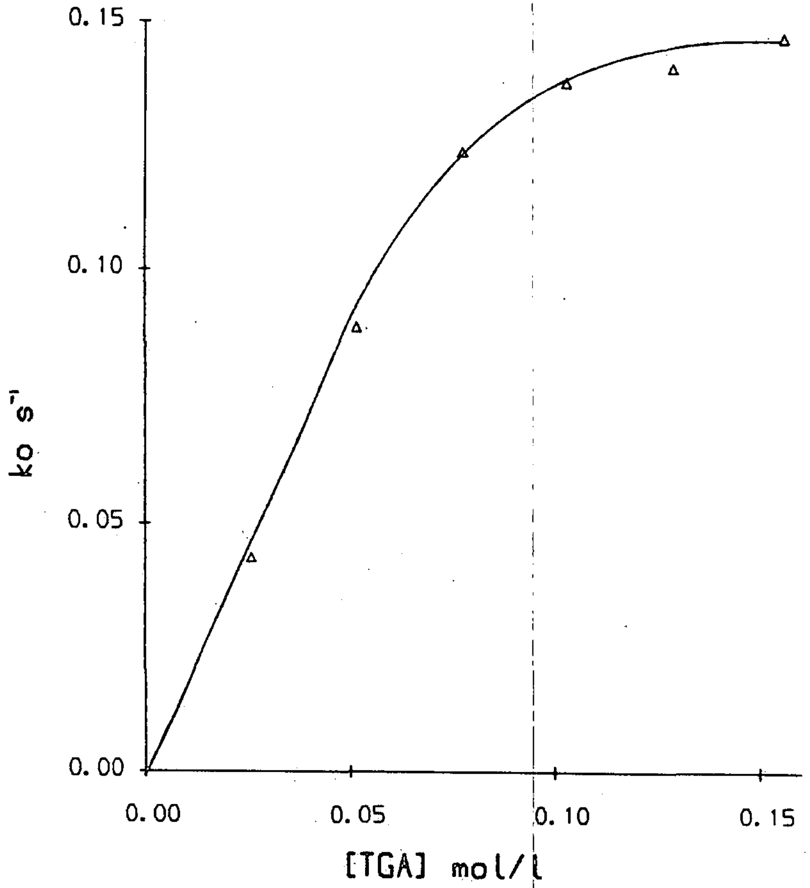
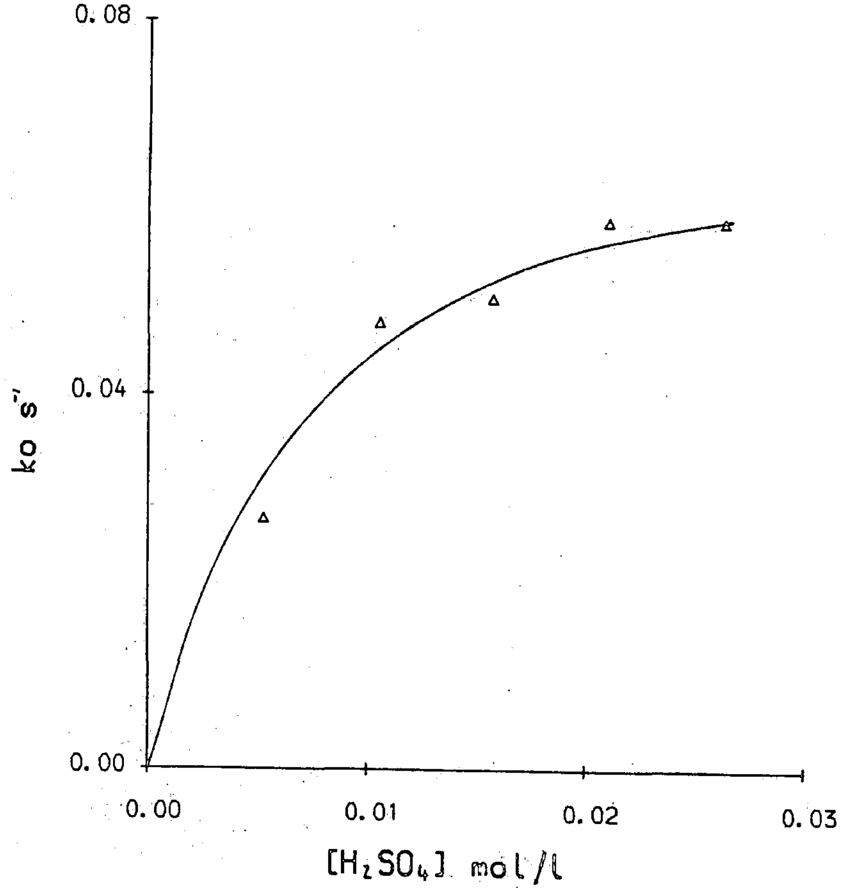


Figure 4.10

Variation of ko with $[H_2SO_4]$ in the presence of $[Et_4NCl]$



other with N-nitrosation. This point will be discussed in Section 4.5 . Evidence against this mechanism comes from the fact that the reaction is no longer first order with respect to both [H_2SO_4] and [TGA] in the presence of Et_4NCl (Figures 4.10 and 4.11). This is also found in the variation of ko with [H_2SO_4] in the presence of Et_4NBr (Table 4.19).

Table 4.19:

Variation of ko with [H_2SO_4] in the presence of Et_4NBr

[^{t}BuONO] = 2.5×10^{-4} mol l^{-1} [TGA] = 0.0259 mol l^{-1}

[Et_4NBr] = 4.34×10^{-3} mol l^{-1}

[H_2SO_4] mol l^{-1}	ko s^{-1}
9.14×10^{-4}	$0.0140 \pm 4 \times 10^{-4}$
1.98×10^{-3}	$0.0209 \pm 3 \times 10^{-4}$
2.97×10^{-3}	$0.0276 \pm 1.0 \times 10^{-3}$
3.97×10^{-3}	$0.0314 \pm 1.2 \times 10^{-3}$
4.96×10^{-3}	$0.0361 \pm 6 \times 10^{-4}$
9.22×10^{-3}	$0.0494 \pm 9 \times 10^{-4}$
0.0149	$0.0598 \pm 1.2 \times 10^{-3}$
0.0198	$0.0704 \pm 1.6 \times 10^{-3}$
0.0248	$0.0792 \pm 1.5 \times 10^{-3}$
0.0496	$0.1004 \pm 3 \times 10^{-4}$

The problem with the analysis of Scheme (4.15) is that it assumes a knowledge of both [H^+] and [Cl^-]. From the earlier results is seems that the approximation of [H^+]$\simeq$[H_2SO_4] is valid, but the analysis assumes that Et_4NCl is fully dissociated in the alcohol solvent. Values of the dissociation constants of several halide salts in alcohol solutions have been determined [24] previously and are shown in Table (4.20).

Table 4.20:

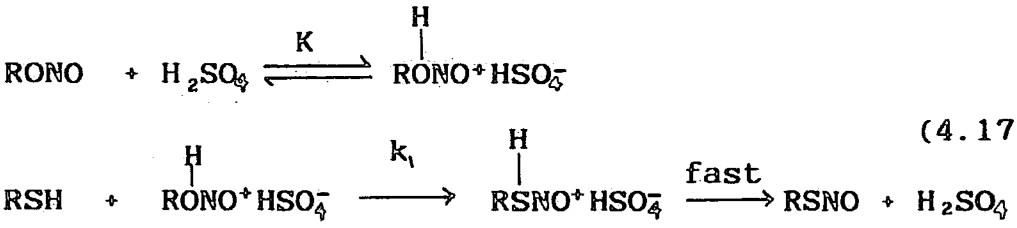
Dissociation constants of several chloride and bromide salts in alcohol solution at 25°C

	^iPrOH	^tBuOH	n-BuOH
		K_d (mol l^{-1})	
HCl	7.94×10^{-4}	3.16×10^{-6}	
HBr	1×10^{-2}	1×10^{-5}	
Et_4NBr	9×10^{-4}		7.5×10^{-4}
~~Me_4NCl~~	~~4.4×10^{-4}~~	~~1×10^{-6}~~	
Me_4NBr	5.5×10^{-4}		
Bu_4NBr	1.1×10^{-8}	5.3×10^{-6}	

The dissociation constants of the salts in alcohols are very small and so there will not be a significant ammount of free chloride ion present in these solutions.

An alternative explanation of the levelling off of ko with added chloride and bromide ion is that the formation of the nitrosyl halide becomes almost quantitative at high chloride ion concentrations. This requires that the value of the equilibrium constant, K_X, be in the order of $10^3 - 10^4$ l^2 mol^{-2}. This is known not to be the case for chloride and bromide ion with nitrous acid in methanol solution [3] and is unlikely to apply in this case.

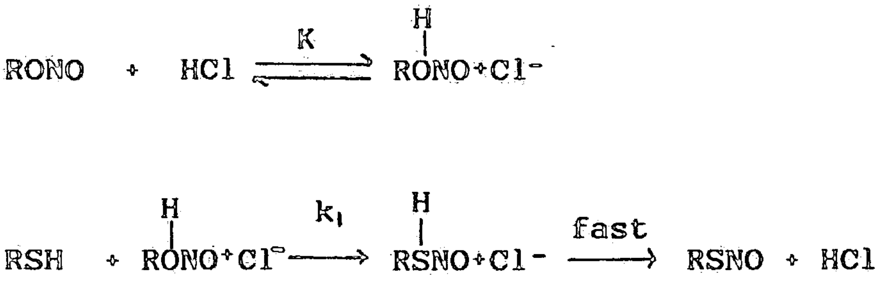
A further explanation is that at high Et_4NCl concentrations there is a significant amount of association of the chloride ion with any cations present in the solution, most importantly the proton. A similar explanation was put forward for the chloride and bromide ion catalysis of the reactions of 1-methyl heptyl nitrite in various alcohols [1]. The catalysis observed on addition of chloride to the solution could therefore be due to the formation of HCl which can act as a general acid catalyst in the same way as H_2SO_4. This is represented in Schemes (4.17) and (4.18).



$$RONO + H_2SO_4 \overset{K}{\rightleftharpoons} R\overset{H}{\overset{|}{O}}NO^+HSO_4^-$$

$$RSH + R\overset{H}{\overset{|}{O}}NO^+HSO_4^- \xrightarrow{k_1} R\overset{H}{\overset{|}{S}}NO^+HSO_4^- \xrightarrow{\text{fast}} RSNO + H_2SO_4$$

(4.17)



$$\mathrm{RONO} + \mathrm{HCl} \overset{K}{\rightleftharpoons} \mathrm{R}\overset{\overset{\displaystyle \mathrm{H}}{|}}{\mathrm{O}}\mathrm{NO}^{+}\mathrm{Cl}^{-}$$

$$\mathrm{RSH} + \mathrm{R}\overset{\overset{\displaystyle \mathrm{H}}{|}}{\mathrm{O}}\mathrm{NO}^{+}\mathrm{Cl}^{-} \xrightarrow{k_1} \mathrm{R}\overset{\overset{\displaystyle \mathrm{H}}{|}}{\mathrm{S}}\mathrm{NO}^{+}\mathrm{Cl}^{-} \xrightarrow{\text{fast}} \mathrm{RSNO} + \mathrm{HCl}$$

(4.18)

Catalysis could arise from an increase in K or in k_1 on the addition of Et_4NBr and Et_4NCl. The results in Table (4.21) show that HCl also acts as a catalyst for these reactions and the reaction is first order in HCl. The derived value of k_1 from this data is 810 l^2 mol^{-2} s^{-1} which is over 100 times larger than the corresponding value using H_2SO_4.

Table 4.21:

Variation of ko with [HCl] in the nitrosation of TGA

[^{t}BuONO] = 5×10^{-4} mol l^{-1} [TGA] = 7.234×10^{-3} mol l^{-1}

[HCl] mol l^{-1}	ko s^{-1}
2.18×10^{-3}	0.0135
4.35×10^{-3}	0.0274
8.70×10^{-3}	0.0523
0.0131	0.0778

slope = 5.85 ± 0.07 l mol^{-1} s^{-1}

intercept = $1.3 \times 10^{-3} \pm 6 \times 10^{-1}$ s^{-1}

This type of mechanism can also account for the lack of catalysis by Et_4NCl when $[Et_4NCl] \gg [H_2SO_4]$ as HCl could be expected to be formed quantitatively and so its concentration would remain constant even though $[Et_4NCl]$ is increased. The non linear dependence of k_o on $[H_2SO_4]$ in the presence of Et_4NCl is also explicable in these terms, as other equilibria (eg. Equation 4.19) have to be taken into account.

$$H_2SO_4 + Et_4\overset{+}{N}\bar{Cl} \xrightleftharpoons{K} HCl + HSO_4^-Et_4N^+ \qquad (4.19)$$

4.3.2 Thiourea catalysis

The effect on the rate of nitrosation of TGA was investigated. Table (4.22) shows the effect of [thiourea] on the observed first order rate constant, k_o . A plot of k_o against [thiourea] gave a curve, tending towards a limiting value of k_o , with a positive intercept (Figure 4.12). The intercept corresponds to the uncatalysed rate. On analysing the results in terms of an initial reversible nitrosation and subsequent proton transfer to the solvent (Scheme 4.15), a plot of $(k_o\text{-intercept})^{-1}$ against [thiourea] gave a straight line with slope = $0.304 \pm 3 \times 10^{-3}$ mol l^{-1} s and intercept = 10.9 ± 0.3 s^{-1}. This gives a value of k_2/k_{-1} of 0.028 mol l^{-1} which is

Table 4.22:

Variation of k_o with [thiourea] at 30°C

$[^t\mathrm{BuONO}] = 2.5 \times 10^{-4}$ mol l^{-1} $[\mathrm{H_2SO_4}] = 0.0660$ mol l^{-1}

$[\mathrm{TGA}] = 0.0144$ mol l^{-1}

[thiourea] mol l^{-1}	k_o s^{-1}
0	$6.4 \times 10^{-3} \pm 2 \times 10^{-4}$
0.006	$0.0226 \pm 9 \times 10^{-4}$
0.012	$0.0341 \pm 1.6 \times 10^{-3}$
0.018	$0.0420 \pm 6 \times 10^{-4}$
0.024	$0.0495 \pm 7 \times 10^{-4}$
0.030	$0.0531 \pm 4 \times 10^{-4}$

again in good agreement with the values found for chloride ion and also the k_2/k_{-1} values found for nitrosation of the aniline derivatives in n-propanol [2]. This approach, however, does not take into account the protonation of thiourea. Also with thiourea, since the equilibrium constant is large, curvature of a plot of k_o against [thiourea] could be expected if at high [thiourea], S-nitrosothiourea is formed rapidly and almost quantitatively before reaction with TGA occurs. This is taken into account in reaction Scheme (4.20).

$$ {}^{t}BuONO + H^{+} + (NH_2)_2CS \overset{K}{\rightleftharpoons} (NH_2)_2\overset{+}{C}S\text{-}NO \qquad (4.20) $$

$$ (NH_2)_2\overset{+}{C}S\text{-}NO + RSH \xrightarrow{k_1} (NH_2)_2CS + RSNO + H^{+} $$

$$ \text{Rate} = k_1[RSH][(NH_2)_2CS\text{-}NO^{+}] $$

$$ \text{but} \quad [{}^{t}BuONO]_o = [(NH_2)_2CS\text{-}NO^{+}] + [{}^{t}BuONO] $$

$$ [{}^{t}BuONO]_o = [(NH_2)_2CS\text{-}NO^{+}]\left(1 + \frac{1}{K\,[H^{+}][(NH_2)_2CS]}\right) $$

$$ \text{Rate} = \frac{k_1K[H^{+}][(NH_2)_2CS][TGA][{}^{t}BuONO]_o}{1 + K[(NH_2)_2CS][H^{+}]} $$

$$ k_o = \frac{k_1K\,[H^{+}][(NH_2)_2CS][TGA]}{1 + [(NH_2)_2CS][H^{+}]K} \qquad (4.21) $$

Equation (4.21) predicts that if $K.[(NH_2)_2CS][H^{+}] \gg 1$ then the value of k_o should be independent of [thiourea]. The actual concentrations of $[H^{+}]$, assumed to be equal to $[H_2SO_4]$ and free thiourea, $[(NH_2)_2CS]$ can be calculated, using the Ka value of 0.075 mol l^{-1} and so a plot of k_o against $K[H^{+}][(NH_2)_2CS]/(1 + K[(NH_2)_2CS][H^{+}])$ can be obtained (Figure 4.13), using K = 2215 l^{2} mol $^{-2}$. The results are shown in Table (4.23).

Table 4.23:

$[H_2SO_4]_T$ = 0.0660 mol l^{-1} [TGA] = 0.0141 mol l^{-1}

$[\text{thiourea}]_T$ mol l^{-1}	$[(NH_2)_2C\overset{+}{S}-H]$ mol l^{-1}	$[(NH_2)_2CS]$ mol l^{-1}	$[H_2SO_4]$actual mol l^{-1}	$\frac{K[H^+][(NH_2)_2CS]}{(1 + K[(NH_2)_2CS][H^+])}$	ko s^{-1}
0	0	0	0.0660	0	6.4×10^{-3}
0.006	2.75×10^{-3}	3.25×10^{-3}	0.0628	0.315	0.0226
0.012	5.36×10^{-3}	6.64×10^{-3}	0.0594	0.470	0.0341
0.018	7.86×10^{-3}	0.0101	0.0559	0.560	0.0420
0.024	0.0102	0.0138	0.0522	0.618	0.0495
0.030	0.0125	0.0175	0.0485	0.656	0.0531

slope = 0.0713 ± 5.7×10^{-3} s

intercept = 3.4×10^{-3} ± 2.8×10^{-3}

Figure 4.13

Catalysis by thiourea allowing for protonation

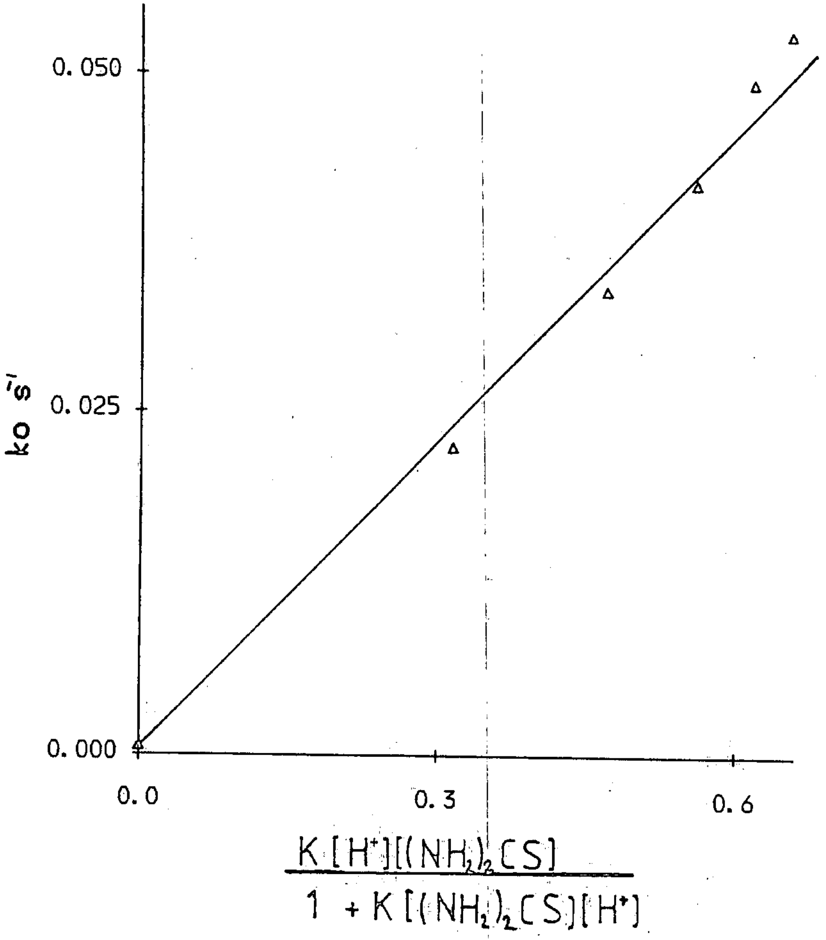
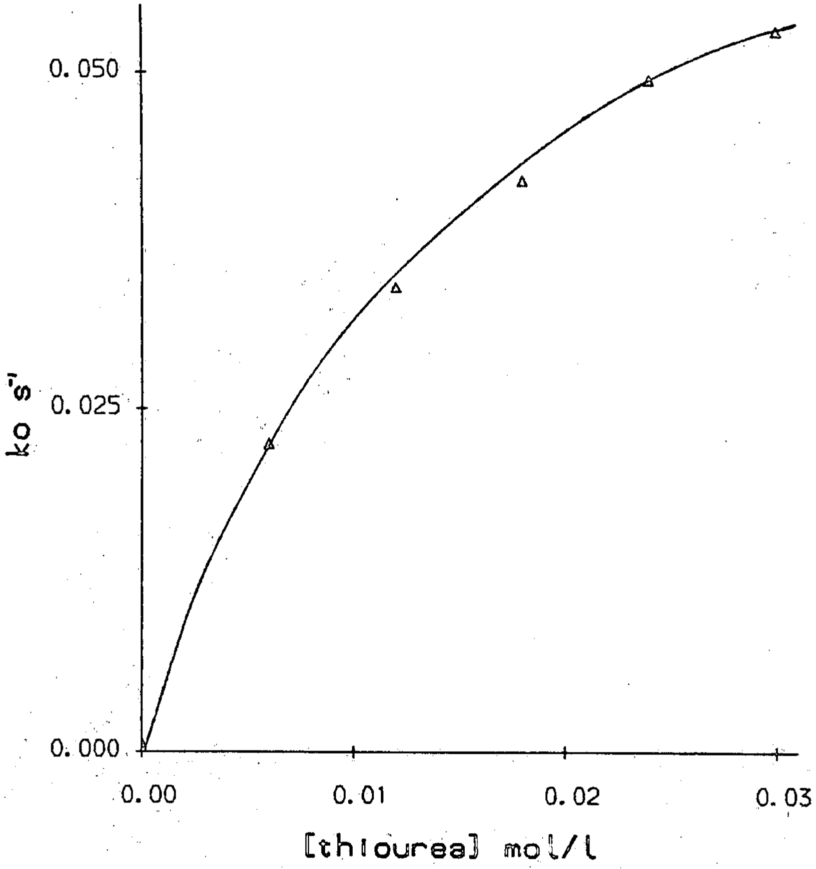


Figure 4.12

Plot of ko against [thiourea]



The plot (Figure 4.13) gives a reasonable straight line with a fair amount of scatter. The value of k_1, the second order rate constant for attack of S-nitrosothiourea on thioglycolic acid can be calculated as 5.0 l mol^{-1} s^{-1}. The results are consistent with the formation of an equilibrium concentration of S-nitrosothiourea which then reacts with TGA in the rate determining step. The curvature found on plots of ko against thiourea can be explained by this mechanism and by allowing for protonation equilibria.

4.4. Nucleophilic catalysis of the nitrosation of thioglycolic acid by isopropyl nitrite in isopropanol at 30°C

4.4.1 Chloride ion catalysis

The variation of ko with added Et_4NCl was studied in the nitrosation of TGA by ^{i}PrONO at 30°C. The results are shown in Table (4.24) and in Figure (4.14). The plot of ko against $[Et_4NCl]$ shows a marked curvature, tending towards a limiting value of ko. A plot of $(ko - intercept)^{-1}$ against $[Et_4NCl]^{-1}$ gave a good straight line with slope = 0.482 ± 6 x 10^{-3} mol l^{-1} s and intercept = 13.9 ± 2.1 s. This corresponds to a value of k_1/k_{-1} of 3.5 x 10^{-2} mol l^{-1}, which is again consistent

Table 4.24:

Variation of ko with $[Et_4NCl]$ at 30°C

$[TGA] = 9.2 \times 10^{-3}$ mol l^{-1} $[H_2SO_4] = 0.119$ mol l^{-1}

$[{}^{i}PrONO] = 2.5 \times 10^{-4}$ mol l^{-1}

$[Et_4NCl]$ mol l^{-1}	ko s^{-1}
0	$7.01 \times 10^{-3} \pm 2.1 \times 10^{-4}$
1.06×10^{-3}	$9.13 \times 10^{-3} \pm 2.3 \times 10^{-4}$
3.19×10^{-3}	$0.0136 \pm 9 \times 10^{-5}$
6.38×10^{-3}	$0.0185 \pm 8 \times 10^{-5}$
8.85×10^{-3}	$0.0214 \pm 7 \times 10^{-4}$
9.58×10^{-3}	$0.0219 \pm 4 \times 10^{-4}$
0.0128	$0.0272 \pm 2 \times 10^{-4}$
0.0159	$0.0289 \pm 9 \times 10^{-4}$
0.0177	$0.0298 \pm 9 \times 10^{-4}$
0.0266	$0.0356 \pm 7 \times 10^{-4}$
0.0443	$0.0485 \pm 8 \times 10^{-4}$

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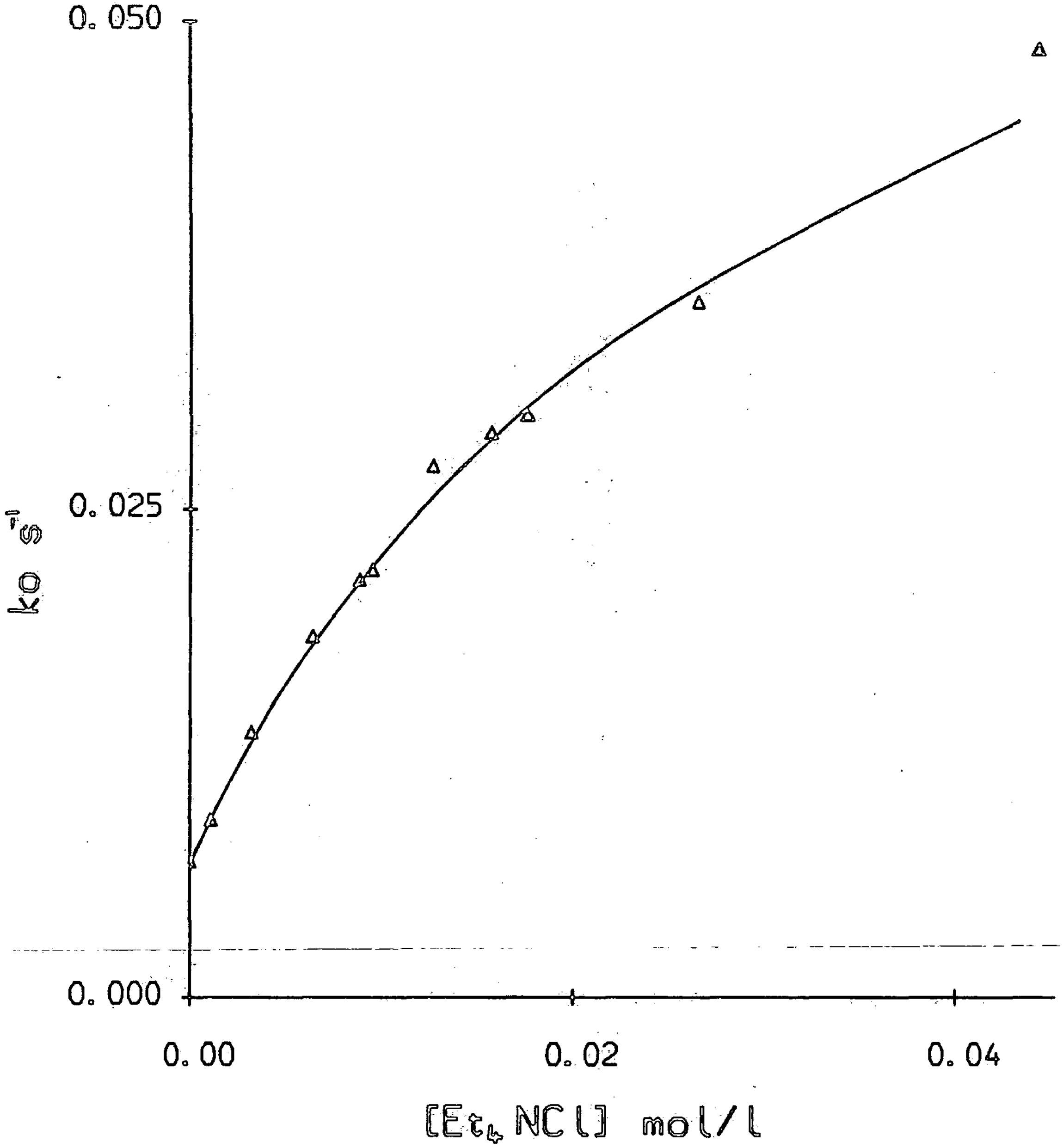
with those previously found, but again assumes that the initial S-nitrosation of TGA is reversible.

Figure 4.14

Plot of ko against [Et$_4$NCl]



4.4.2 Thiourea catalysis

The value of ko was obtained at various [thiourea] and the results are shown in Table 4.25. The plot of ko against [thiourea] gives a curve with a positive intercept that corresponds to the uncatalysed rate.

Table 4.25:

Variation of ko with [thiourea] at 30°C

$[H_2SO_4]$ = 0.119 mol l^{-1} [TGA] = 9.2 x 10^{-3} mol l^{-1}

$[{}^iPrONO]$ = 2.5 x 10^{-4} mol l^{-1}

[thiourea] mol l^{-1}	ko s^{-1}
2.45 x 10^{-3}	0.0155
7.35 x 10^{-3}	0.0288
0.0147	0.0401
0.0220	0.0556
0.0294	0.0609
0.0367	0.0605

A plot of $(ko - \text{intercept})^{-1}$ against $[\text{thiourea}]^{-1}$ gives a good straight line with slope = 0.263 mol l^{-1} s and intercept = 10.44 s. This corresponds to a k_2/k_{-1} value

Table 4.26:

$[H_2SO_4]_T$ = 0.0119 mol l^{-1} [TGA] = 9.2 x 10^{-3} mol l^{-1}

$[\text{thiourea}]_T$ mol l^{-1}	$[(NH_2)_2C\overset{+}{S}-H]$ mol l^{-1}	$[(NH_2)_2CS]$ mol l^{-1}	$[H_2SO_4]$actual mol l^{-1}	$\frac{Kx[H^+][(NH_2)_2CS]}{(1 + Kx[(NH_2)_2CS][H^+])}$	ko s^{-1}
2.45 x 10^{-3}	1.80 x 10^{-3}	6.5 x 10^{-4}	0.1170	0.122	0.0155
7.35 x 10^{-3}	5.35 x 10^{-3}	2.00 x 10^{-3}	0.1135	0.293	0.0288
0.0147	0.0106	4.10 x 10^{-3}	0.1082	0.447	0.0401
0.0220	0.0156	6.4 x 10^{-3}	0.1032	0.546	0.0556
0.0294	0.0206	8.8 x 10^{-3}	0.0982	0.612	0.0609
0.0367	0.0253	0.0114	0.0935	0.660	0.0605

slope = 0.0899 ± 6.4 x 10^{-3} s

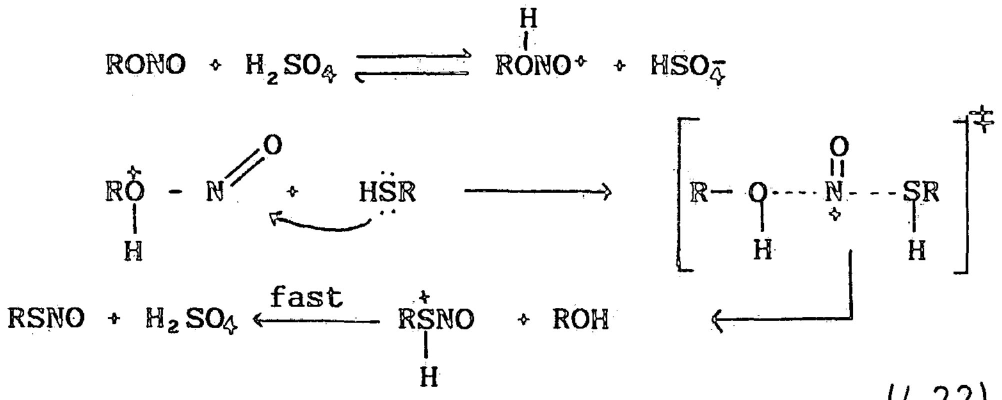
intercept = 3.37 x 10^{-3} ± 3.12 x 10^{-3} s^{-1}

of 2.5 x 10^{-2} mol l^{-1}, which is again similar to those previously found, but again this approach does not take into account the protonation of thiourea. Assuming the value of 0.0422 mol l^{-1} for Ka of thiourea and 1823 l^{2} mol $^{-2}$ for K_X for the formation of S-nitrosothiourea, the data can be analysed allowing for the protonation of thiourea in a similar way to the results in ^{t}BuOH. The results are shown in Table 4.26. A plot of k_o against $K_X[H^+][(NH_2)_2CS]/(1 + K_X[(NH_2)_2CS][H^+])$ gave a reasonable straight line with slope = 0.899 ± 6.4 x 10^{-3} s and intercept = 3.37 x 10^{-3} ± 3.12 x 10^{-3} s^{-1}. From the slope the value of k, the second order rate constant for attack of S-nitrosothiourea on TGA can be calculated as 9.8 l mol^{-1} s^{-1}.

4.5 Discussion

Both ^{i}PrONO and ^{t}BuONO in their respective alcohol as solvent appear to react by a similar mechanism with both thiourea and thioglycolic acid. In the absence of any added nucleophilic catalyst the reaction appears to proceed by nucleophilic attack of the sulphur atom of the substrate on the nitrogen centre of the protonated alkyl nitrite. The mechanism is shown in Scheme (4.22).

Acid catalysis occurs but it is not clear whether the solvated proton, H^+, or sulphuric acid itself acts



(4.22)

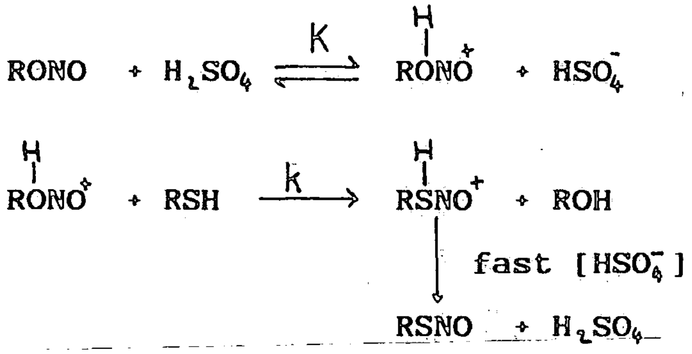
as the catalyst. The data obtained analysed well if the acidity of the solution is represented by $[H_2SO_4]$. The main arguement for this being true comes from the fact that the dissociation constants of several strong acids are known to be ca. 100 times smaller in ^{t}BuOH than ^{i}PrOH [17,21], therefore, assuming a similar trend for sulphuric acid, the rate of reaction in ^{t}BuOH would be expected to be significantly smaller than that in ^{i}PrOH if H^+ was the catalyst. This can be seen not to be the case by comparing the values of the rate and equilibrium constants obtained (Table 4.27). It is not possible to deduce the reactivity order of the protonated alkyl nitrites as the pKa values are not known. It can be seen though that both alkyl nitrites appear to have a very similar reactivity, and that the reaction with TGA is significantly slower than that with thiourea, indicating that the reaction with TGA does not approach the encounter controlled limit [22], as is observed in the reaction of TGA [19] and thiourea [6] with nitrous acid in water.

Table 4.27:

Values of rate and equilibrium constants obtained at 30°C

	Thiourea			TGA
Alcohol	K_N (mol^2 l^{-2})	k_1 l^2 mol^{-2}s^{-1}	k_{-1} s^{-1}	k l^{2}mol^{-2}s^{-1}
^{n}BuOH	2215	237	0.107	7.8
^{i}PrOH	1823	248	0.136	6.1

If H_2SO_4 acts as the acid catalyst, then any protonation equilibrium must depend on $[HSO_4^-]$, which would lead to non-first order kinetics (scheme 4.23).



$$RONO + H_2SO_4 \overset{K}{\rightleftharpoons} RON\overset{H}{\overset{|}{O}}{}^+ + HSO_4^-$$

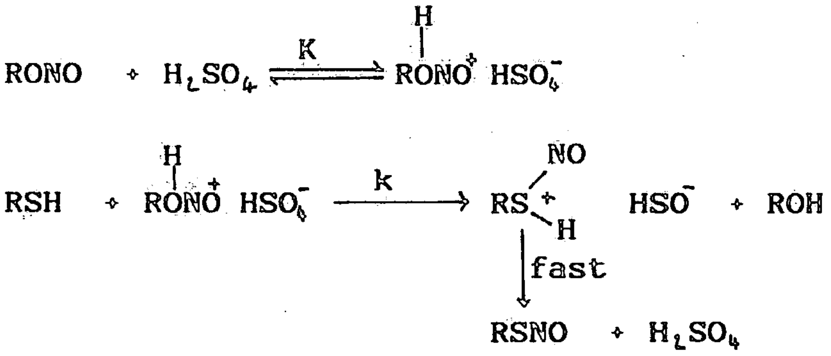
$$RON\overset{H}{\overset{|}{O}}{}^+ + RSH \xrightarrow{k} RSN\overset{H}{\overset{|}{O}}{}^+ + ROH$$

$$\downarrow \text{fast } [HSO_4^-]$$

$$RSNO + H_2SO_4 \qquad (4.23)$$

$$ko = \frac{k\,[RSH]K[H_2SO_4]}{K[H_2SO_4] + [HSO_4^-]} \qquad (4.24)$$

Equation (4.24) predicts that the reaction should not be first order since $[HSO_4^-]$ is not constant throughout the reaction. It also predicts a non first order dependence upon $[H_2SO_4]$. Another possible explanation is if there is extensive ion pairing in these solutions (Scheme 4.25) . This would then lead to a strict first order dependence upon $[H_2SO_4]$.



$$RONO + H_2SO_4 \xrightleftharpoons{K} R\overset{H}{O}NO^{+}\ HSO_4^-$$

$$RSH + R\overset{H}{O}NO^{+}\ HSO_4^- \xrightarrow{k} R\overset{NO}{\underset{H}{S^{+}}}\quad HSO^- + ROH$$

$$\downarrow \text{fast}$$

$$RSNO + H_2SO_4$$

(4.25)

Catalysis by added halide and thiourea also occurs. The curvature of plots of ko against [thiourea] can be accounted for by allowing for protonation of thiourea and assuming that the reaction occurs via the formation of an equilibrium concentration of S-nitrosothiourea, which can effect nitrosation of TGA.

The curvature ~~a~~ of the plots of ko against [halide ion] can also be explained in a similar way if the halide ion is being extensively protonated. Evidence against the halide ion being the effective catalyst in these solutions comes from the fact that the dissociation constants for the type of salts used are all very small in these solvents and further, they are ca 100 times smaller in ^{t}BuOH than in ^{i}PrOH. Therefore a much larger effect on the rate in ^{i}PrOH than ^{t}BuOH would be expected, but as can be seen by the data in Tables (4.14) and (4.24) a similar catalytic effect is observed in each case. The results are best explained in terms of formation of HCl and HBr in these solutions which can then act as a general acid catalyst.

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CHAPTER 5

REACTIONS OF ALKYL NITRITES IN ACETONITRILE AND CHLOROFORM

Chloroform and acetonitrile are examples of dipolar aprotic solvents. Some physical properties of these solvents are given in Table (5.1).

Table 5.1:

Physical properties

	Dielectric Constant (at 25°C)	Dipole Moment D	Freezing Point °C	Boiling Point °C
Acetonitrile	36.0	3.37	-45.72	81.60
Chloroform	4.81	1.01	-63.5	61.7
Water	78.54	1.85	0	100

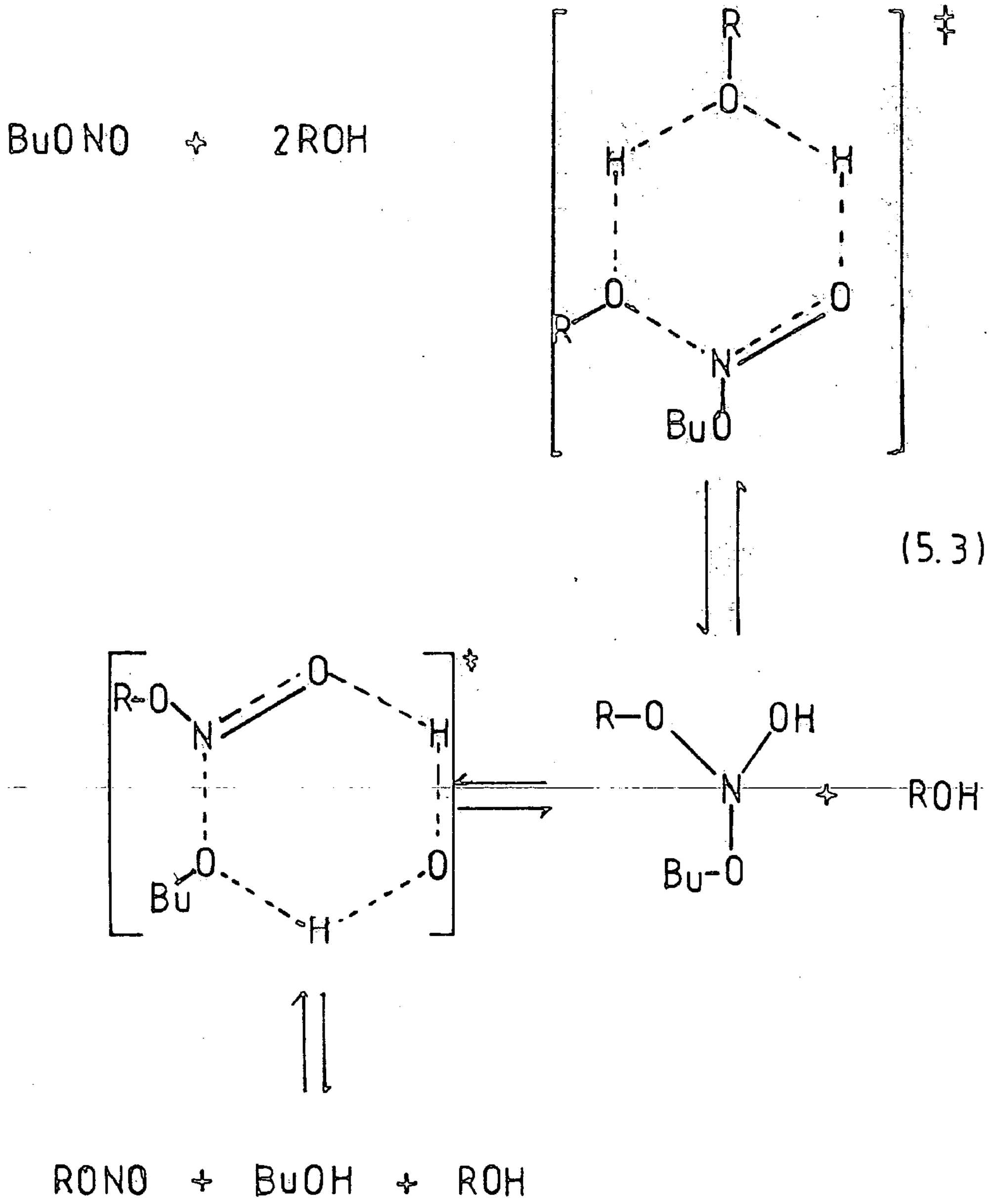
Acetonitrile is not strictly speaking an aprotic solvent as in its pure liquid state it is known to undergo autoprotolysis [1] as shown in equation (5.1), the autoprotolysis constant being ca. 3×10^{-29}. The value of the constant is so small that acetonitrile can be considered to be essentially an aprotic solvent.

$$2CH_3C{\equiv}N \overset{K}{\rightleftharpoons} [CH_2C{\equiv}N]^- + [CH_3C{\equiv}NH]^+ \qquad (5.1)$$

Chloroform, acetonitrile and dipolar aprotic solvents generally, have been used to some extent in nitrosation reactions of alkyl nitrites. In one previous study [2] the reaction of various alkyl nitrites with acetamide in various solvents was explained in terms of nucleophilic attack of the amino group of the amide on the nitrogen centre of the alkyl nitrite in an S_N2 type process. The rate of reaction was found to increase as the polarity and dielectric constant of the solvent increased. Other studies [3,4] have investigated the transnitrosation reaction of alkyl nitrites with alcohols by a NMR technique (equation 5.2). In all cases the reaction proceeded readily in the absence of any acid catalyst.

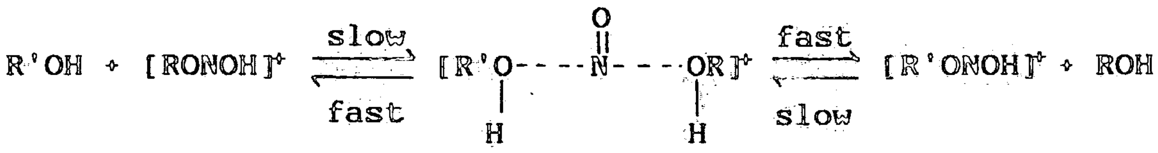
$$RONO + R'OH \overset{K}{\rightleftharpoons} ROH + R'ONO \qquad (5.2)$$

Using tertiary butyl nitrite as the nitrosating agent in chloroform [3], primary alkyl nitrites were formed with K≃ 10 and secondary nitrites were formed with K≃4, indicating that steric effects are again important in these reactions. No mechanistic work was carried out on this reaction which was assumed to occur via a six membered transition state (scheme 5.3), involving two alcohol molecules [3] or via a simple nitrosyl exchange reaction [4] (scheme 5.4).



(5.3)

$$\mathrm{RONO} + \mathrm{H^+} \underset{}{\overset{\text{fast}}{\rightleftharpoons}} [\mathrm{RONOH}]^+$$



$$\mathrm{R'OH} + [\mathrm{RONOH}]^+ \underset{\text{fast}}{\overset{\text{slow}}{\rightleftharpoons}} [\mathrm{R'\underset{H}{O}\text{---}\overset{O}{\underset{}{N}}\text{---}\underset{H}{O}R}]^+ \underset{\text{slow}}{\overset{\text{fast}}{\rightleftharpoons}} [\mathrm{R'ONOH}]^+ + \mathrm{ROH}$$

$$[\mathrm{R'ONOH}]^+ \xrightarrow{\text{fast}} \mathrm{R'ONO} + \mathrm{H^+} \qquad (5.4)$$

5.1 Equilibrium constants for the formation of alkyl nitrites in acetonitrile and chloroform

The equilibrium constants for the reactions of alkyl nitrites with various alcohols, equation (5.5), have now been determined spectrophotometrically in the 330-420 nm region. The results are given in Tables (5.2) and (5.3)

$$\mathrm{RONO} + \mathrm{R'OH} \overset{K}{\rightleftharpoons} \mathrm{R'ONO} + \mathrm{ROH} \qquad (5.5)$$

In each case equilibrium was obtained rapidly, without the addition of any external source of acid. The results show the trend that the equilibrium constant increases as the alcohol changes from a tertiary to

Table 5.2:

Equilibrium constants in acetonitrile at 25°C

R	R'	K
^{t}Butyl	Methyl	13.0
^{i}Propyl	Methyl	3.8
^{iso}Amyl	Methyl	2.5

Table 5.3:

Equilibrium constants in chloroform at 25°C

R	R'	K	
^{t}Butyl	^{i}Propyl	3.97 ± 0.14	4.2^{a}
^{i}Propyl	^{t}Butyl	0.301	
^{t}Butyl	Ethyl	10.1 ± 0.9	10.6^{a}
^{t}Butyl	Methyl	20.5	

a) from reference [3]

secondary to primary, ie a primary alkyl nitrite is preferred over a secondary and tertiary one, indicating that steric effects are important. The values obtained in chloroform are in good agreement with those found previously by NMR methods [3].

5.2 Kinetics and mechanism of the transnitrosation reaction

5.2.1 Chloroform as solvent

The reaction of tertiary butyl nitrite (^{t}BuONO) and isopropyl nitrite (^{i}PrONO) with methanol (MeOH) was studied in chloroform ($CHCl_3$) as solvent. The reaction was followed at 400 nm, where only ^{t}BuONO and ^{i}PrONO absorb significantly. In the absence of any acid catalyst the reaction proceeded readily to form methyl nitrite (MeONO). Good first order behaviour was obtained by following the disappearance of the alkyl nitrite when the $[\text{alkyl nitrite}] \ll [\text{MeOH}]$. However the observed first order rate constant, ko, was found to increase markedly with the age of the stock solution of the alkyl nitrite as shown in Tables (5.4) and (5.5).

This effect can be explained if the alkyl nitrite is decomposing to produce an acid, possibly nitrous acid which can act as an acid catalyst or effect nitrosation itself (equation 5.6). A similar explanation has been given to account for the reactions of alkyl nitrites [5] in neutral solution.

Table 5.4:

Effect of time on the value of ko for ^{t}BuONO

[MeOH] = 0.067 mol l^{-1} [^{t}BuONO] = 0.010 mol l^{-1}

25°C 400 nm

time min	ko s^{-1}
0	0.114
5	0.157
15	0.170
ca 30	0.225
ca 60	0.278
ca 120	0.475

Table 5.5:

Effect of time on the value of ko for ^{i}PrONO

[MeOH] = 0.251 mol l^{-1} [^{i}PrONO] = 0.018 mol l^{-1}

25°C 400 nm

time min	ko s^{-1}
15	8.89×10^{-3}
22	0.0129
29	0.0100
43	0.0138
58	0.0144

$$ {}^{t}BuONO + H_2O \rightleftharpoons BuOH + HNO_2 \qquad (5.6) $$

5.2.2 Acetonitrile as solvent

The reactions of ^{t}BuONO, ^{i}PrONO and isoamyl nitrite (^{iso}AmONO) with methanol were studied in acetonitrile (CH_3CN) as solvent. In the absence of any acid catalyst the reaction proceeded readily to form MeONO. Good first order behaviour was obtained by following the disappearance of the alkyl nitrite at 400 nm. The observed first order rate constant, ko, was again found to increase markedly with the age of the stock solution of the alkyl nitrite. The results for ^{i}PrONO are shown in Table (5.6)

Table 5.6:

Effect of time on the value of ko for ^{i}PrONO

[MeOH] = 0.356 mol l^{-1} [^{i}PrONO] = 9.8 x 10^{-3} mol l^{-1}

25°C 400 nm

time min	ko s^{-1}
8	0.0240
16	0.0469
27	0.0496
34	0.0501

This effect can be explained again by decomposition of the alkyl nitrite to produce an acid catalyst. Further evidence for this comes from the fact that the reactions are catalysed by the addition of H_2SO_4. With fresh solutions of H_2SO_4 in CH_3CN reproducible values of ko could be obtained only after the acid solution had stood for ca 10-15 minutes. This 'time-effect' will be discussed in detail in section 5.5. The reaction of all three alkyl nitrites with MeOH was found to be approximately first order with respect to $[H_2SO_4]$ (Tables 5.7 - 5.9)

Table 5.7 (a):

Variation of ko with $[H_2SO_4]$ for reaction of ^tBuONO

$[^tBuONO] = 0.010$ mol l^{-1} $[MeOH] = 0.118$ mol l^{-1}

25°C 400 nm

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
2.18×10^{-3}	33.3 ± 0.5
4.36×10^{-3}	79.8 ± 2.8
6.53×10^{-3}	137 ± 4
8.71×10^{-3}	193 ± 6
0.0109	217 ± 9
0.0131	273 ± 7

Table 5.7 (b):

Variation of ko with [H_2SO_4] for reaction of ^{t}BuONO

[^{t}BuONO] = 0.010 mol l^{-1} [MeOH] = 0.109 mol l^{-1}

25°C 400 nm

[H_2SO_4] mol l^{-1}	ko s^{-1}
1.97×10^{-3}	39.4 ± 1.5
3.94×10^{-3}	98.4 ± 1.7
5.92×10^{-3}	150 ± 3
7.89×10^{-3}	193 ± 4
9.86×10^{-3}	234 ± 8

Table 5.7 (c):

Variation of ko with [H_2SO_4] for reaction of ^{t}BuONO

[^{t}BuONO] = 0.010 mol l^{-1} [MeOH] = 0.110 mol l^{-1}

25°C 400 nm

[H_2SO_4] mol l^{-1}	ko s^{-1}
1.16×10^{-3}	16.2 ± 0.4
2.33×10^{-3}	38.4 ± 1.9
3.49×10^{-3}	56.9 ± 2.4

Table 5.8:

Effect of [H_2SO_4] on ko for reaction of ^{i}PrONO

[^{i}PrONO] = 0.010 mol l^{-1} [MeOH] = 0.117 mol l^{-1}

25°C 400 nm

[H_2SO_4] mol l^{-1}	ko s^{-1}
3.28×10^{-3}	24.4 ± 0.4
6.56×10^{-3}	59.3 ± 1.0
9.84×10^{-3}	89.6 ± 2.8
0.0131	131 ± 9
0.0164	165 ± 4
0.0197	210 ± 4

Table 5.9:

Effect of [H_2SO_4] on ko for reaction of ^{iso}AmONO

[^{iso}AmONO] = 0.015 mol l^{-1} [MeOH] = 0.113 mol l^{-1}

25°C 400 nm

[H_2SO_4] mol l^{-1}	ko s^{-1}
3.28×10^{-3}	17.0 ± 0.7
6.56×10^{-3}	42.8 ± 1.0
9.84×10^{-3}	59.7 ± 1.3
0.0131	90.6 ± 2.6
0.0164	118 ± 5
0.0197	148 ± 3

The data for ^{t}BuONO (Tables 5.7 (a) - (c)) are shown in Figure (5.1). The graph shows that there is only reasonable agreement between the three sets of data. When the experiment was repeated 1 week later using the same acid stock solution, the values of ko obtained were markedly smaller than those obtained previously. The results are shown in Table (5.10) and Figure (5.1). This shows that there is a substantial ageing effect occurring in the sulphuric acid solutions.

Table 5.10:

Effect of $[H_2SO_4]$ after 1 week

$[^tBuONO]$ = 0.010 mol l^{-1} $[MeOH]$ = 0.118 mol l^{-1}

400nm 25°C

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
3.42×10^{-3}	8.92 ± 0.13
1.03×10^{-2}	15.66 ± 0.07
1.71×10^{-2}	19.74 ± 0.16

The rate constant was found to decrease markedly over several days even though the total stoichiometric concentration of sulphuric acid remained constant over that period, as shown by titration with standard sodium

Figure 5.2

Acid catalysis in the nitrosation of methanol by alkyl nitrites

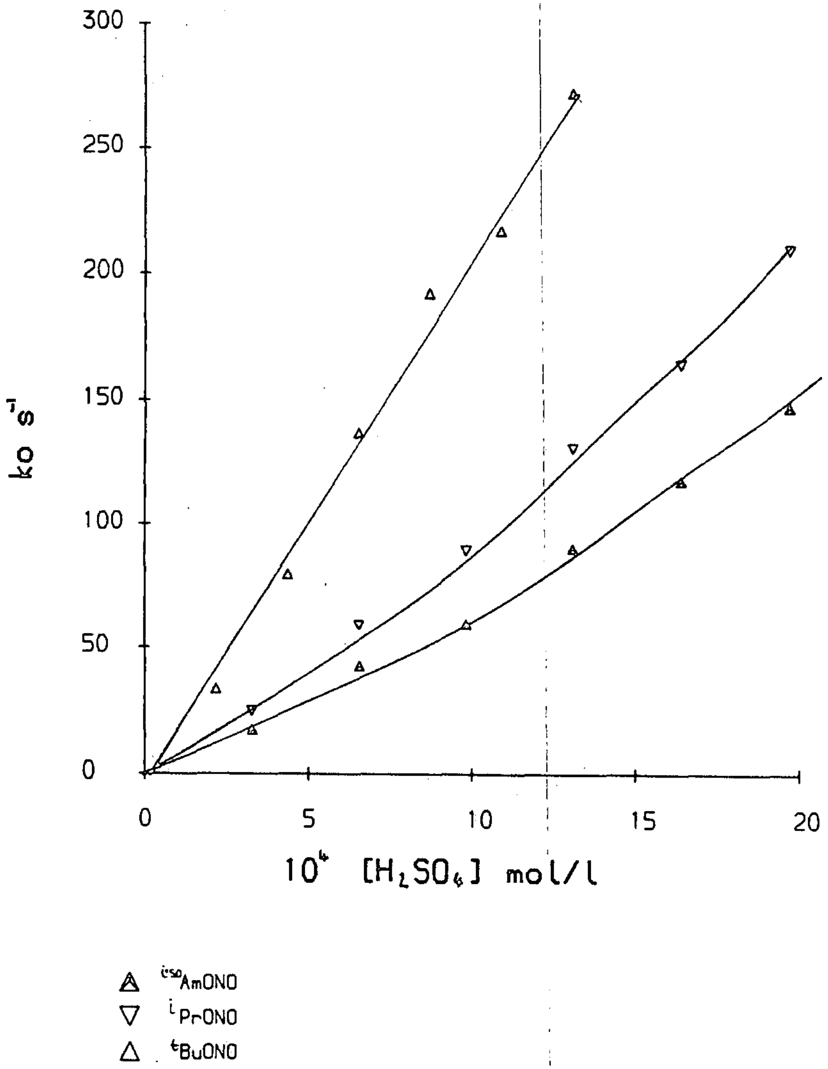
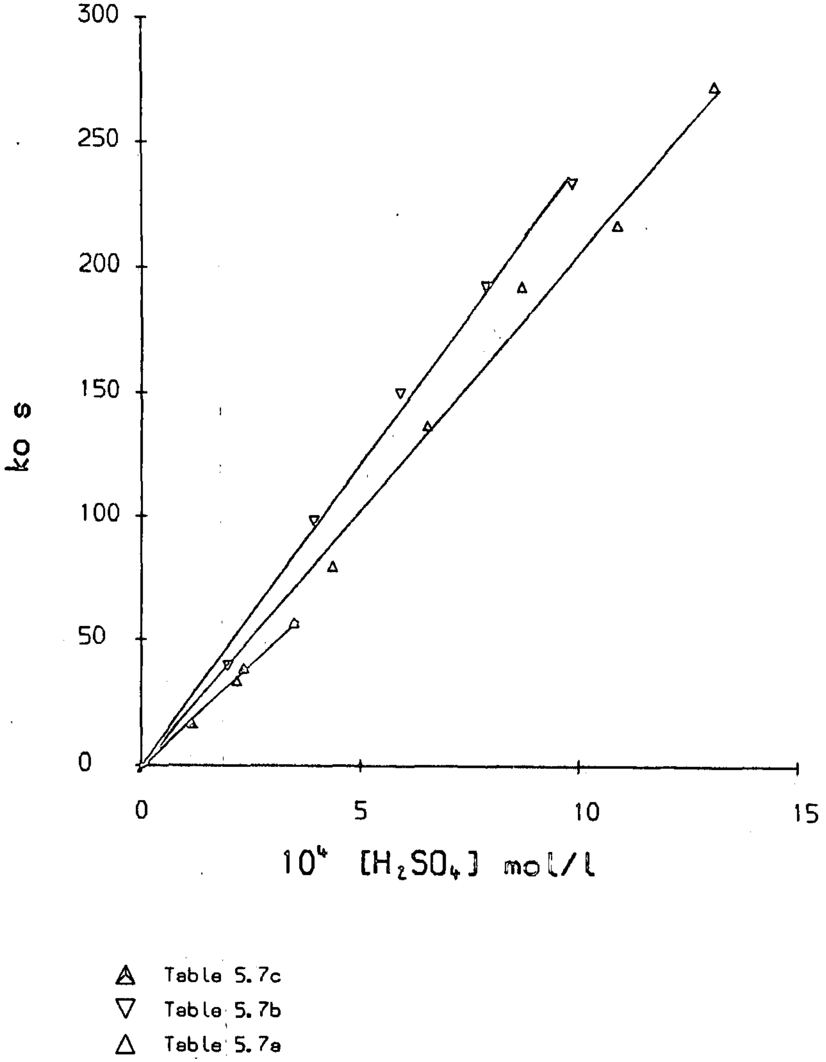


Figure 5.1

Variation of ko with acid



hydroxide solution. This effect will be discussed in section 5.5, but indicates that the reaction is probably subject to catalysis by hydrogen ions rather than by H_2SO_4 molecules. The data in all the other tables were obtained with freshly prepared solutions of sulphuric acid and were used within 6-8 hours of preparation, where this 'ageing effect' is not significant. This is shown by the reasonable agreement between the three sets of data in Figure (5.1).

When the data for the three different alkyl nitrites are plotted (Figure 5.2) it can be seen that the reactivity order towards formation of MeONO is ^{t}BuONO $>$ ^{i}PrONO $>$ ^{iso}AmONO, the relative reactivity order being approximately 3 : 1.5 : 1 .

Strikingly the reactions of ^{t}BuONO and ^{i}PrONO were found to be completely zero order with respect to [MeOH]. Results are shown in Tables (5.11) and (5.12).

The zero order dependence of the rate upon [MeOH] suggests that the rate limiting step occurs before the attack of the nitrosating species on MeOH. Two possible explanations exist. The first explanation is that the protonated alkyl nitrite is the reactive species and that the rate limiting step is protonation of the alkyl nitrite (Scheme 5.7)

Table 5.11:

Variation of ko with [MeOH] for reaction of ^{t}BuONO

[^{t}BuONO] = 0.010 mol l^{-1} [H_2SO_4] = 2.18 x 10^{-3} mol l^{-1}

400 nm 25°C

[MeOH] mol l^{-1}	ko s^{-1}
0.0233	31.7 ± 0.7
0.0466	35.8 ± 1.2
0.0699	31.5 ± 1.4
0.0933	32.2 ± 0.5
0.117	33.3 ± 0.5

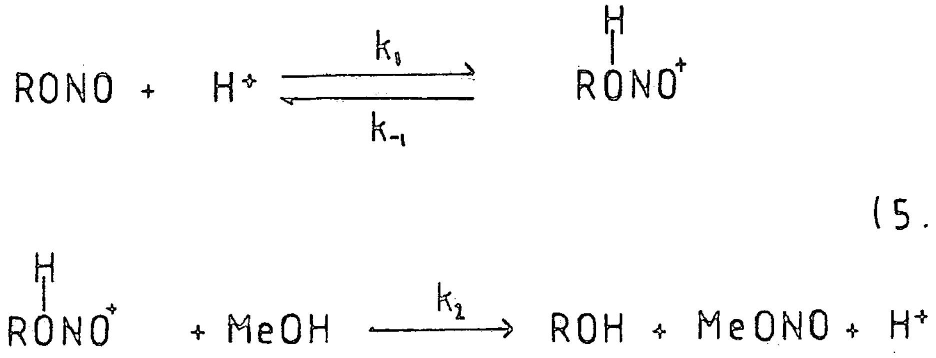
Table 5.12:

Variation of ko with [MeOH] for reaction of ^{i}PrONO

[^{i}PrONO] = 5 x 10^{-3} mol l^{-1} [H_2SO_4] = 1.43 x 10^{-3} mol l^{-1}

400 nm 25°C

[MeOH] mol l^{-1}	ko s^{-1}
0.0434	11.9 ± 0.3
0.0651	12.9 ± 0.3
0.0996	11.5 ± 0.2
0.199	9.3 ± 0.4
0.299	7.5 ± 0.1



$$\mathrm{RONO} + \mathrm{H^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{R\overset{H}{O}NO^+}$$

$$\mathrm{R\overset{H}{O}NO^+} + \mathrm{MeOH} \xrightarrow{k_2} \mathrm{ROH} + \mathrm{MeONO} + \mathrm{H^+}$$

(5.7)

Since the equilibrium constants for the formation of MeONO are large, under the conditions used the reaction can be considered to be effectively irreversible. If the value of k_2 [MeOH] $\gg$ k_{-1} then the rate determining step will become protonation of alkyl nitrite. If this is the case then a primary kinetic isotope effect ($k_H/k_D > 1$) would be expected. Experiments were carried out using D_2SO_4 in acetonitrile as catalyst in the reactions of ^{t}BuONO and ^{i}PrONO with MeOD. The results are shown in Tables (5.13) - (5.14).

The results are displayed in Figure (5.3), along with the results obtained using H_2SO_4. It is clear that the reaction is slightly faster in D_2SO_4 than H_2SO_4 indicating that proton transfer is not involved in the rate determining step. These results therefore rule out the mechanism in Scheme (5.7). Again in these experiments there is a considerable 'ageing effect' of the acid solution such that when the experiments were repeated after 6 days the value of ko had dropped by a factor of ca 10 (Table 5.13 (c)).

Table 5.13 (a):

Effect of D_2SO_4 on ko for reaction of ^tBuONO

$[^tBuONO]$ = 0.010 mol l^{-1} $[MeOD]$ = 0.114 mol l^{-1}

400 nm 25°C

$[D_2SO_4]$ mol l^{-1}	ko s^{-1}
2.65×10^{-3}	54.4 ± 3.0
5.30×10^{-3}	129 ± 2
7.96×10^{-3}	201 ± 6
0.0106	284 ± 12
0.0133	369 ± 25

Table 5.13 (b):

Effect of D_2SO_4 on ko for reaction with ^tBuONO

$[^tBuONO]$ = 0.010 mol l^{-1} $[MeOD]$ = 0.130 mol l^{-1}

400 nm 25°C

$[D_2SO_4]$ mol l^{-1}	ko s^{-1}
1.82×10^{-3}	36.8 ± 1.1
	38.1 ± 1.8✲
3.65×10^{-3}	76.8 ± 2.4
5.27×10^{-3}	124 ± 4

✲ $[MeOD]$ = 0.0652 mol l^{-1}

Table 5.13 (c):

Effect of D_2SO_4 after 6 days for reaction with ^tBuONO

[^tBuONO] = 0.010 mol l^{-1} [MeOD] = 0.114 mol l^{-1}

400 nm 25°C

[D_2SO_4] mol l^{-1}	ko s^{-1}
5.30×10^{-3}	15.8
0.0106	24.8
0.0133	32.0

Table 5.14:

Effect of D_2SO_4 on ko for reaction with ^iPrONO

[^iPrONO] = 0.010 mol l^{-1} [MeOD] = 0.114 mol l^{-1}

400 nm 25°C

[D_2SO_4] mol l^{-1}	ko s^{-1}
4.86×10^{-3}	61.6 ± 3.2
9.72×10^{-3}	142 ± 8
0.0146	188 ± 7

Figure 5.4

Effect of added alcohol on ko

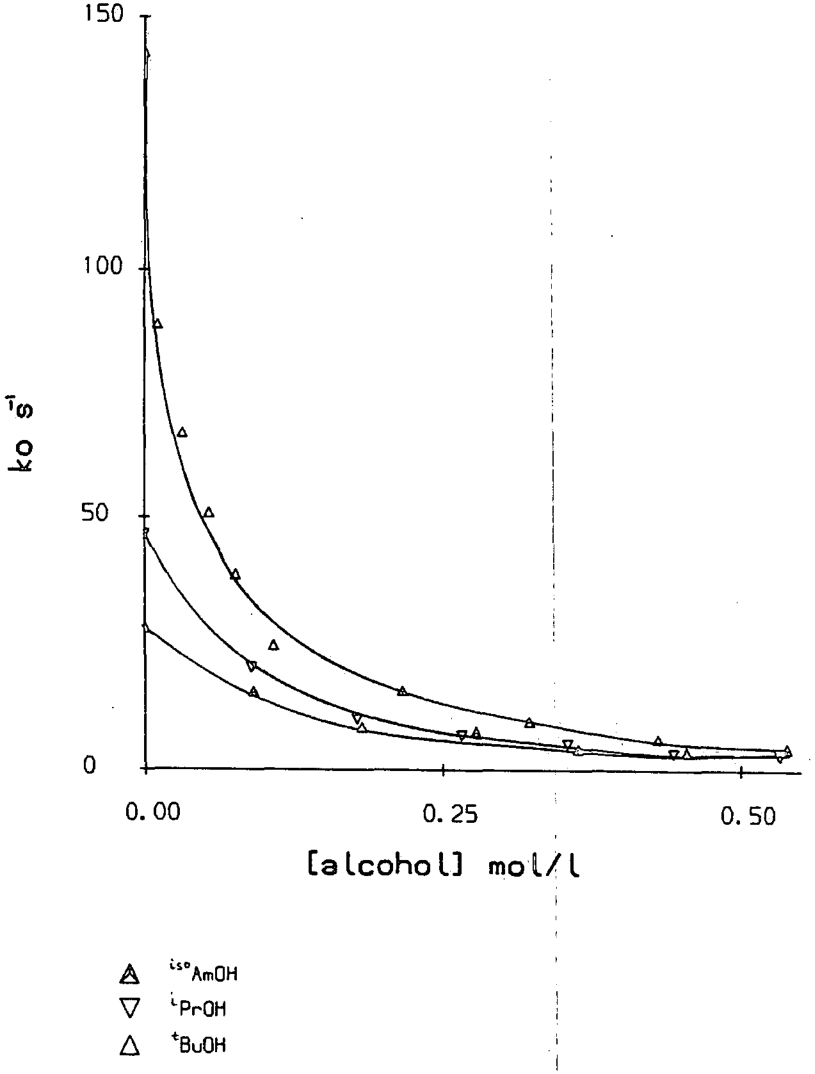
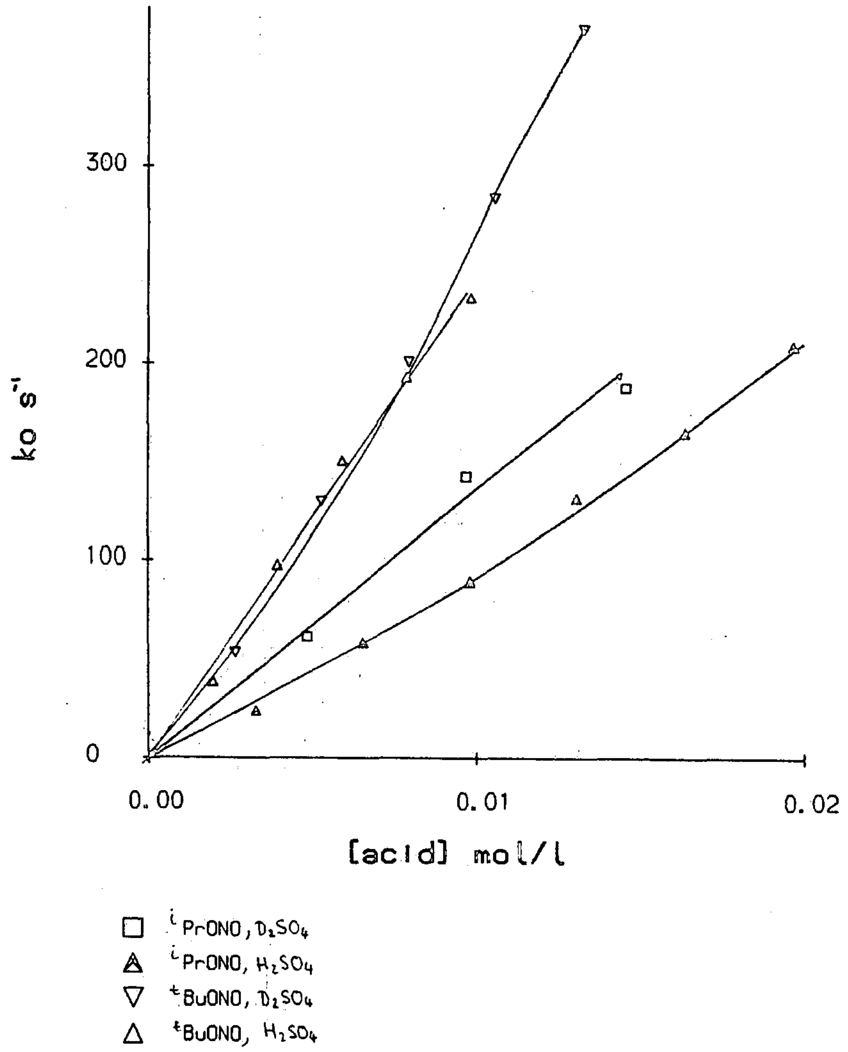
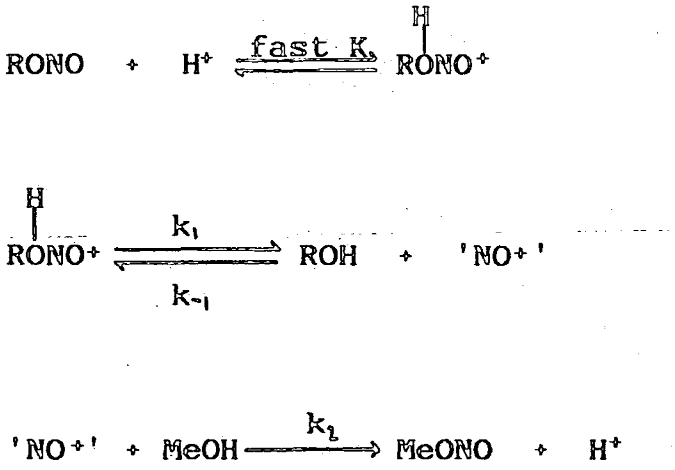


Figure 5.3

Deuterium isotope effect



An alternative explanation is that the rate limiting step is the formation of a nitrosating agent from the protonated alkyl nitrite (Scheme 5.8)



$$\mathrm{RONO} + \mathrm{H^+} \xrightleftharpoons{\text{fast } K} \mathrm{R\overset{H}{O}NO^+}$$

$$\mathrm{R\overset{H}{O}NO^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ROH} + \mathrm{'NO^+'} \qquad (5.8)$$

$$\mathrm{'NO^+'} + \mathrm{MeOH} \xrightarrow{k_2} \mathrm{MeONO} + \mathrm{H^+}$$

The nitrosating species is written here as NO^+, but other possibilities exist, namely nitrous acid or the nitrous acidium ion, which could be formed if there are traces of water in the solvent. The derived rate equation for Scheme (5.8) is given in equation (5.9).

$$ko = \frac{k_1 k_2 K\ [H^+][MeOH]}{k_{-1}[{}^tBuOH] + k_2[MeOH]} \qquad (5.9)$$

This predicts that if $k_2[MeOH] \gg k_{-1}[{}^tBuOH]$ then $ko = k_1 K[H^+]$ and so the rate constant would be independent of [MeOH].

The reaction rate constant was found to decrease markedly on the addition of the parent alcohol. The results for the three alkyl nitrites are shown in Tables (5.15) - (5.17) and Figure (5.4).

Table 5.15:

Effect of ^{t}BuOH on the rate of nitrosation by ^{t}BuONO

[^{t}BuONO] = 0.010 mol l^{-1} [MeOH] = 0.113 mol l^{-1}

[H_2SO_4] = 6.84 x 10^{-3} mol l^{-1} 400 nm 25°C

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0	143 ± 2
0.0108	88.9 ± 2.1
0.0323	67.2 ± 1.2
0.0539	51.2 ± 1.0
0.0755	39.1 ± 0.5
0.108	25.1 ± 0.3
0.216	16.0 ± 0.4
0.323	9.8 ± 0.2
0.431	6.3 ± 0.1
0.539	4.5 ± 0.1

Table 5.16:

Effect of ^{i}PrOH on the rate of nitrosation by ^{i}PrONO

[^{i}PrONO] = 0.010 mol l^{-1} [MeOH] = 0.113 mol l^{-1}

[H_2SO_4] = 6.84 x 10^{-3} mol l^{-1} 400 nm 25°C

[^{i}PrOH] mol l^{-1}	ko s^{-1}
0	46.6 ± 1.0
0.0887	20.6 ± 0.4
0.178	10.3 ± 0.2
0.266	7.0 ± 0.1
0.355	5.22 ± 0.12
0.444	3.41 ± 0.03
0.532	2.99 ± 0.04

Table 5.17:

Effect of ^{iso}AmOH on the rate of nitrosation by ^{iso}AmONO

[^{iso}AmOH] = 0.010 mol l^{-1} [MeOH] = 0.128 mol l^{-1}

[H_2SO_4] = 6.84 x 10^{-3} mol l 400 nm 25°C

[^{iso}AmOH] mol l^{-1}	ko s^{-1}
0	28.5 ± 0.2
0.0909	15.8 ± 0.1
0.182	8.59 ± 0.10
0.278	7.81 ± 0.04
0.364	4.27 ± 0.10
0.455	3.72 ± 0.15

Further in the presence of high concentrations of ^{t}BuOH or ^{i}PrOH the reaction was found to be no longer zero order with respect to [MeOH] (Tables 5.18 and 5.19).

Table 5.18:

Effect of [MeOH] in the presence of ^{t}BuOH

[^{t}BuOH] = 5 x 10^{-3} mol l^{-1} [H_2SO_4] = 1.43 x 10^{-3} mol l^{-1}

[^{t}BuOH] = 0.414 mol l^{-1} 400 nm 25°C

[MeOH] mol l^{-1}	ko s^{-1}
0.0417	0.788 ± 6 x 10^{-3}
0.0626	0.944 ± 0.017
0.0958	1.07 ± 0.05
0.192	1.33 ± 0.01
0.287	1.52 ± 0.04

Table 5.19:

Effect of [MeOH] in the presence of ^{i}PrOH

[^{i}PrONO] = 5 x 10^{-3} mol l^{-1} [^{i}PrOH] = 0.444 mol l^{-1}

[H_2SO_4] = 1.43 x 10^{-3} mol l^{-1} 400 nm 25°C

[MeOH] mol l^{-1}	ko s^{-1}
0.0434	0.704 ± 0.050
0.0651	0.789 ± 0.055
0.0996	0.969 ± 0.047
0.199	1.18 ± 0.04
0.299	1.26 ± 0.02

This is to be expected as equation (5.9) predicts that the rate constant should decrease on addition of ROH and should become first order in [MeOH], ie $k_{-1}[{}^{t}BuOH]$ can be made to compete with k_2[MeOH]. This means that the reaction under these conditions must be considered to be reversible (Scheme 5.10). The derived rate equation for such a scheme is given in equation (5.11).

$$\begin{aligned} &RONO + H^{+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} ROH + \text{'}NO^{+}\text{'} \\ &\text{'}NO^{+}\text{'} + MeOH \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} MeONO + H^{+} \end{aligned} \qquad (5.10)$$

$$ko = \frac{k_1 k_2[H^{+}][MeOH]}{k_{-1}[ROH] + k_2[MeOH]} + \frac{k_{-1} k_{-2}[H^{+}][ROH]}{k_{-1}[ROH] + k_2[MeOH]} \qquad (5.11)$$

The first term in equation (5.11) corresponds to the rate of nitrosation of MeOH by the alkyl nitrite and the second term corresponds to the rate of nitrosation of ROH by methyl nitrite. If the first term is much larger than the second term, as it must be due to the size of the equilibrium constant, it can be seen to a first approximation that if k_{-1} [ROH] $\approx$ k_2[MeOH] the rate constant should decrease on addition of ROH and should increase on addition on MeOH.

The observed first order rate constant was also found to decrease on addition of water. The results are shown in Table (5.20). The effect possibly results

Table 5.20:

Effect of water on ko for reaction with ^{t}BuONO

[^{t}BuONO] = 0.010 mol l^{-1} [MeOH] = 0.110 mol l^{-1}

[H_2SO_4] = 1.08 x 10^{-3} mol l^{-1} 400 nm 25°C

[H_2O] mol l^{-1}	ko s^{-1}
0	13.4 ±0.2
0.0520	9.44 ±0.1
0.104	6.71 ±0.13
0.156	4.38 ±0.10
0.300	2.55 ±0.14

from the basicity of water in this solvent, ie. water reduces the hydrogen ion activity in this solvent. This explanation has also been given to explain a similar effect in the reactions of alkyl nitrites in alcohol solvent [5,6]. The decrease in ko on addition of ROH could therefore be explained in a similar way and this possibility is discussed further in Section 5.5.

All the data obtained for the reactions of the three alkyl nitrites are consistent with a mechanism involving rate limiting formation of a nitrosating agent, possibly NO^+, followed by a rapid nitrosation of methanol. The reactivity order is $^{t}BuONO > {}^{i}PrONO > {}^{iso}AmONO$.

5.3 Kinetics and mechanism of the nitrosation of thioglycolic acid in acetonitrile

In view of the zero order dependence upon [Substrate] in the nitrosation of MeOH it was thought to be of interest to see if a similar effect was observed with other substrates. Thioglycolic acid [7] (TGA) was chosen as this had proved to be a suitable substrate in both aqueous and alcohol solution. Reactions were carried out in acetonitrile at 25°C. Good first order behaviour was obtained under the conditions used ([RONO]<<[TGA]), by following the appearance of the thionitrite at 330 nm. The value of ko was found to be independent of [TGA] at high [TGA] for all three alkyl nitrites studied ($^{t}BuONO$, $^{i}PrONO$, $^{iso}AmONO$). The results are given in Tables (5.21) - (5.23). The slight upward trend in ko as [TGA] is increased is probably due to the fact that TGA will

Table 5.21 (a):

Effect of [TGA] on ko for reaction with ${}^tBuONO$

$[{}^tBuONO] = 2 \times 10^{-4}$ mol l^{-1} $[H_2SO_4] = 2.33 \times 10^{-3}$ mol l^{-1}

[TGA] mol l^{-1}	ko s^{-1}
4.73×10^{-3}	27.9 ± 1.4
9.46×10^{-3}	38.7 ± 0.4
0.0142	37.1 ± 1.0

Table 5.21 (b):

Effect of [TGA] on ko for reaction with ${}^tBuONO$

$[{}^tBuONO] = 1 \times 10^{-4}$ mol l^{-1} $[H_2SO_4]^{*} = 6.84 \times 10^{-3}$ mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
1.14×10^{-3}	15.6 ± 0.9
2.29×10^{-3}	18.0 ± 0.5
4.58×10^{-3}	20.2 ± 1.1
9.15×10^{-3}	21.0 ± 0.4
0.0137	22.2 ± 0.9
0.0183	23.8 ± 0.5
0.0229	23.1 ± 0.8

* Acid solution was three days old

Table 5.22:

Effect of [TGA] on ko for reaction with ^{i}PrONO

[^{i}PrONO] = 2 x 10^{-4} mol l^{-1} [H_2SO_4] = 5.61 x 10^{-4} mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
5.85 x 10^{-3}	3.08 ± 0.12
0.0117	2.97 ± 0.087
0.0176	2.99 ± 0.06

Table 5.23:

Effect of [TGA] on ko for reaction with ^{iso}AmOH

[H_2SO_4] = 3.07 x 10^{-4} mol l^{-1} [^{iso}AmONO] = 1 x 10^{-4} mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
8.67 x 10^{-3}	0.604 ± 0.015
0.0260	0.828 ± 0.036
0.0347	0.889 ± 0.029
0.0434	0.924 ± 0.029
0.0607	1.06 ± 0.02

act as a weak acid in these solutions, so increasing the hydrogen ion activity. It can also be seen that the reaction is subject to the same 'ageing effect' of the sulphuric acid solutions as was the case with the methanol reactions. This can be seen by comparing the results for the reaction of ^tBuONO using fresh H_2SO_4 (Table 5.21 (a)) and using three day old H_2SO_4 (Table 5.21 (b)). In all cases the reaction was subject to acid catalysis. Results are shown in Table (5.24)-(5.26) and in Figure (5.5).

Table 5.24:

Catalysis by H_2SO_4 in the reaction with ^tBuONO

$[^tBuONO] = 2 \times 10^{-4}$ mol l^{-1} $[TGA] = 0.0122$ mol l^{-1}

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
9.27×10^{-4}	14.3 ± 0.1
1.85×10^{-3}	33.3 ± 0.7
2.78×10^{-3}	45.7 ± 0.8
3.71×10^{-3}	60.7 ± 1.4
5.56×10^{-3}	105 ± 8

Table 5.25:

Catalysis by H_2SO_4 in the reaction with $^{i}PrONO$

$[^{i}PrONO] = 2 \times 10^{-4}$ mol l^{-1} $[TGA] = 0.0117$ mol l^{-1}

330 nm 25°C

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
2.80×10^{-4}	1.13 ± 0.02
5.61×10^{-4}	2.97 ± 0.09
8.41×10^{-4}	4.59 ± 0.05
1.12×10^{-3}	6.73 ± 0.10
1.40×10^{-3}	8.20 ± 0.21

Table 5.26:

Catalysis by H_2SO_4 in the reaction with $^{iso}AmONO$

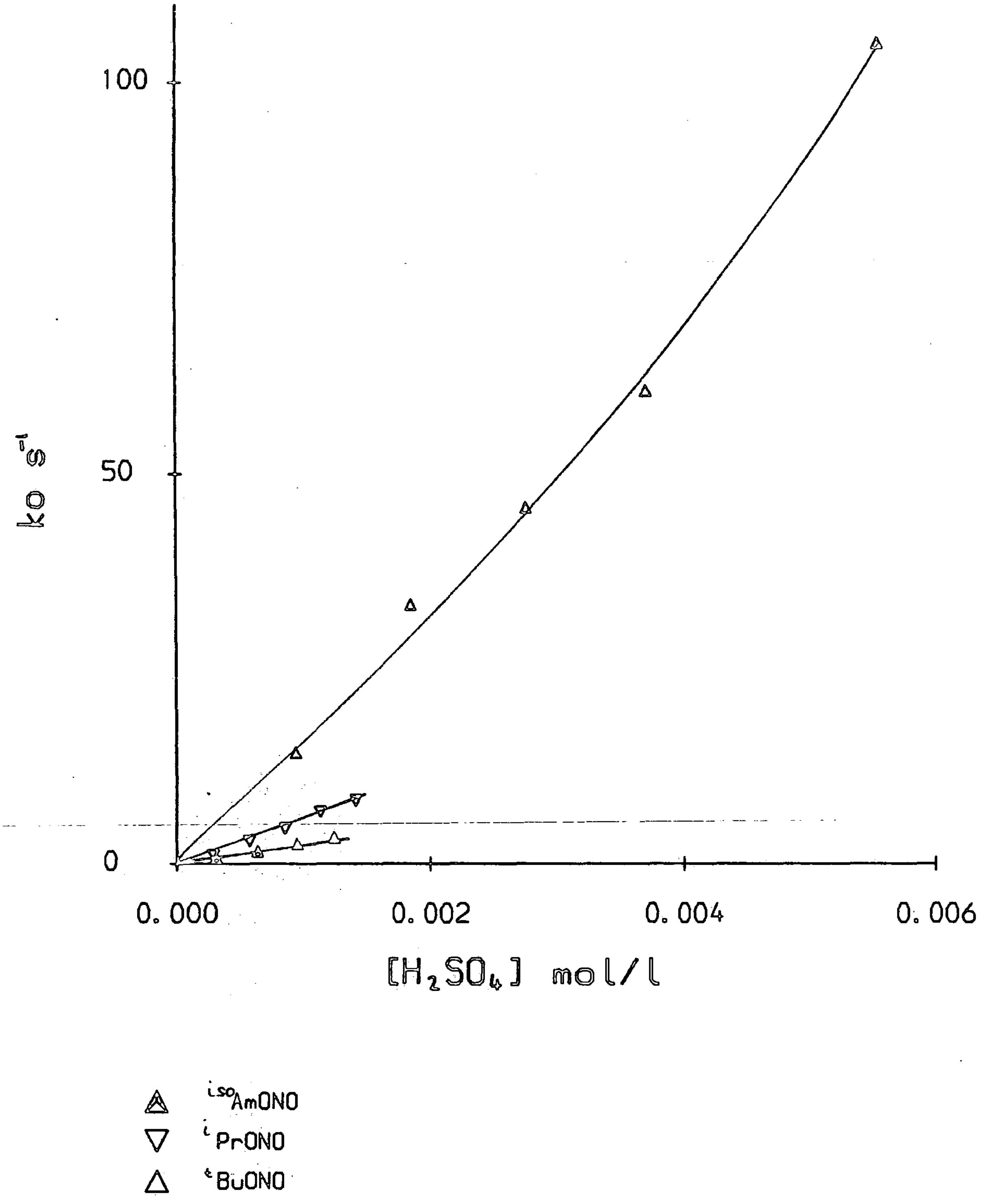
$[^{iso}AmONO] = 1 \times 10^{-4}$ mol l^{-1} $[TGA] = 0.0260$ mol l^{-1}

330 nm 25°C

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
3.07×10^{-4}	0.828 ± 0.036
6.15×10^{-4}	1.65 ± 0.03
9.22×10^{-4}	2.62 ± 0.05
1.23×10^{-3}	3.46 ± 0.03

Figure 5.5

Acid catalysis in the nitrosation of TGA



Since the rate constant for reaction is independent of the [TGA], this again implies that the rate determining step is the formation of the nitrosating species from the protonated alkyl nitrite, the k_1 step (scheme 5.12).

$$\mathrm{RONO} + \mathrm{H^+} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathrm{ROH} + \mathrm{'NO^{+}'}$$

$$\mathrm{NO^+} + \mathrm{RSH} \xrightarrow{k_2} \mathrm{RSNO} + \mathrm{H^+} \qquad (5.12)$$

The rate of this step would be expected to be different for different alkyl nitrites but should only depend on the acidity of the medium, and not on the substrate used, for any one alkyl nitrite. By comparison of the limiting rates of reaction at the same acidity this can be seen to be the case. Thus for ^{t}BuONO at [H_2SO_4] = 2.33 x 10^{-3} mol l^{-1} the limiting value of ko is ca. 38 s^{-1} with TGA as substrate and the value of ko measured using the same sulphuric acid solution with methanol is 38.4 ± 1.9 s^{-1} ([MeOH]=0.110 mol l^{-1} , [^{t}BuONO]=0.01 mol l^{-1}). Similarly for ^{i}PrONO the limiting values obtained by using MeOH and TGA are identical (Table 5.27)

As expected the rate constant for reaction of ^{t}BuONO with TGA was found to decrease markedly on the addition of ^{t}BuOH. In the presence of ^{t}BuOH the reaction became no longer zero order with respect to [TGA], again as for the reactions with methanol. The results are shown in Table (5.28)

Table 5.27:
Limiting values of ko for reaction of ^{i}PrONO

$[H_2SO_4] = 4.56 \times 10^{-3} mol\ l^{-1}$

[MeOH] mol l^{-1}	ko s^{-1}	[TGA] mol l^{-1}	ko s^{-1}
0.07	31.5 ± 4.9	0.03	30.1 ± 0.7
0.14	32.8 ± 2.5	0.06	31.9 ± 0.4

These results therefore add weight to the argument in favour of a reaction mechanism involving rate limiting formation of a nitrosating species, possibly nitrous acid (by analogy with the reactions in water) or the nitrosonium ion. In order to try to distinguish between these two possibilities the reaction of ^{i}PrONO with added water was studied.

In the reactions so far studied, traces of water will always be present in the solvent (even though it was dried and distilled prior to use) and also due to the fact that traces will be added due to the H_2SO_4 catalyst.

Table 5.28:

Effect of [TGA] in the presence of ^{t}BuOH

[^{t}BuONO] = 1 x 10^{-4} mol l^{-1} [H_2SO_4] = 1.45 x 10^{-3} mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1} a	 b	 c
4.06 x 10^{-3}	13.6 ± 0.1	0.0505 ± 7 x 10^{-4}	0.0127 ± 5 x 10^{-4}
8.11 x 10^{-3}	15.5 ± 0.2	0.0820 ± 1.1 x 10^{-3}	0.0176 ± 2 x 10^{-4}
0.0122	16.1 ± 0.3	0.103 ± 4 x 10^{-3}	0.0255 ± 5 x 10^{-4}
0.0162	17.8 ± 0.2	0.141 ± 3 x 10^{-3}	0.0308 ± 3 x 10^{-4}
0.0203	20.6 ± 0.2	0.156 ± 8 x 10^{-3}	0.0381 ± 9 x 10^{-4}

a) [^{t}BuOH] = 0

b) [^{t}BuOH] = 0.216 mol l^{-1}

c) [^{t}BuOH] = 0.431, [H_2SO_4] solution is 24 hrs old

This was shown by the fact that ^{i}PrONO, when mixed with the sulphuric acid solutions rapidly produced an equilibrium concentration of nitrous acid, as detected spectrophotometrically. This reaction was studied kinetically at 410 nm, following the disappearance of the alkyl nitrite. Good first order behaviour was observed in all cases. The results are shown in Table (5.29).

Table 5.29:

Nitrosation of water by ^{i}PrONO

$[H_2SO_4]$ = 1.61 x 10^{-3} mol l^{-1} $[^{i}PrONO]$ = 0.04 mol l^{-1}

410 nm 25°C

$[H_2O]$ mol l^{-1}	ko s^{-1}
0	22.3 ± 1.4
0.0555	23.4 ± 0.4
0.111	21.5 ± 1.2
0.277	7.4 ± 0.3
1.111	1.73 ± 0.03

Above $[H_2O]$ ≃ 1.1 mol l^{-1} the reactions were no longer first order with respect to ^{i}PrONO and were not investigated further.

The results show that at low [H_2O] the reaction is independent of [H_2O], but the value of ko found is higher than those previously found, ie. ko ≃ 22 s^{-1} at [H_2SO_4] = 1.61 x 10^{-3} mol l^{-1} compared with ko ≃ 31 s^{-1} at [H_2SO_4] = 4.56 x 10^{-3} mol l^{-1} for the reaction of ^{i}PrONO with MeOH and TGA. This discrepancy probably arises from the fact that the reaction with water is significantly reversible under the conditions used (as detected by a marked increase in the absorbance change as [H_2O] is increased). This means that the value of ko will contain significant contributions from both the rate of nitrosation of H_2O by ^{i}PrONO and also the rate of nitrosation of ^{i}PrOH by HNO_2 (cf. equation (5.11)). The decrease in ko with [H_2O] when [H_2O] > 0.1 mol l^{-1} can be attributed to a medium effect as described previously. These results show that under the conditions used in all the nitrosation experiments in acetonitrile the presence of water can lead to the formation of nitrous acid. These results however do not necessarily prove that the nitrosating species formed in the rate limiting step in the reactions of alkyl nitrites is nitrous acid.

The reaction of ^{i}PrONO with TGA also occurs without the addition of any external acid (TGA is itself an acid). Experiments were carried out using (a) acetonitrile that was specially dried and used under a dry nitrogen atmosphere, and (b) acetonitrile that was purified by the usual procedure [8] (see Chapter 7). The results are shown in Table 5.30. These show that the reaction

Table 5.30:

Reaction in 'Super dry' acetonitrile

$[TGA] = 7.16 \times 10^{-3}$ mol l^{-1} $[{}^{i}PrONO] = 5 \times 10^{-6}$ mol l^{-1}

'super dry' acetonitrile ko = 3.6×10^{-6} s^{-1}
'normal' acetonitrile ko = 1.4×10^{-6} s^{-1}

still proceeds readily even in the absence of traces of water, indicating that the rate limiting step is unlikely to be formation of HNO_2, rather it is more likely to be formation of NO^+.

Further evidence of this comes from the fact that the reaction was markedly catalysed by a solution containing dry HCl gas in CH_3CN (Table 5.31). The reaction was found to be zero order with respect to [TGA], indicating that the rate limiting step is again formation of a nitrosating species.

Table 5.31:

Effect of HCl on rate of reaction of ^{i}PrONO with TGA

[^{i}PrONO] = 2 x 10^{-6} mol l^{-1} [TGA] = 0.0114 mol l^{-1}

330 nm 25°C

[HCl] mol l^{-1}	ko s^{-1}
7.82 x 10^{-4}	1.36 ± 0.05
1.57 x 10^{-3}	3.16 ± 0.07
2.35 x 10^{-3}	4.66 ± 0.37
3.13 x 10^{-3}	6.27 ± 0.07
4.70 x 10^{-3}	9.29 ± 0.22

Table 5.32:

Dependence of ko on [TGA]

[^{i}PrONO] = 2 x 10^{-4} mol l^{-1} [HCl] = 2.35 x 10^{-3} mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
5.7 x 10^{-3}	4.15 ± 0.04
0.0114	4.66 ± 0.37
0.0171	3.95 ± 0.05

5.4 Kinetics and mechanism of the reaction of nitrous acid in acetonitrile

In order to obtain further evidence for the identity of the active nitrosating agent in these solutions, the reactions of nitrous acid itself were studied under similar conditions to those used for the alkyl nitrites. Solutions of nitrous acid in acetonitrile were formed by addition of sulphuric acid in acetonitrile to a solution of sodium nitrite in acetonitrile. The presence of nitrous acid was identified by the characteristic 'finger' absorbtion bands in the 330 - 400 nm region [9]. The exact concentration of nitrous acid used in the kinetic experiments was difficult to determine due to the very low solubility of sodium nitrite. Nitrous acid was reacted with MeOH (to form MeONO), ^{i}PrOH (to form ^{i}PrONO), ^{t}BuOH (to form ^{t}BuONO) and TGA (to form S-nitrosothioglycolic acid). In all cases good first order behaviour was found by following the appearance of the product when the reactions were carried out with $[HNO_2] \ll [\text{Substrate}]$. The results are shown in Tables (5.33) - (5.36).

For MeOH, ^{i}PrOH and TGA, the reaction is zero order in [Substrate], within the experimental error. For ^{t}BuOH the value of ko decreases slightly as [^{t}BuOH] is increased. This probably arises due to a medium effect and will be discussed later. The limiting rate constant

Table 5.33:

Variation of ko with [MeOH] for reaction with HNO_2

$[NaNO_2] < 10^{-6}$ mol l^{-1} $[H_2SO_4] = 8.68 \times 10^{-4}$ mol l^{-1}

260 nm 25°C

[MeOH] mol l^{-1}	ko s^{-1}
9.96×10^{-3}	21.9 ± 0.9
0.0199	21.2 ± 1.2
0.0249	26.9 ± 2.7
0.0498	24.8 ± 1.9
0.0767	22.8 ± 1.1

Table 5.34:

Variation of ko with [^{i}PrOH] for reaction with HNO_2

$[NaNO_2] < 10^{-6}$ mol l^{-1} $[H_2SO_4] = 8.68 \times 10^{-4}$ mol l^{-1}

260 nm 25°C

[^{i}PrOH] mol l^{-1}	ko s^{-1}
0.0149	24.6 ± 1.3
0.0298	30.6 ± 1.9
0.0446	26.0 ± 1.3
0.0593	22.7 ± 1.3
0.0744	21.9 ± 1.1

Table 5.35:

Variation of ko with [^{t}BuOH] for reaction with HNO_2

$[NaNO_2] < 10^{-6}$ mol l^{-1} $[H_2SO_4] = 8.46 \times 10^{-6}$ mol l^{-1}

260 nm 25°C

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0.0161	23.5 ± 0.6
0.0323	16.3 ± 0.5
0.0484	14.3 ± 0.4

Table 5.36 (a):

Variation of ko with TGA for reaction with HNO_2

$[NaNO_2] < 10^{-6}$ mol l^{-1} $[H_2SO_4] = 8.46 \times 10^{-6}$ mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
8.87×10^{-3}	15.8 ± 0.6
0.0177	19.6 ± 0.4
0.0266	21.7 ± 0.4
0.0443	23.4 ± 0.5

Table 5.36 (b):

Variation of ko with TGA for reaction with HNO_2

$[NaNO_2] < 10^{-6}$ mol l^{-1} $[H_2SO_4] = 6.20 \times 10^{-3}$ mol l^{-1}

330 nm 25°C

[TGA] mol l^{-1}	ko s^{-1}
5.36×10^{-3}	254 ± 16
0.0107	278 ± 25
0.0161	283 ± 24
0.0443	349 ± 16

is the same for all the substrates at the same acidity (assuming that the value of ko at $[^{t}BuOH] = 0.0161$ mol l^{-1} represents the limiting rate). This means that the reaction proceeds via rate limiting formation of the nitrosonium ion from nitrous acid (Scheme 5.13). The rate

$$HNO_2 + H^+ \overset{K}{\rightleftharpoons} H_2NO_2^+$$

$$H_2NO_2^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2O + NO^+ \qquad (5.13)$$

$$NO^+ + S \xrightarrow{k_2} Products$$

equation derived from Scheme (5.13) is equation (5.14).

$$ko = \frac{k_1[S][H^+]K}{k_{-1}[H_2O] + k_2[S]} \qquad (5.14)$$

If $k_2[S] \gg k_{-1}[H_2O]$, then $ko = k_1K[H^+]$ and so the rate limiting step becomes formation of the nitrosonium ion. This is directly analogous to the formation of the nitronium ion in nitration reactions using nitric acid [10]. Here the rate of nitration of reactive aromatic substrates, eg. toluene, was found to be zero order with respect to toluene. This occured in a variety of solvents, including nitromethane [11], concentrated sulphuric acid [12] and carbon tetrachloride [13]. The results identified the nitronium ion as the reactive species. The reaction scheme is shown in Scheme (5.15).

$$H_2SO_4 + HNO_3 \rightleftharpoons HSO_4^- + H_2NO_3^+$$

$$H_2NO_3^+ \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2O + NO_2^+ \qquad (5.15)$$

$$NO_2^+ + ArH \xrightarrow[\text{fast}]{k_2} \text{Products}$$

As would be expected the reactions of nitrous acid in acetonitrile are subject to acid catalysis. Results are shown in Table (5.37)

Table 5.37 (a):

Acid catalysis in the nitrosation of TGA

$[NaNO_2] < 10^{-4}$ mol l^{-1} [TGA] = 0.0177 mol l^{-1}

330 nm 25°C

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
8.46×10^{-4}	19.6 ± 0.4
1.69×10^{-3}	46.7 ± 1.5
2.54×10^{-3}	80.2 ± 4.3

Table 5.37 (b):

Acid catalysis in the nitrosation of TGA

$[NaNO_2] < 10^{-4}$ mol l^{-1} [TGA] = 0.0443 mol l^{-1}

330 nm 25°C

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
1.55×10^{-3}	71.7 ± 2.1
3.10×10^{-3}	159 ± 9
6.20×10^{-3}	349 ± 16

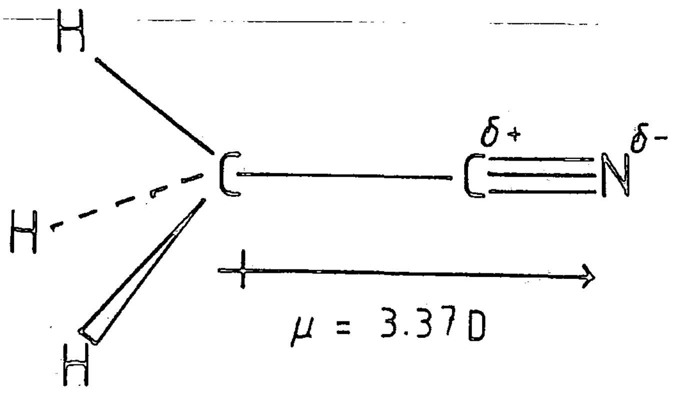
5.5 Discussion

5.5.1 Acid-base behaviour in acetonitrile

In order to try to understand the acid catalysis observed in these reactions, especially the 'ageing effects' of the solutions it is necessary to review some of the work previously reported on acid-base equilibria in acetonitrile [14].

Sulphuric acid [15], and strong acids in general, are known to be incompletely dissociated in this solvent. The one exception to this is perchloric acid [16], which is believed to exist completely in the dissociated form in this solvent. Because of the polar nature of acetonitrile (Figure 5.6), the solvent is very good at solvating

Figure 5.6



cations, but is only a poor solvator of anions, hence most anions in acetonitrile are stabilized by homoconjugation. The major dissociation equilibria of sulphuric acid [17] in this solvent are shown in equation (5.16). A similar series of equilibria exist for the hydrogen halides in this solvent [15] and the values of the equilibrium constants are shown in Table (5.38).

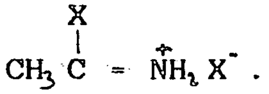
$$H_2SO_4 \overset{Ka}{\rightleftharpoons} H^+ + HSO_4^- \text{(acid dissociation)} \tag{5.16}$$

$$H_2SO_4 + HSO_4^- \overset{K}{\rightleftharpoons} H_2SO_4HSO_4^- \text{ (homoconjugation)}$$

Table 5.38:

Values of pKa and -pK in acetonitrile

Acid	-pK	pKa
Perchloric		2
Hydrobromic	2.4	5.5
Sulphuric	3.0	7.3
Nitric	2.3	8.9
Hydrochloric	2.2	8.9

Experiments have been carried out to measure the hydrogen ion activity of solutions of strong mineral acids in acetonitrile. In these experiments the measured hydrogen ion activity [17,22] was found to give drifting values over the first 30 minutes and then reached a steady value. Over a longer time scale the hydrogen ion activity was found to drop markedly over periods of months [16,18], even though the stoichiometric concentrations of acid (as determined by titration) remained constant over the same period. The initial increase can be explained [19,20] in terms of a slow equilibrium process of some kind, possibly involving proton transfer from the acid to the solvent or the formation of nitrilium-like salts, of empirical formula $CH_3CN.2HX$ or formation of salts of the type [19,20]  $CH_3\overset{\overset{X}{|}}{C}=\overset{+}{N}H_2X^-$. The decrease in hydrogen ion activity over a longer period of time was explained [15,16] in terms of the formation of a basic species in acetonitrile, possibly acetamide or a polymer of acetonitrile [18], which then reduces the hydrogen ion activity. Since the acid catalysis observed in the nitrosation reactions in acetonitrile follows this pattern it seems reasonable that the nitrosation reactions in acetonitrile are catalysed by the hydrogen ion.

The hydrogen ion must necessarily be solvated by acetonitrile molecules. It has been shown that acetonitrile [21] is a very weak base as compared to water and alcohols and so as the concentration of water or alcohol is increased the percentage of hydrogen ions associated with acetonitrile will drop and the percentage of hydrogen ions associated with water or alcohol will increase. This is probably the cause of the medium effect observed when water is added to the reaction medium, as a proton associated with a water molecule must necessarily be less acidic than one associated with acetonitrile. This may also occur to some extent when ^{t}BuOH is added to the solution as the results for nitrosation of ^{t}BuOH with HNO_2 (Table 5.35) show a marked decrease in rate with added ^{t}BuOH.

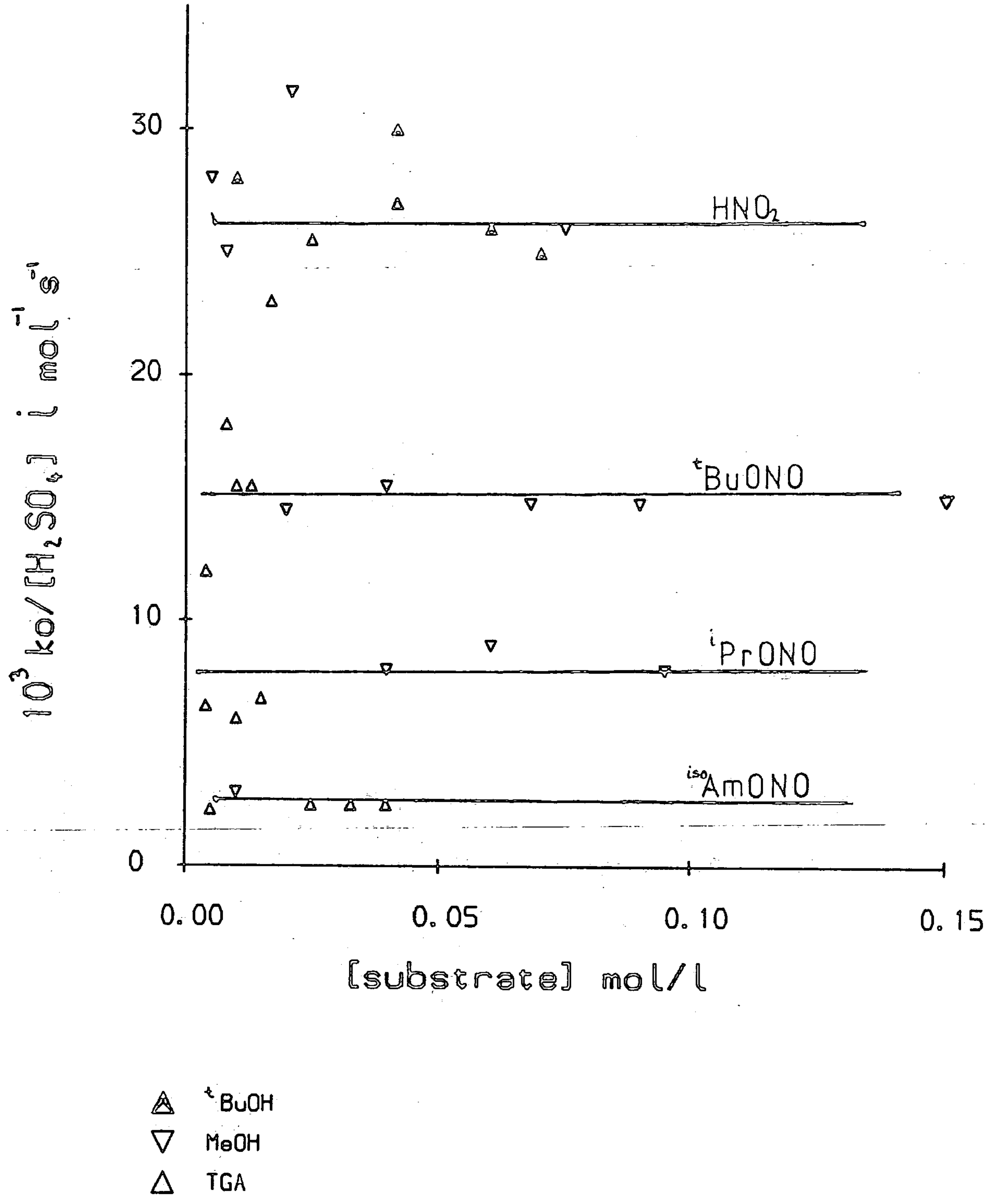
5.5.2 Mechanism of nitrosation in acetonitrile

The results found for nitrous acid nitrosations in acetonitrile show conclusively that the nitrosating species involved is the nitrosonium ion. The nitrosonium ion most likely exists in a solvated form by acetonitrile, but could also be solvated by the bisulphate ion that must be present in solution, ie. from nitrosyl sulphuric acid ($HSO_4^- NO^+$). By analogy with the reaction with HNO_2, the reactions of alkyl nitrites in this solvent are also likely to proceed via rate limiting formation of NO^+.

For all the nitrosating agents used the reactions with methanol and thioglycolic acid proceed via rate limiting formation of NO^+. This rate constant has been shown to be different for the four nitrosating agents used, but for each one it is independent of the nature and concentration of the substrate. Since the reaction is proportional to $[H^+]$ which will in turn be approximately proportional to $[H_2SO_4]$, the values of ko obtained at different acidities can be compared by simply dividing ko by $[H_2SO_4]$. This is only very approximate however since a plot of ko against $[H_2SO_4]$ is a slight curve in most cases, however the results of such an analysis are plotted in Figure (5.7). It can be seen that the value of ko / $[H_2SO_4]$ is approximately constant for each alkyl nitrite and nitrous acid and is not dependent on the substrate used. Further the approximate order of reactivity of HNO_2 : ^{t}BuONO : ^{i}PrONO : ^{iso}AmONO can be deduced as 6 : 3 : 1.5 : 1 . The reactivity order of the alkyl nitrites is easily explained in terms of steric effects, ie. ^{t}BuONO is more sterically crowded than ^{i}PrONO and so formation of the alcohol is favoured more in the case of ^{t}BuONO than ^{i}PrONO. The relative reactivity also includes the pKa of the alkyl nitrite and nitrous acid and since these are unknown it is not possible to comment on the actual rate constant for formation of NO^+ from the protonated alkyl nitrite or protonated nitrous acid.

Figure 5.7

Comparison of the limiting rate constants



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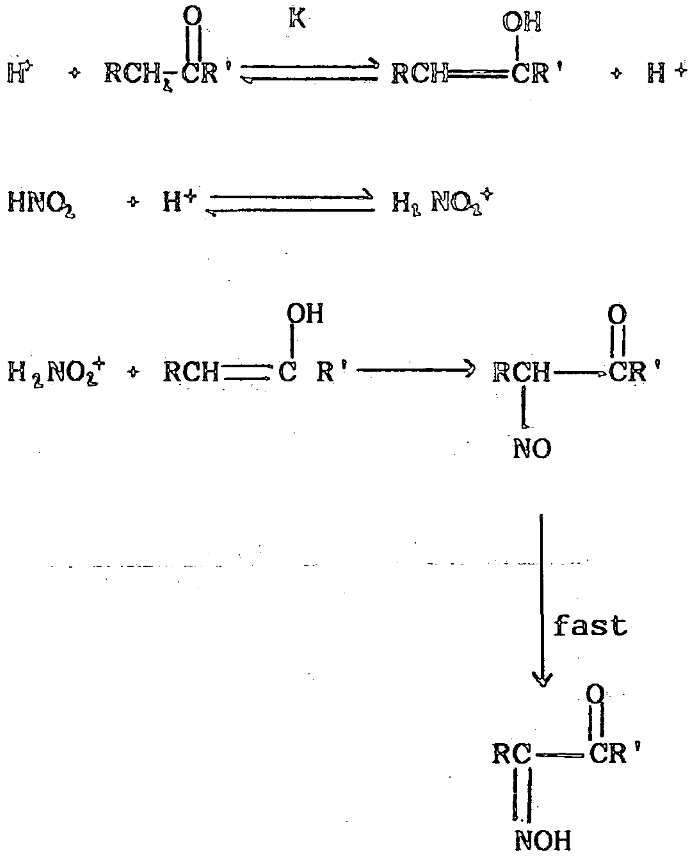
CHAPTER 6

NITROSATION OF AMINES AND KETONES IN ACETONITRILE

In Chapter 5, the reactions of alkyl nitrites and nitrous acid in acetonitrile were shown to be kinetically zero order with respect to [substrate], and were explained in terms of rate limiting formation of the nitrosonium ion. It was expected therefore, that with less reactive substrates the rate determining step might be the nitrosation of the substrate.

6.1 Nitrosation of ß-diketones

The reaction of ketones with nitrous acid have been long known synthetically [1], but it has only recently been shown that the reaction occurs via the enol form [2] (Scheme 6.1). The reactions yield the C-nitroso species, which under acid conditions rapidly isomerise to give the oxime products. The enol form of the ketone was identified [2] as the reactive species in these reactions because under certain experimental conditions the reactions became zero order with respect to the



$$H^+ + RCH_2\overset{\overset{O}{\|}}{C}R' \xrightleftharpoons{K} RCH{=}\overset{\overset{OH}{|}}{C}R' + H^+$$

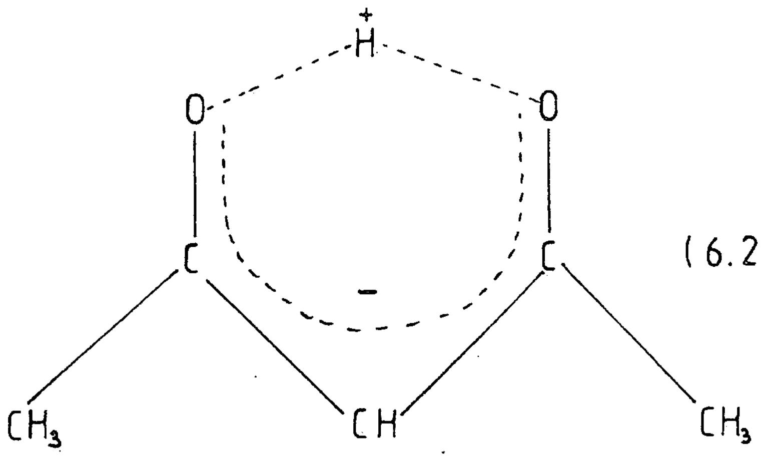
$$HNO_2 + H^+ \rightleftharpoons H_2NO_2^+$$

$$H_2NO_2^+ + RCH{=}\overset{\overset{OH}{|}}{C}\,R' \longrightarrow \underset{\underset{NO}{|}}{RCH}{-}\overset{\overset{O}{\|}}{C}R' \xrightarrow{fast} \underset{\underset{NOH}{\|}}{RC}{-}\overset{\overset{O}{\|}}{C}R'$$

(6.1)

nitrous acid concentration, indicating that the rate limiting step was enolization of the ketone. The measured rate constant for enolization was in good agreement with that obtained for halogenation [3] and hydrogen-exchange reactions [4]. In the case of acetylacetone it was not possible to make the enolization rate limiting due to the lower reactivity of the enol.

In solution, ketones exist in equilibrium with their enol forms. For most simple ketones the percentage of enol in aqueous solution is very small, whereas for ß-diketones much more enol exists, eg. for acetylacetone [5] K is 0.2. However in non-aqueous solutions the percentage [6,7,8] of the enol form is increased markedly. This is explained in terms of enhanced solvation of the most polar form (the ketoform) by the highly polar water molecules. In the case of ß-diketones [9,10] the enol form is stabilized by the formation of a six membered cyclic structure, as shown in equation (6.2).



(6.2)

This explains why in aqueous solution, although the K of acetylacetone is small, it is still many orders of magnitude greater than that of monoketones such as acetone and methylethyl ketone [11]. In non aqueous solution, where the keto form is not stabilized to the same extent as in aqueous solution, the percentage enol is increased markedly.

6.1.3 Nitrosation of acetylacetone in acetonitrile

The percentage enol of acetylacetone (AA) in acetonitrile was estimated from the N.M.R. spectrum. The ^{1}H chemical shifts relative to TMS are shown in Table (6.1) and the estimated percentage enol is ca 67% ($K_E = 2$)

Table 6.1:

^{1}H N.M.R. spectra of AA in CD_3CN

δ ppm	Relative intensity	assignment
1.58	6.0	CH_3 enol
1.76	3.0	CH_3 keto
3.18	1.0	CH_2 keto
5.16	1.0	CH enol

The reaction of acetylacetone with tertiary butyl nitrite (^{t}BuONO) was shown to yield the expected oxime by comparison with the U.V. /visible and infra red spectra of a sample prepared from nitrous acid. The reaction was followed kinetically at 375 - 380 nm where only the alkyl nitrite absorbs significantly. Good first order behaviour was obtained by monitoring the disappearance of the alkyl nitrite under the conditions where [^{t}BuONO]$\ll$[AA]. The reactions were found to be first order with respect to [AA] and also to be approximately first order with respect to [H_2SO_4]. The results are shown in Table (6.2) and (6.3). A plot of ko against [H_2SO_4] (Figure 6.1) shows no significant intercept.

Table 6.2:

Variation of ko with [AA]

[^{t}BuONO] = 2×10^{-3} mol l^{-1} [H_2SO_4] = 4.44×10^{-3} mol l^{-1}

380 nm 25°C

[AA] mol l^{-1}	ko s^{-1}
0.0202	0.922 ± 0.029
0.0808	2.21 ± 0.04
0.143	5.07 ± 0.19
0.287	10.9 ± 0.1
0.430	14.4 ± 0.4

slope = 34.6 ± 2.1 l mol^{-1} s^{-1}

intercept = 0.1 ± 0.5 s^{-1}

Table 6.3:

Variation of ko with [H_2SO_4]

[^{t}BuONO] = 1 x 10^{-3} mol l^{-1} [AA] = 0.0161 mol l^{-1}

375 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0117	3.94 ± 0.14
0.0234	10.4 ± 0.3
0.0351	16.6 ± 0.6
0.0468	22.3 ± 2.1
0.0585	31.6 ± 1.3

These results suggest that the rate determining step is the reaction of the nitrosating species with acetylacetone. The rate constant was also found to decrease markedly on the addition of ^{t}BuOH. Results are shown in Table (6.4).

This indicates that the alkyl nitrite itself is not the nitrosating agent and is consistent with the formation of an equilibrium concentration of the nitrosonium ion which then reacts with the enol form of the ketone in the rate determining step. This will be discussed further in Section 6.1.4.

Table 6.4 (a):

Effect of ^{t}BuOH on ko at low acid concentrations

[^{t}BuONO] = 3 x 10^{-3} mol l^{-1} [AA] = 0.0314 mol l^{-1}

[H_2SO_4] = 8.99 x 10^{-4} mol l^{-1} 25°C 375 nm

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0	0.0373 ± 4.4 x 10^{-3}
0.0205	4.13 x 10^{3} ± 3.2 x 10^{-4}
0.0410	2.43 x 10^{3} ± 3.2 x 10^{-4}

Table 6.4 (b):

Effect of ^{t}BuOH on ko at high acid concentrations

[^{t}BuONO] = 5 x 10^{-4} mol l^{-1} [AA] = 9.64 x 10^{-3} mol l^{-1}

[H_2SO_4] = 0.0351 mol l^{-1} 375 nm 25°C

[^{t}BuOH] mol l^{-1}	ko s^{-1}
0	4.41 ± 0.24
5.26 x 10^{-3}	1.30 ± 0.09
0.0158	0.206 ± 0.029
0.0316	0.155 ± 0.006

Figure 6.1

Plot of ko against $[H_2SO_4]$ for AA

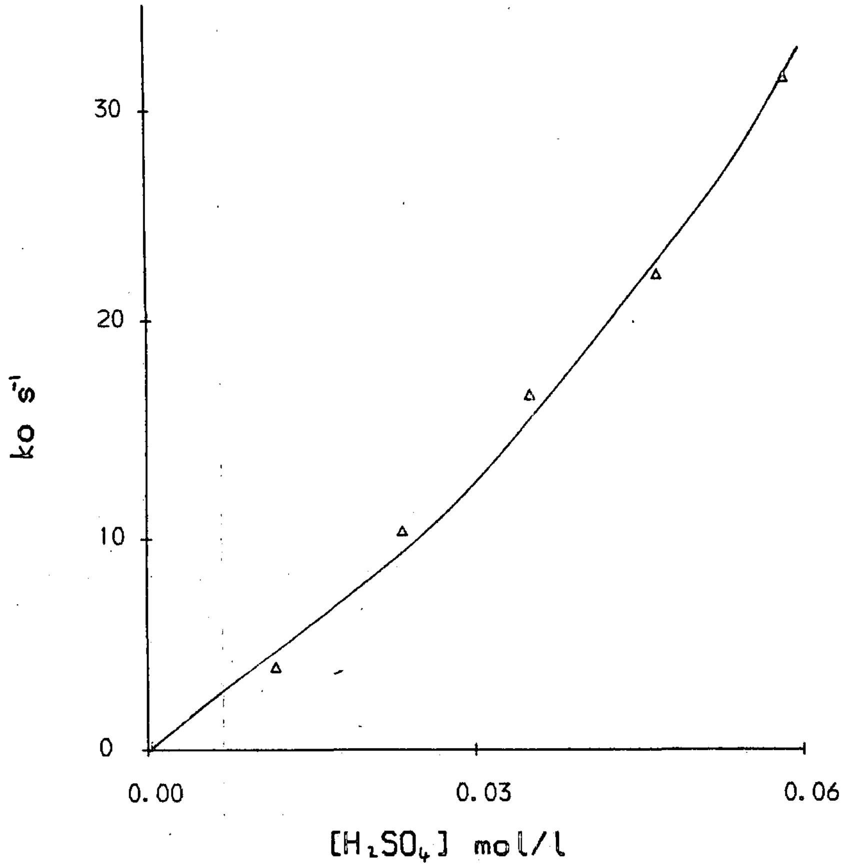
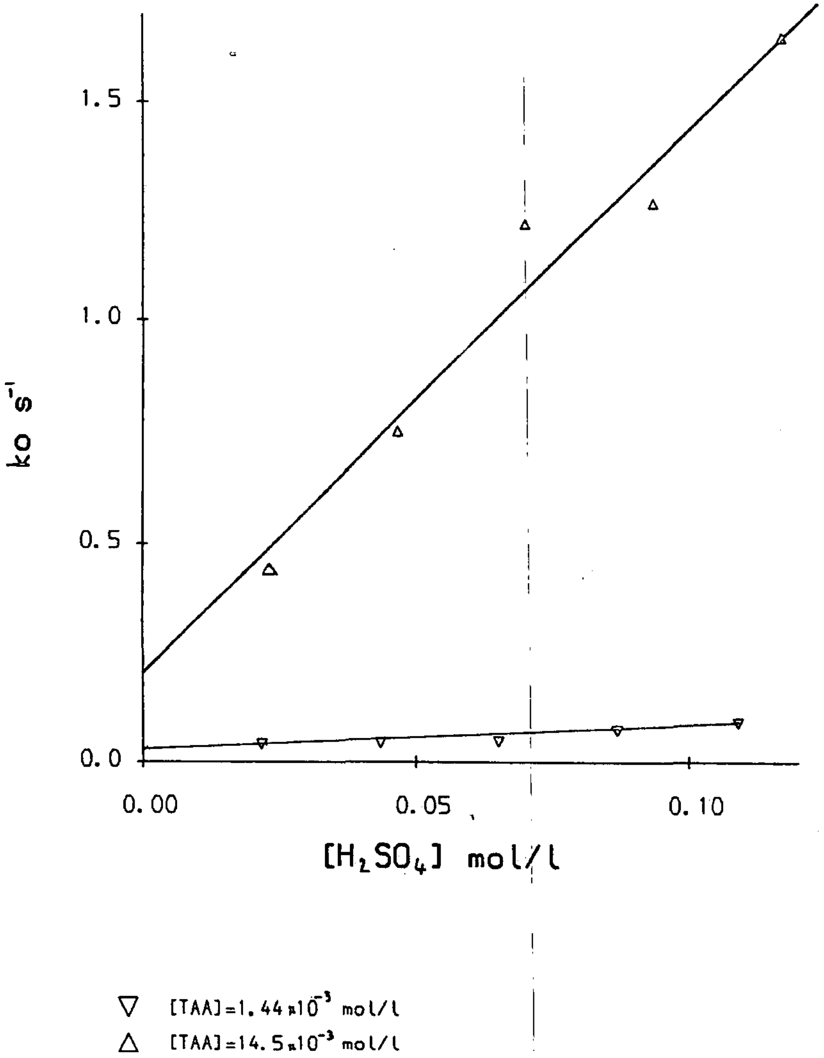


Figure 6.2

Plot of ko against $[H_2SO_4]$ for TAA



6.1.2 Nitrosation of 1,1,1,-trifluoroacetylacetone

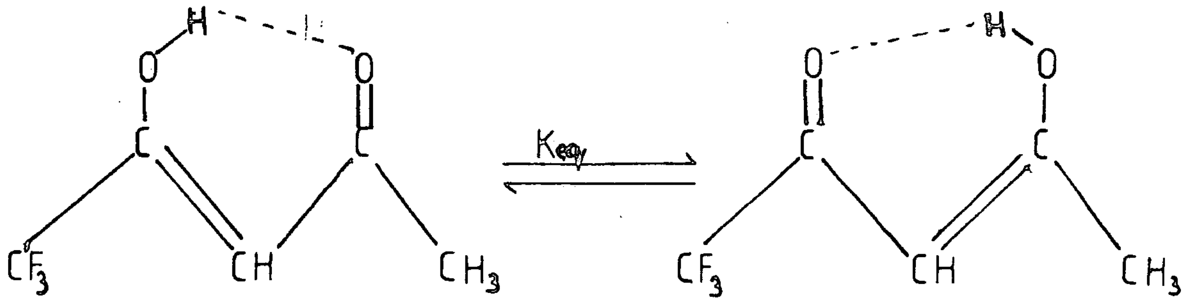
1,1,1,-trifluoroacetylacetone (TAA) is known to exist almost totally as the enol form in non aqueous solution. N.M.R. measurements in d^3-acetonitrile now confirm this is the case (Table 6.5), as there was no detectable signals due to the keto form.

Table 6.5:

^1H N.M.R. data for TAA in CD_3CN

δ ppm	Relative intensity	assignment
1.83	3	CH Enol
5.63	1	CH Enol
13.88	1	O-H Enol

The enol of TAA can exist in two forms. These are shown in equation (6.3). It is known [13] that



(6.3)

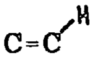
the tautomer on the left hand side of equation (6.3) is the favoured form in the rapid equilibrium, with Keq 0.4 in hexane. The presence of the CF_3- group has the effect of making the enol form electron deficient compared with acetylacetone. This can be seen in an increase in the acidity of the proton of the OH bond, the pKa values in water being 6.7 [14] for TAA and 8.87 [15] for AA.

The reaction of TAA with nitrous acid has been studied very recently in aqueous solution [16]. The product of the reaction, presumably the oxime, was not isolable, and indeed there has been no report of the synthesis of such a compound in the literature. The reaction was found to proceed readily in aqueous solution, the product absorbing in the 220-230 nm region. The results were interpreted in terms of a reaction via both the enol and enolate anion form, from the observed rate constant dependence upon the acidity.

The reaction of ^{t}BuONO and TAA was found to proceed readily also in acetonitrile solvent, the spectrum of the product had a peak in the 220-230 nm region. ^{1}H NMR experiments in deuterochloroform showed that the signal due to the proton of the carbon-carbon double bond disappeared along with the enol O-H proton signal. Also the signal from the CH_3 of the enol disappeared and a new CH_3 signal appeared. The results are shown in Table (6.6). These data show that the nitrosation must occur at the enolic carbon-carbon double bond, and are consistent with the formation of the oxime.

Table 6.6:

^{1}H N.M.R. data for nitrosation of TAA in $CDCl_3$

Enol	assignment	Product	assignment
2.13	CH_3	2.36	CH_3
5.86		11.76	=N-O-H
14.23	O-H		

The reaction of ^{t}BuONO with TAA was studied kinetically in acetonitrile by two methods. Firstly the reaction was studied by following the appearance of the product at 220 nm and secondly the reaction was studied by following the disappearance of the alkyl nitrite at 370 nm. In both cases good first order behaviour was found when the reactions were carried out with [^{t}BuONO]$\ll$[TAA]. The reaction was found to be first order with respect to [TAA] (Table 6.7) and was catalysed by added sulphuric acid (Tables 6.8 and 6.9)

Table 6.7:

Variation of ko with [TAA] at 370 nm

$[H_2SO_4] = 2.34 \times 10^{-2}$ mol l^{-1} $[^tBuONO] = 7 \times 10^{-6}$ mol l^{-1}

25°C

[TAA] mol l^{-1}	ko s^{-1}
7.23×10^{-3}	$0.228 \pm 9 \times 10^{-3}$
14.5×10^{-3}	0.445 ± 0.049
21.7×10^{-3}	0.707 ± 0.040
28.9×10^{-3}	0.976 ± 0.041
36.2×10^{-3}	1.20 ± 0.02

slope = 34.3 ± 0.73 l mol^{-1} s^{-1}

intercept = 0.03 ± 0.02 s^{-1}

Table 6.8:

Variation of ko with [H_2SO_4] at 370 nm

[TAA] = 14.5 x 10^{-3} mol l^{-1} [^{t}BuONO] = 7 x 10^{-4} mol l^{-1}

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0234	0.445 ± 0.049
0.0467	0.751 ± 0.047
0.0701	1.22 ± 0.03
0.0935	1.27 ± 0.06
0.117	1.65 ± 0.08

slope = 12.5 ± 1.4 l mol^{-1} s^{-1}

intercept = 0.189 ± 0.119 s^{-1}

Table 6.9:

Variation of ko with [H_2SO_4] at 220 nm

[TAA] = 1.44 x 10^{-3} mol l^{-1} [^{t}BuONO] = 1 x 10^{-4} mol l^{-1}

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0217	0.0406 ± 1.2 x 10^{-3}
0.0435	0.0436 ± 3.2 x 10^{-3}
0.0652	0.0470 ± 3.4 x 10^{-3}
0.0869	0.0728 ± 3.6 x 10^{-3}
0.109	0.0895 ± 0.0129

slope = 0.585 ± 0.127 l mol^{-1} s^{-1}

intercept = 0.0205 ± 9.1 x 10^{3} s^{-1}

Plots of ko against $[H_2SO_4]$ (Figure 6.2) at the two different [TAA] both gave straight lines with substantial positive intercepts. Such plots can be explained if the reaction of TAA occurs via both the enol and enolate anion forms. This is shown in Scheme (6.4).

$$\underset{E}{\text{Enol}} \overset{Ka}{\rightleftharpoons} \underset{E^-}{\text{Enolate}} + H^+$$

$$\text{RONO} + H^+ + E \xrightarrow{k_1} \text{Oxime}$$

$$\text{RONO} + H^+ + E^- \xrightarrow{k_2} \text{Oxime} \qquad (6.4)$$

$$\text{Rate of reaction} = k_1[\text{RONO}][H^+][E] + k_2[\text{RONO}][H^+][E^-]$$

$$\text{but } Ka = \frac{[E^-][H^+]}{[E]}$$

$$\text{and } [\text{TAA}] = [E^-] + [E]$$

$$\text{so } [E] = \frac{[\text{TAA}][H^+]}{Ka + [H^+]} \text{ and } [E^-] = \frac{[\text{TAA}]Ka}{Ka + [H^+]}$$

$$\text{therefore Rate} = \frac{k_1[H^+]^2[\text{TAA}][\text{RONO}]}{Ka + [H^+]} + \frac{k_2[H^+][\text{TAA}]Ka[\text{RONO}]}{Ka + [H^+]}$$

(6.5)

If $[H^+] \gg Ka$, equation (6.5) leads to the derived value of ko (equation 6.6). This predicts that a plot of

$$ko = k_1[TAA][H^+] + k_2[TAA]Ka \qquad (6.6)$$

ko against [TAA] should give a straight line with zero intercept and a plot of ko against $[H^+]$ should give a straight line with slope = k_1 [TAA] and intercept = k_2 [TAA]Ka. From the data in table (6.8) and (6.9), the values of k_1 (by assuming $[H^+] \simeq [H_2SO_4]$) and k_2Ka can be obtained. Using the average value of k_2Ka the value of k_1 can also be obtained from the data in Table (6.7). The results are shown in Table (6.10). The agreement between the three sets of data is reasonably good. These results will be discussed further in Section 6.1.4.

Table 6.10:

Values of k_1 and k_2Ka at 25°C

Data	k_1 l^2 mol^{-2} s^{-1}	k_2Ka l mol^{-1} s^{-1}
Table 6.8	862 ± 97	13 ± 8
Table 6.9	406 ± 89	14 ± 6
Table 6.7	867 ± 32	

6.1.3 Nitrosation of 1,1,1, 5,5,5 hexafluoroacetylacetone

1,1,1, 5,5,5, hexafluoroacetylacetone (HAA) also exists almost entirely as the enol form in non aqueous solution [10,12]. ^1H N.M.R. measurements in acetonitrile confirm that this is the case (Table 6.11), and the enol content is estimated at 97%. As was the case with TAA, there has been no report in the literature of the nitrosation of HAA. The reaction of HAA with ^{t}BuONO did proceed readily in acetonitrile, the product forming at 240 nm. Attempts to isolate the product failed. ^1H N.M.R. experiments in CD_3CN showed that the signal due to the enol proton at δ = 6.1 ppm disappeared indicating that reaction occured at the enolic carbon-carbon double bond.

Table 6.11:

^1H N.M.R. data for HAA

δ ppm	Relative intensity	assignment
2.85	1	CH_2
6.1	14	C=CH

The reaction of ^{t}BuONO with HAA was studied kinetically in acetonitrile by both following the appearance of the product at 220 nm and the disappearance of the alkyl nitrite at 370 nm. In both cases good first order behaviour was found when the reactions were carried out with [^{t}BuONO] $\ll$ [HAA]. The reaction was found to be first order with respect to HAA (Table 6.12) but was not catalysed by sulphuric acid (Table 6.13).

Table 6.12 (a):

Variation of ko with [HAA] at 220 nm

[^{t}BuONO] = 5×10^{-5} mol l^{-1} [H_2SO_4] = 4.92×10^{-3} mol l^{-1}

25°C

[HAA] mol l^{-1}	ko s^{-1}
7.23×10^{-4}	$0.0287 \pm 8 \times 10^{-4}$
1.45×10^{-3}	$0.0546 \pm 2.3 \times 10^{-3}$
4.34×10^{-3}	0.172 ± 0.014

slope = 39.9 ± 0.8 l mol^{-1} s^{-1}

intercept = $1 \times 10^{-3} \pm 2 \times 10^{-3}$ s^{-1}

Table 6.12 (b):

Variation of ko with [HAA] at 370 nm

$[{}^{t}BuONO] = 5 \times 10^{-4}$ mol l^{-1} $[H_2SO_4] = 0.0109$ mol l^{-1}

25°C

[HAA] mol l^{-1}	ko s^{-1}
5.03×10^{-3}	0.163 ± 0.012
7.55×10^{-3}	0.331 ± 0.018
0.0127	0.401 ± 0.019
0.0167	0.606 ± 0.034
0.0201	0.751 ± 0.019

slope = 36.4 ± 4.1 l mol^{-1} s^{-1}

intercept = $1 \times 10^{3} \pm 0.05$ s^{-1}

Table 6.13 (a):

Variation of ko with $[H_2SO_4]$ at 220 nm

$[{}^{t}BuONO] = 5 \times 10^{-5}$ mol l^{-1} $[HAA] = 7.23 \times 10^{-4}$ mol l^{-1}

$[H_2SO_4]$ mol l^{-1}	ko s^{-1}
4.92×10^{-4}	$0.0196 \pm 7 \times 10^{-4}$
1.24×10^{-3}	$0.0247 \pm 3 \times 10^{-4}$
2.48×10^{-3}	$0.0320 \pm 2.0 \times 10^{-3}$
3.72×10^{-3}	$0.0236 \pm 1.1 \times 10^{-3}$
4.92×10^{-3}	$0.0287 \pm 8 \times 10^{-4}$

Table 6.13 (b):

Variation of ko with [H_2SO_4] at 370 nm

[^tBuONO] = 5 x 10^{-4} mol l^{-1} [HAA] = 5.81 x 10^{-3} mol l^{-1}

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0115	0.198 ± 9 x 10^{-3}
0.0229	0.192 ± 8 x 10^{-3}
0.0344	0.172 ± 0.014
0.0458	0.182 ± 0.017
0.0573	0.202 ± 8 x 10^{-3}

The absence of acid catalysis can be explained if the reaction occurs via the enolate anion only. By analogy with equation (6.6) the derived value of ko is equation (6.7), which predicts that the reaction rate

$$ko = k_2 Ka\ [HAA] \qquad (6.7)$$

should be first order in [HAA] and should be independent of [H^+]. The values of $k_2 Ka$ obtained from the four sets of data are, 39.9 ± 0.8, 36.4 ± 4.1, 35.5 ± 5.9 and 32.5 ± 1.9 l mol^{-1} s^{-1}, which are all in good agreement with each other.

6.1.4 Discussion

All the results obtained for the reaction of ^{t}BuONO with the three acetylacetone derivatives are consistent with reaction involving the enol or enolate form of the ketone. The nitrosating species involved, by analogy with the results obtained in Chapter 5, is likely to be the nitrosonium ion. This is shown by the decrease in reaction rate on the addition of ^{t}BuOH (although some of this decrease probably arises from a medium effect). The reaction scheme is shown in Scheme (6.8) and the derived rate equation is equation (6.9)

$$^{t}\mathrm{BuONO} + \mathrm{H}^{+} \overset{K}{\rightleftharpoons} \mathrm{NO}^{+} + {}^{t}\mathrm{BuOH}$$

$$\begin{tikzcd}
\mathrm{NO}^{+} + \mathrm{E} \arrow[r, "k_1"] \arrow[d, shift right, "Ka"'] & \text{Product} \\
\mathrm{NO}^{+} + \mathrm{E}^{-} \arrow[r, "k_2"] \arrow[u, shift right, "\mathrm{H}^{+}"'] & \text{Product}
\end{tikzcd} \qquad (6.8)$$

$$ko = \frac{k_1 K[\mathrm{H}^{+}][\mathrm{AA}]}{K[\mathrm{H}^{+}] + [\mathrm{ROH}]} + \frac{k_2 K Ka[\mathrm{AA}]}{K[\mathrm{H}^{+}] + [\mathrm{ROH}]} \qquad (6.9)$$

Clearly in the absence of added [^{t}BuOH], the value of ko should not be constant throughout the reaction as [^{t}BuOH] will increase as the reaction proceeds. This is contrary to what is observed experimentally as good first order behaviour is observed over 2-3 halflives. A possible explanation of this is if $K[H^{+}] \gg [ROH]$, but this would lead to the observation of no acid catalysis for the reaction with the enol and a retardation of the rate by acid for the reaction with the enolate anion. A further explanation is if the alkyl nitrite is undergoing a rapid hydrolysis to nitrous acid with the traces of water present in the solution and then the nitrous acid can then react by forming NO^{+} which reacts with the substrate. In other words water is effectively competing with the enol for reaction with the alkyl nitrite. Evidence for this comes from the fact that when an alkyl nitrite and sulphuric acid are mixed in acetonitrile an equilibrium concentration of nitrous acid is rapidly formed (see Table 5.29). The reaction scheme is shown in Scheme (6.10) and the derived rate equation is shown in equation (6.11).

$$^{t}BuONO + H_2O + H^{+} \overset{K}{\rightleftharpoons} {}^{t}BuOH + HNO_2 + H^{+}$$

(6.10)

$$HNO_2 + H^{+} + E \xrightarrow{k_1} \text{Products}$$

$$ko = \frac{k_1 K[H_2O][H^+][E]}{K[H_2O] + [{}^tBuOH]} \qquad (6.11)$$

If the value of $K[H_2O] \gg [{}^tBuOH]$ then $ko = k_1[H^+][E]$ and so ko will be constant throughout the kinetic run despite the increasing $[{}^tBuOH]$. Further evidence for this type of mechanism comes from the fact that when ^{i}PrONO and AA are reacted under the same conditions the reactions are not first order with respect to [^{i}PrONO], but on the addition of ^{i}PrOH to the solution the reactions do become first order. This is shown in Table (6.14). In this case the value of K is likely to be smaller than that for ^{t}BuONO by analogy with the results found in aqueous solution [17].

The three acetylacetone derivatives show interesting trends in their reactivity in acetonitrile. For acetylacetone the reaction appears to occur through the enol form only, for hexafluoroacetylacetone the reaction appears to occur through the enolate anion only and trifluoroacetylacetone appears to react through both forms. The values of k_1, for reaction with the enol form (obtained by assuming $[H^+] \simeq [H_2SO_4]$) and k_2Ka for reaction of the enolate form are shown in Table (6.15).

Table 6.1.4:

Reaction of ^{1}PrONO with AA

[^{1}PrONO] = 2 x 10^{-3} mol l^{-1} 380 nm
[H_2SO_4] = 4.44 x 10^{-3} mol l^{-1}
[AA] = 0.0809 mol l^{-1}

time s	Vt (mv)	ko s^{-1}
0	14.5	
0.5	10.1	0.86
1.0	7.6	0.79
1.5	6.1	0.73
2.0	5.1	0.69
2.5	4.5	0.63
3.0	4	0.59
3.5	3.6	0.57
4.0	3.3	0.54
	1.9	

mean ko = 0.68 ± 0.11 s^{-1}

[^{1}PrONO] = 2 x 10^{-3} mol l^{-1} 380 nm
[H_2SO_4] = 4.64 x 10^{-3} mol l^{-1}
[AA] = 0.0808 mol l^{-1}
[^{1}PrOH] = 0.02 mol l^{-1}

time s	Vt (mv)	ko s^{-1}
0	12.60	
5	11.00	0.041
10	9.80	0.039
15	8.76	0.039
20	7.90	0.039
25	7.40	0.036
30	6.80	0.037
35	6.40	0.036
40	5.90	0.037
	3.90	

mean ko = 0.038 ± 2 x 10^{-3} s^{-1}

Table 6.15:

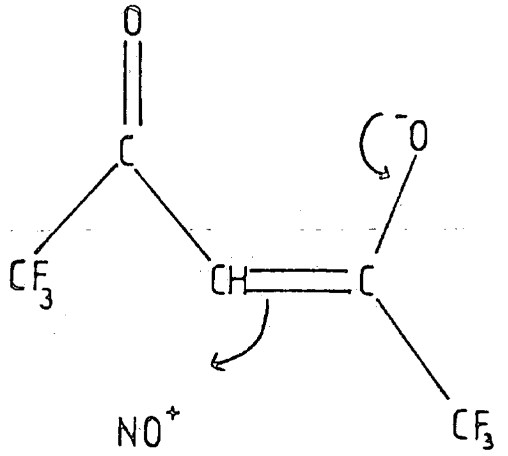
Values of k_1 and k_2Ka

	k_1 l mol^{-2} s^{-1}	k_2Ka l mol^{-1} s^{-1}
AA	~ 3 x 10^6	
TAA	800	13
HAA	~ 0	40

It is clear that the enol of acetylacetone is much more reactive than that of trifluoroacetylacetone, as expected considering the powerful electron withdrawing effect of a trifluoromethyl group. For reaction with the enolate anion it is not possible to obtain the actual values of k_2 since the Ka values are not known. In aqueous solution the Ka value of HAA [18] (pKa = 4.71) is ca 100 times larger than that of TAA (pKa = 6.7). If such a difference occurs in this solvent then the value of k_2 for TAA would be greater than that of HAA, again in accordance with the electron withdrawal effect of two trifluoromethyl groups compared with one.

The fact that HAA only reacts via the enolate anion can be explained in terms of a very low reactivity of the enol form, due to the presence of two CF_3- groups, but the presence of negative charge in the enolate anion would be expected to assist the nucleophilic attack of the carbon-carbon double bond on the nitrosonium ion. This is shown in Figure (6.3). For acetylacetone, the pKa

Figure 6.3



value in water is much larger (pKa = 8.87) [15] and so the concentration of the enolate anion may be too small under the conditions used for reaction to occur via this form.

For TAA two possible isomers can exist in solution (equation 6.3). One isomer has a CF_3 group adjacent to the C=C bond and would be expected to behave more like the HAA derivative, whereas the other isomer, with the CH_3 group adjacent to the C=C bond would be expected to behave more like the AA derivative. This would explain why TAA shows behaviour that is a mixture of that found for the other two derivatives.

6.2 Reaction of alkyl nitrites with amines in acetonitrile

Due to the large amount of literature on the synthetic uses of alkyl nitrites in the nitrosation of amines [19] it was thought to be of interest to investigate the mechanism of these reactions in acetonitrile as solvent. Many procedures in the literature use an alkyl nitrite (typically amyl nitrite or tertiary butyl nitrite) and the amine, in a solvent such as acetonitrile or chloroform without any acid catalyst. When this was tried in acetonitrile the reaction proceeded readily with primary aromatic amines (aniline, p-toluidine, p-chloroaniline), but the reactions were complicated by the formation of triazines by coupling of the diazonium ion with the unreacted amine. When an aromatic secondary amine was used (N-methylaniline or diphenylamine), the reaction proceeded readily to form the nitrosamine but the nitrosamine reacted further in both cases again making it impossible for the reaction to be studied. The side reactions in this case are unknown but the same reactions could be effected by using a sample of the nitrosamine in acetonitrile indicating that the nitrosamine must be formed in the first step. No reaction was observed with primary and secondary aliphatic amines under the conditions used.

When an excess of sulphuric acid was used in the reaction of the primary aromatic amines, the expected diazonium ion was formed quantitatively with the absence of any side reactions. The diazonium ion was identified by coupling with 2-naphthol-6-8-disulphonic acid in borax buffer. This was calibrated by using the diazonium ion produced from the reaction of p-toluidine and nitrous acid in aqueous solution. The extinction coefficient of the coupled product was 464 ± 1 mol^{-1} cm^{-1} at 510 nm. The results using $^{t}BuONO$ and p-toluidine in acetonitrile are shown in Table (6.16)

Table 6.16:

Formation of the diazonium ion from p-toluidine in CH_3CN

[toluidine] mol l^{-1}	[H_2SO_4] mol l^{-1}	[$^{t}BuONO$] mol l^{-1}	Abs 510	[ArN_2^+] mol l^{-1}
0.0113	0.12	2.76×10^{-4}	0.113	$2.5 \times 10^{-4} \pm 2 \times 10^{-5}$
0.0113	0.12	5.52×10^{-4}	0.271	$5.8 \times 10^{-4} \pm 3 \times 10^{-5}$

The reaction of $^{t}BuONO$ with N-methylaniline (NMA) also occurred readily in the presence of H_2SO_4, but the nitrosamine underwent further reactions (possibly the Fischer-Hepp rearrangement). It was, however, possible to study the initial nitrosation reaction because under the conditions used the rate of formation of the nitrosamine was much faster than its subsequent reactions.

The reactions of ^{t}BuONO with aniline, p-toluidine and NMA were studied kinetically in acetonitrile. Reactions were carried out under conditions where [^{t}BuONO]<<[Amine] and also [H_2SO_4]>7[Amine]. Under these conditions the amine is essentially completely protonated, as detected by the U.V. spectrum. Good first order behaviour was observed by following the appearance of the diazonium ion or the nitrosamine in the 280-330 nm region. For all three amines the reaction was first order with respect to the amine concentration. Results are shown in Tables (6.17)-(6.19)

Table 6.17:
Variation of ko with [aniline] in CH_3CN

[^{t}BuONO] = 1 x 10^{-4} mol l^{-1} [H_2SO_4] = 0.0573 mol l^{-1}

330 nm   25°C

[aniline] mol l^{-1}	ko s^{-1}
2.18 x 10^{-3}	0.0223 ± 1.9 x 10^{-3}
4.36 x 10^{-3}	0.0549 ± 4.3 x 10^{-3}
6.54 x 10^{-3}	0.0919 ± 1.4 x 10^{-3}
8.72 x 10^{-3}	0.131 ± 0.010
0.0109	0.187 ± 0.018

slope = 18.6 ± 1.2 l mol^{-1} s^{-1} intercept = 0.02 ± 0.01 s^{-1}

Table 6.18:

Variation of ko with [p-toluidine] in CH_3CN

$[^tBuONO] = 5 \times 10^{-5}$ mol l^{-1} $[H_2SO_4] = 0.0507$ mol l^{-1}

330 nm 25°C

[toluidine] mol l^{-1}	ko s^{-1}
2.25×10^{-3}	$0.0346 \pm 1.3 \times 10^{-3}$
4.51×10^{-3}	$0.0638 \pm 1.6 \times 10^{-3}$
6.76×10^{-3}	$0.0797 \pm 6.4 \times 10^{-3}$
9.01×10^{-3}	$0.106 \pm 5 \times 10^{-3}$
0.0135	0.182 ± 0.014

slope = 12.8 ± 1.1 l mol^{-1} s^{-1}

intercept = $1 \times 10^{-3} \pm 9 \times 10^{-3}$ s^{-1}

Table 6.19:

Variation of ko with [NMA] in CH_3CN

$[^tBuONO] = 5 \times 10^{-5}$ mol l^{-1} $[H_2SO_4] = 0.189$ mol l^{-1}

330 nm 25°C

[NMA] mol l^{-1}	ko s^{-1}
1.63×10^{-3}	$0.0494 \pm 1.3 \times 10^{-3}$
3.26×10^{-3}	$0.0826 \pm 5.0 \times 10^{-3}$
4.89×10^{-3}	$0.114 \pm 3 \times 10^{-3}$
6.52×10^{-3}	$0.173 \pm 5 \times 10^{-3}$
8.16×10^{-3}	$0.199 \pm 2 \times 10^{-3}$

slope=23.9 ± 1.7 l mol^{-1} s^{-1} intercept=$7 \times 10^{-3} \pm 9 \times 10^{-3}$ s^{-1}

An experiment was carried out using [toluidine]<< [^{t}BuONO]. Again good first order behaviour was obtained by following the appearance of the diazonium ion and the reaction was first order with respect to [^{t}BuONO]. These results are shown in Table (6.20).

Table 6.20:

Variation of ko with [^{t}BuONO] for reaction with p-toluidine

[p-toluidine] = 5 x 10^{-5} mol l^{-1} [H_2SO_4] = 0.0222 mol l^{-1}

330 nm 25°C

[^{t}BuONO] mol l^{-1}	ko s^{-1}
6.92 x 10^{-3}	0.0225
0.0234	0.0551
0.0395	0.0706
0.0566	0.0892
0.0811	0.106

slope = 1.1 ± 0.1 l mol^{-1} s^{-1}

intercept = 0.023 ± 6 x 10^{-3} s^{-1}

The effect of acidity on ko was also investigated. For aniline, at low acid concentrations the reaction rate was independent of [H_2SO_4], but at higher concentrations the rate increased as [H_2SO_4] increased. The results are shown in Tables (6.21) - (6.23)

Table 6.21:

Effect of [H_2SO_4] on rate of nitrosation of aniline

[^tBuONO] = 1×10^{-4} mol l^{-1} [aniline] = 2.18×10^{-3} mol l^{-1}
330 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0176	$0.0211 \pm 1.7 \times 10^{-3}$
0.0352	$0.0241 \pm 1.9 \times 10^{-3}$
0.0528	$0.0239 \pm 1.4 \times 10^{-3}$
0.0704	$0.0174 \pm 2 \times 10^{-4}$
0.0880	$0.0265 \pm 2.2 \times 10^{3}$

Table 6.22:

Effect of [H_2SO_4] on the rate of nitrosation of aniline

[^tBuONO] = 1×10^{-4} mol l^{-1} [aniline] = 1.9×10^{-3} mol l^{-1}
330 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0155	$0.0234 \pm 1.1 \times 10^{-3}$
0.0310	$0.0262 \pm 9 \times 10^{-4}$
0.0466	$0.0256 \pm 1.9 \times 10^{-3}$
0.0776	$0.0392 \pm 2.5 \times 10^{-3}$
0.109	$0.0471 \pm 1.1 \times 10^{-3}$
0.140	$0.0599 \pm 2.2 \times 10^{-3}$
0.233	$0.130 \pm 9 \times 10^{-3}$

Table 6.23:

Effect of [H_2SO_4] on the rate of nitrosation of aniline

[^tBuONO] = 1 x 10^{-4} mol l^{-1} [aniline] = 5.9 x 10^{-3} mol l^{-1}

330 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0322	0.100 ± 7 x 10^{-3}
0.0643	0.169 ± 7 x 10^{-3}
0.0966	0.210 ± 0.011
0.129	0.290 ± 7 x 10^{-3}
0.161	0.382 ± 0.031
0.241	0.686 ± 0.029

The results in Tables (6.21) and (6.23) are shown graphically in Figure (6.4).

A very similar effect was found in the nitrosation of NMA. The results are shown in Table (6.26)

In the case of p-toluidine the reaction was catalysed by acid over the entire concentration range studied. The results are shown in Table (6.25) and also in Figure (6.5)

These results can be readily understood by comparison with results found for nitrosation of aromatic amines in water with nitrous acid. At low or moderate acidities [20] it is known that the free base form of the amine is

Figure 6.5

Effect of acid in the nitrosation of p-toluidine

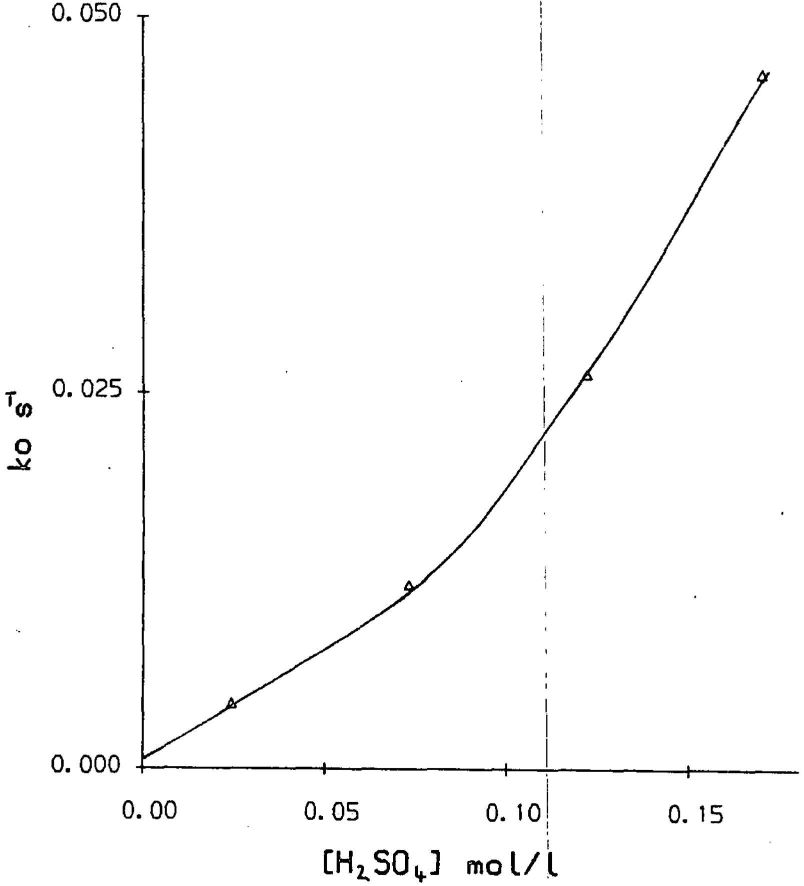


Figure 6.4

Effect of acid in the nitrosation of aniline

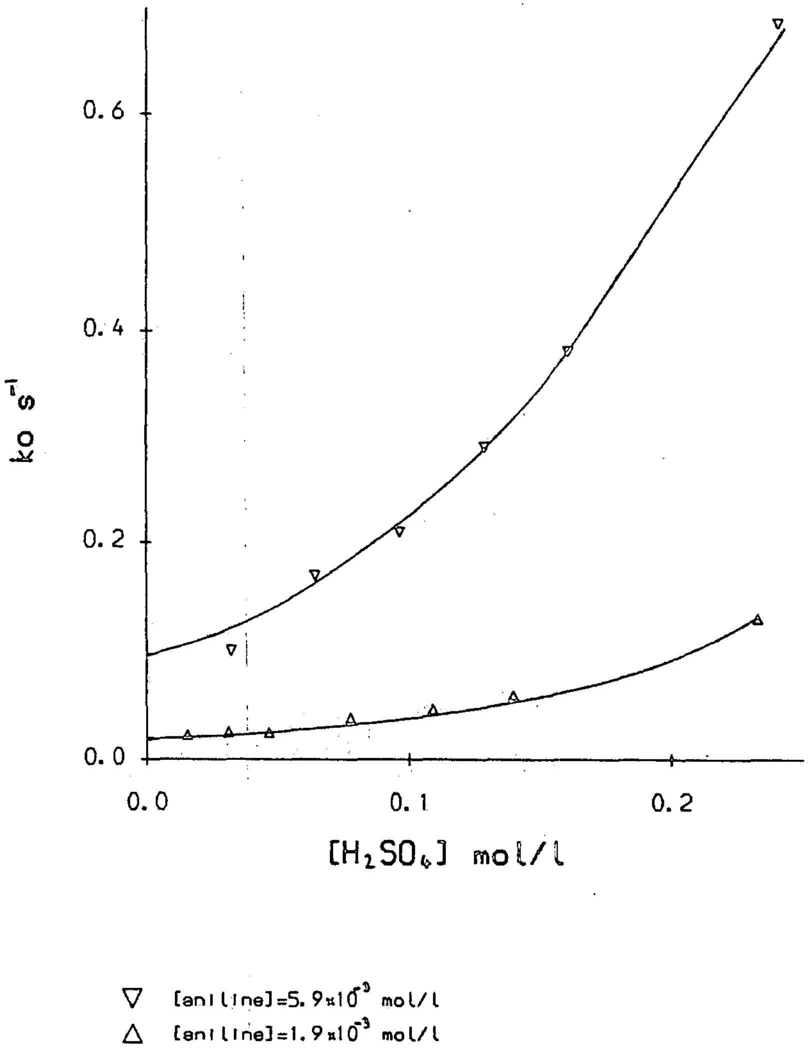


Table 6.24:

Effect of [H_2SO_4] on the rate of nitrosation of NMA

[^tBuONO] = 5 x 10^{-5} mol l^{-1} [NMA] = 1.63 x 10^{-3} mol l^{-1}

330 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0595	0.0254 ± 8 x 10^{-4}
0.0893	0.0248 ± 1.2 x 10^{-3}
0.119	0.0345 ± 7 x 10^{-4}
0.149	0.0403 ± 1.5 x 10^{-3}
0.189	0.0494 ± 1.3 x 10^{-3}

Table 6.25:

Effect of [H_2SO_4] on the rate of nitrosation of p-toluidine

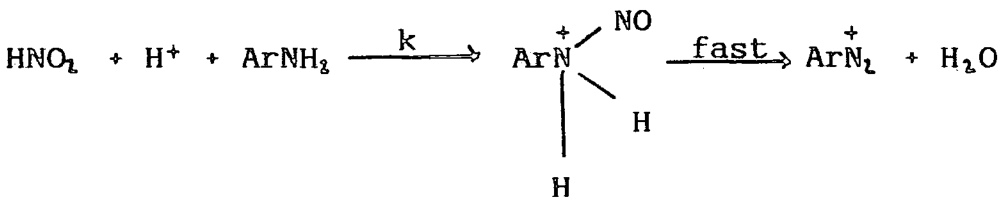
[^tBuONO] = 5 x 10^{-5} mol l^{-1} [p-toluidine] = 6.76x10^{-4} mol l^{-1}

285 nm 25°C

[H_2SO_4] mol l^{-1}	ko s^{-1}
0.0243	4.30x10^{-3} ± 1.8x10^{-4}
0.0729	0.0121 ± 7 x 10^{-4}
0.122	0.0264 ± 1.9x10^{-3}
0.170	0.0463 ± 3.5 x 10^{-3}

the reactive species in aqueous solution and a zero order dependence upon the concentration of acid is observed. This is shown in Scheme (6.12). The derived first order rate constant is shown in equation (6.13), where under the conditions used $[Ar\overset{+}{N}H_3] = [ArNH_2]_T$, the total stoichiometric concentration of amine used. A very similar

$$Ar\overset{+}{N}H_3 \xrightleftharpoons{Ka} ArNH_2 + H^+ \qquad (6.12)$$

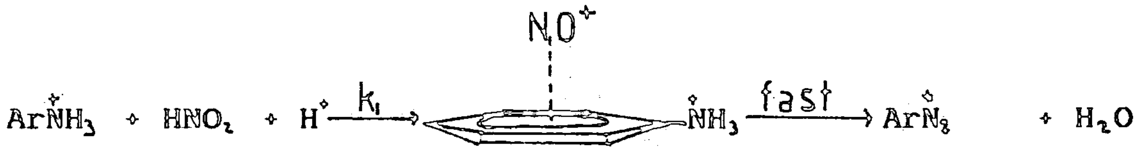


$$HNO_2 + H^+ + ArNH_2 \xrightarrow{k} Ar\overset{+}{N}(NO)(H)H \xrightarrow{fast} Ar\overset{+}{N}_2 + H_2O$$

$$ko = k\, Ka\, [ArNH_2]_T \qquad (6.13)$$

reaction must be occurring in acetonitrile and so explains the zero order dependence of the rate upon $[H_2SO_4]$ at low $[H_2SO_4]$. The actual nitrosating species involved, by analogy with the results of Chapter 5, is likely to be the nitrosonium ion, but this could either be formed from the alkyl nitrites or from an equilibrium concentration of nitrous acid (see section 6.1.4). At higher acid concentrations, where the concentration of free amine is very low, another reaction pathway occurs in aqueous solution [20,21], namely the protonated amine becomes the reactive species. This is shown in equation

(6.14). The derived value of ko (equation 6.15) shows that the reaction should be first order with respect to both [amine]$_T$ and [H$^+$]. This would also explain the



(6.14)

$$ko = k_1 [Ar\overset{+}{N}H_3] [H^+] \qquad (6.15)$$

observed acid catalysis seen in these reactions. Further evidence for this comes from the fact that the acid catalysis is most marked for the most basic amine, p-toluidine, (pKa = 5.08 [22]) which would be expected to have the lowest concentration of free amine of the amines studied and hence is most likely to react via the alternative mechanism. The pKa of several amines [23,24] have been determined in acetonitrile. It was found that the aromatic amines are all ca 5-6 pKa units more basic in acetonitrile than water, i.e. Aniline; pKa = 10.56 in CH_3CN, pKa = 4.63 in H_2O [22] and p-toluidine; pKa = 11.25 in CH_3CN, pKa = 5.08 in H_2O [22], and so the pKa values in water give a good measure of the relative order of basicity in acetonitrile. The pKa values of aliphatic amines are all ca 7-8 pKa units more basic in acetonitrile than H_2O and so the concentration of free amine in these solutions will be very small indeed. This explains why the aliphatic amines are apparently unreactive under similar conditions to those used for the aromatic amines.

For aniline, N-methyl aniline and p-toluidine the values of kKa for reaction with the free amine can be estimated by extrapolation of a plot of ko against $[H_2SO_4]$ to zero acid concentration. The results are shown in Table (6.2b). As can be seen the values of kKa decrease

Table 6.2b:

Values of kKa for nitrosation of amines in acetonitrile

Amine	[Amine] mol l^{-1}	Extrapolated ko s^{-1}	k Ka l mol^{-1} s^{-1}	pKa [22] (water)
Aniline	2.18×10^{-3}	0.023	10.4	4.63
	1.9×10^{-3}	0.022	11.6	
	5.9×10^{-3}	0.065	11.0	
NMA	1.63×10^{-3}	0.011	6.8	4.85
p-toluidine	6.76×10^{-3}	0	~ 0	5.07

as the basicity of the amine increases. This may indicate that the reactions are diffusion controlled [25], as is the case in water, ie. the value of k may be very similar for all three amines, but as accurate values of Ka are not known it is not possible to say for certain if this is the case.

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CHAPTER 7

EXPERIMENTAL DETAILS

7.1 Reagents used

7.1.1 Aqueous solutions (Chapters 2 and 3)

Solutions of perchloric acid were prepared by diluting the required amount of 60 - 62 % perchloric acid solution with distilled water. The acid solutions were then standardized by titration with standard sodium hydroxide solution, using phenolphthalein indicator. Isopropanol (laboratory reagent grade) and tertiary butanol (analar grade) were both purified by fractional distillation. Analar grades of sodium chloride, sodium bromide, sodium azide, sulphamic acid, disodium ortho—phosphate and sodium nitrite were used without further purification. N-methyl aniline was purified by fractional distillation under reduced pressure. Thioglycolic acid was obtained as a commercial sample and was used without any further purification. The alkyl nitrites used, isopropyl nitrite and tertiary butyl nitrite, were prepared from sodium nitrite by the usual procedure [1] and were purified by fractional distillation (at reduced pressure for tertiary butyl nitrite). The samples were stored in the dark at 0-4°C. In some experiments the pH of the solutions were measured using a PTI-6 universal pH meter with glass electrode.

7.1.2 Alcohol Solution

The alkyl nitrites, alcohols and thioglycolic acid used were as described in Section 7.1.1. Solutions of sulphuric acid in alcohol solvent were prepared by dissolving sulphuric acid (98%-analytical reagent) in the alcohol with ice bath cooling. The solutions were standardized by titration with standard sodium hydroxide solution, using phenolphthalein indicator. Solutions of HCl were prepared by passing dry gaseous HCl into the alcohol with cooling. The HCl gas was produced by reaction of concentrated sulphuric acid with sodium chloride and was dried by passing through concentrated sulphuric acid. Thiourea, tetraethyammonium bromide and tetraethylammonium chloride were all of the highest purity available and the tetraethylammonium salts were stored desiccated.

7.1.3 Aprotic Solutions (Chapters 5 and 6)

Chloroform (laboratory reagent grade) was purified [2] by repeated extraction with water to remove the ethanol. It was then dried for 24 hours over calcium chloride and fractionally distilled, the fraction boiling between 60 and 62°C being collected. The chloroform was then stored over type 4A molecular sieves. Acetonitrile (H.P.L.C.grade) was purified [2] by reflux with calcium hydride for eight hours followed by fractional distillation from calcium hydride, the constant boiling point fraction being collected and stored over type 4A molecular sieves. Methanol (anaLar grade) was purified by fractional distillation. Aniline, N-methyl aniline, acetyl acetone and iso-amyl alcohol were purified by distillation under reduced pressure and p-toluidine was recrystallized before use. Isoamyl nitrite was obtained as a commercial sample and was fractionally distilled under reduced pressure before use. Commercial samples of 1,1,1,5,5,5, - hexafluoro - 2,4, - pentanedione and 1,1,1 - trifluoro -2,4,-pentanedione were used without further purification.

Solutions of H_2SO_4 or HCl in acetonitrile were prepared in a similar way to that described in section 7.12. Commercial samples of sulphuric acid - d_2 (99.5+ atom %) and methanol-OD (99 atom %) were used without further purification. All acid solutions, unless otherwise stated, were used within 6-8 hours of preparation.

7.2 Rate Measurements

7.2.1. Stopped-flow spectrophotometry

Stopped-flow spectrophotometry is a technique for measuring the rate constants of fast reactions, typically values of first order rate constants of between 0.01s^{-1} and 200s^{-1} can be measured. A schematic diagram of the apparatus is shown in Figure (7.1). The two solutions to be mixed are stored in the reservoirs and from there they enter two identical syringes. A single piston drives the two syringes so that equal volumes of the solution are mixed. When the plunger of the third syringe hits the stop, the flow stops and the collection of data is triggered. The two solutions usually consisted of a solution containing the alkyl nitrite only and a solution containing all the other reagents. A typical example is shown in Table (7.1).

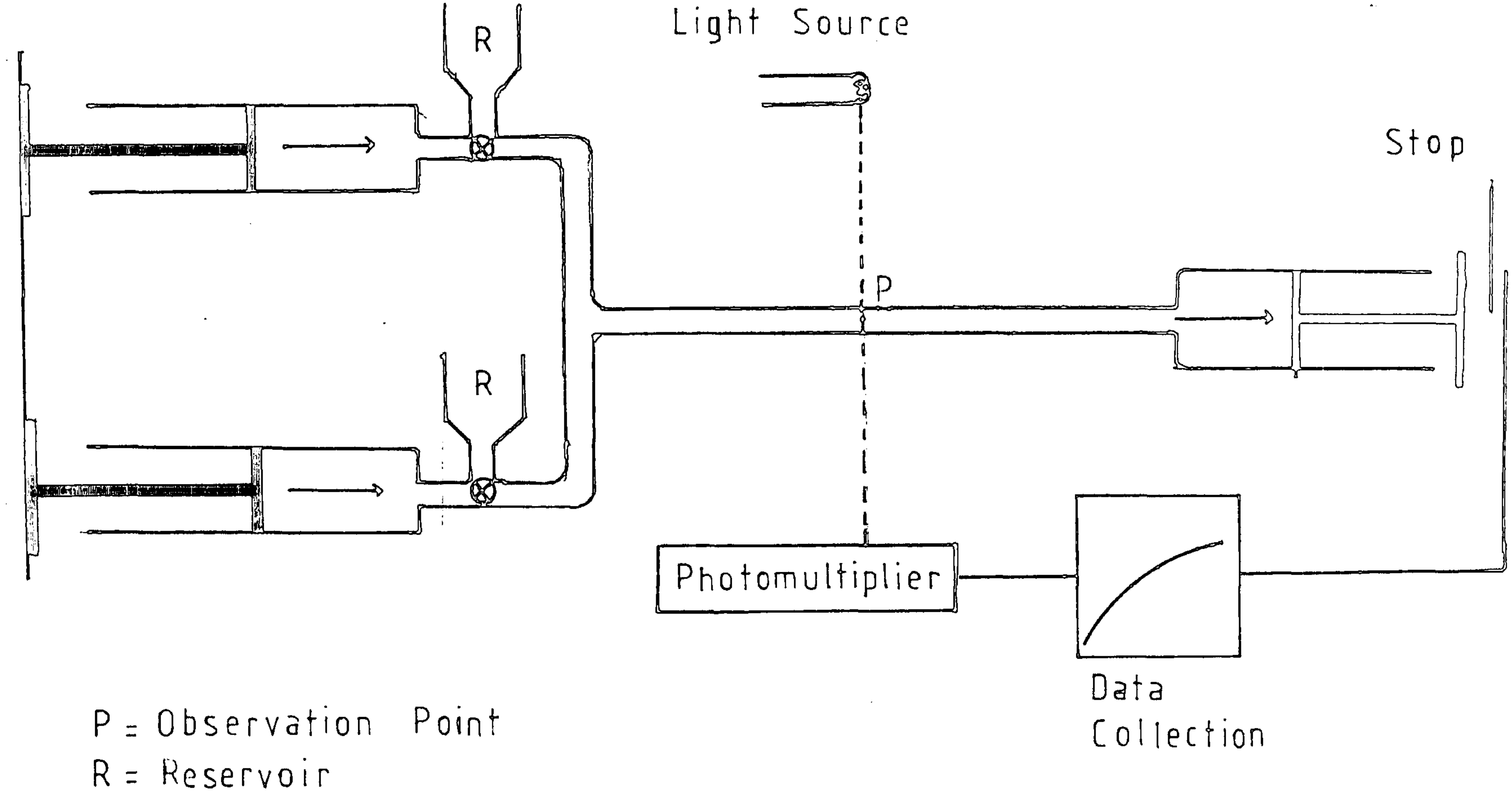
Table 7.1:

A typical set of solutions for stopped-flow spectrophotometry

Solution A	Concentration after mixing
[^{i}PrONO] = 2.4 x 10^{-6} mol l^{-1}	1.2 x 10^{-6} mol l^{-1}
Solution B	
[TGA] = 0.988 mol l^{-1}	0.494 mol l^{-1}
[$HClO_4$] = 0.406 mol l^{-1}	0.203 mol l^{-1}
[^{i}PrOH] = 0.414 mol l^{-1}	0.207 mol l^{-1}

The reaction is monitored by using a beam of monochromatic light which passes through the cell. This signal is amplified by a photomultiplier, which has a voltage of about -6 volts across it. As the voltage change is small in the reaction, an equal but opposite voltage (the bias voltage) of +6 volts is added to

Figure 7.1 : Stopped Flow Spectrophotometer



P = Observation Point
R = Reservoir

the signal. Therefore with just non-absorbing solution at the observation point, the final voltage is zero, and any voltage change observed results from the absorbance change during the reaction. The voltage changes with time were recorded on a storage oscilloscope, or in some cases were fed directly into an Apple IIe microcomputer where the rate constant was calculated using a Hi-Tech Scientific stopped-flow data aquisition and analysis system (SFOSI.0/05).

All the reactions were carried out under first order conditions.

For the reaction $R \xrightarrow{k} P$

$$\frac{-d[R]}{dt} = \frac{d[P]}{dt} = k_o[R]$$

On integration equation (7.1) is obtained,

$$\ln\frac{[R]_o}{[R]_t} = k_o t \qquad (7.1)$$

where $[R]_o$ = concentration of R at time = 0

$[R]_t$ = concentration of R at time = t

Under the conditions used in the stopped flow spectrophotometer, the voltage change during the reaction is less than 10% of the signal voltage (-6v) and so the output signal voltage is proportional to the absorbance. Absorbance (A) can be related to the concentration (c) of the absorbing species by the Beer Lambert law (equation 7.2) by knowledge of the extinction coefficient (ε). The voltage is

$$A = \varepsilon c l \qquad (7.2)$$

therefore directly proportional to concentration

$$V \propto \varepsilon c l$$

$V = a \varepsilon c l$ where a= constant of proportionality

The voltage at any time t is then given by

$$Vt = a \varepsilon_R [R]_t l + a \varepsilon_P [P]_t l$$

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

$$\therefore \quad V_t = a \varepsilon_R [R]_t l + a \varepsilon_P ([R]_o - [R]_t) l$$

$$= [R]_t l (a \varepsilon_R - a \varepsilon_P) + [R]_o a \varepsilon_P l$$

but $[R]o = [P]_\infty$, where $[P]_\infty$ = concentration of P at time $= \infty$

so $[R]o \; a\,\varepsilon_P l = [P]_\infty \; a\,\varepsilon_P l = V_\infty$

$$[R]_t = \frac{V_t - V_\infty}{(a\,\varepsilon_R - a\,\varepsilon_P)l}$$

also at time $t=0$, $[P]o = 0$

so $Vo = a\,\varepsilon_R [R]o \; l$

and $V_\infty = a\,\varepsilon_P [P]_\infty \; l = a\,\varepsilon_P [R]o \; l$

so $Vo - V_\infty = [R]o(a\,\varepsilon_R l - a\,\varepsilon_P l)$

$$\frac{[R]t}{[R]o} = \frac{Vt - V_\infty}{Vo - V_\infty}$$

substitution into equation (7.1) gives equation (7.2)

$$\mathrm{In}\ \frac{Vt - V_\infty}{Vo - V_\infty} = -kot \qquad (7.2)$$

Therefore if $\mathrm{In}(Vt - V_\infty)$ is plotted against time a straight line should be obtained, with gradient = $-k_o$ The values of the observed first order rate constant, ko, quoted are the mean of at least five separate measurements, and the error quoted is the standard deviation between the individual ko values. Typical kinetic runs are shown in Tables (7.2) and (7.7)

Table 7.2:

A typical kinetic run for nitrosation of thioglycolic acid in water by ^{i}PrONO

[^{i}PrONO] = 2 x 10^{-6} mol l^{-1} [^{i}PrOH] = 0.592 mol l^{-1}

[TGA] = 0.0297 mol l^{-1} [$HClO_4$] = 0.2 mol l^{-1}

t / s	Vt mv	ko s^{-1}
0	92.5	
0.02	130	9.97
0.04	162.5	10.29
0.06	190	10.57
0.08	210	10.44
0.10	226	10.31
0.12	240	10.34
0.16	252.5	10.53
	300	

mean ko = 10.35 ± 0.18 s^{-1}

Table 7.4:

A typical kinetic run for the nitrosation of thiourea by ^{t}BuONO in ^{t}BuOH

[^{t}BuONO] = 1 x 10^{-3} mol l^{-1} [H_2SO_4] = 0.0660 mol l^{-1}

[thiourea] = 0.012 mol l^{-1}

t s	Vt mv	ko s^{-1}
0	44	
0.5	61	0.399
1	74	0.384
1.5	86	0.395
2	95	0.391
2.5	104	0.407
3	110	0.403
3.5	115.6	0.408
	138	

mean ko = 0.398 ± 0.008 s^{-1}

Table 7.3:

A typical kinetic run for the nitrosation of hydrazoic acid in water by ^{t}BuONO

[^{t}BuONO] = 1.2 x 10^{-3} mol l^{-1} [H^+] = 0.50 mol l^{-1}

[HN_3] = 0.0125 mol l^{-1}

t s	Vt mv	ko s^{-1}
0	156	
0.1	136	1.89
0.2	122	1.73
0.3	108	1.78
0.4	96	1.82
0.5	87	1.80
0.6	80	1.77
0.7	74	1.75
	40	

mean ko = 1.79 ± 0.05 s^{-1}

Table 7.6:

A typical kinetic run for the nitrosation of aniline by ^{t}BuONO in acetonitrile

$[^{t}BuONO] = 1 \times 10^{-4}$ mol l^{-1} [H SO] = 0.161 mol l^{-1}

[aniline] = 5.9×10^{-3} mol l^{-1}

t s	Vt mv	ko s^{-1}
0	17.5	
0.5	47.5	0.365
1.0	72.5	0.365
1.5	95.0	0.375
2.0	111.0	0.366
2.5	127.5	0.378
3.0	140	0.380
	197.5	

mean ko = 0.372 ± 0.006 s^{-1}

Table 7.5:

A typical kinetic run for the nitrosation of methanol by isopropyl nitrite in acetonitrile

$[^{i}PrONO]$ = 0.010 mol l^{-1} [MeOH] = 0.113 mol l^{-1}

$[H_2SO_4] = 6.24 \times 10^{-3}$ mol l^{-1}

t s	Vt mv	ko s^{-1}
0.005	155	
0.010	122	50.8
0.015	100	46.9
0.020	81	46.7
0.025	65	47.4
0.030	54	46.5
0.035	45	46.0
0.040	38	45.4
	8	

mean ko = 47.1 ± 1.6 s^{-1}

Table 7.8:

A typical kinetic run for the nitrosation of 1,1,1, 5,5,5, hexafluoroacetylacetone by ^{t}BuONO in acetonitrile

[HAA] = 7.23 x 10^{-4} mol l^{-1} [^{t}BuONO] = 5 x 10^{-5} mol l^{-1}

[H_2SO_4] = 1.24 x 10^{-3} mol l^{-1}

t s	Abs t	ko s^{-1}
0	0.060	
10	0.098	0.0240
20	0.129	0.0245
30	0.152	0.0242
40	0.171	0.0244
50	0.186	0.0246
60	0.197	0.0245
70	0.206	0.0245
80	0.213	0.0245
90	0.218	0.0243
100	0.222	0.0241
110	0.226	0.0245
	0.238	

mean ko = 0.0244 ± 2 x 10^{-4} s^{-1}

Table 7.7:

A typical kinetic run for the nitrosation of thioglycolic acid by nitrous acid in acetonitrile

[HNO_2] $<$ 10^{-4} mol l^{-1} [H_2SO_4] = 3.08 x 10^{-3} mol l^{-1}

[TGA] = 0.0184 mol l^{-1}

t s	Vt mv	ko s^{-1}
0	26	
0.002	53	134
0.004	73	132
0.006	88	129
0.008	100	129
0.010	109	128
0.012	113	118
	141	

mean ko = 128 ± 5 s^{-1}

7.2.2 Conventional U.V./Visible Spectrophotometry

Rate measurements for the slower reactions ($k_o < 0.01\ s^{-1}$) were usually carried out using a thermostatted recording spectrophotometer. The machines used were a Beckman model 25, Pye Unicam SP8 - 100, Perkin-Elmer lambda 3 and a Philips PU 8725. A typical reaction procedure was to thermostat a solution of the alkyl nitrite and a solution containing all the other reagents (total volume = 24 ml) at the required temperature. A 1 cm silica cell containing a sample of the solvent used in the reaction was placed in the reference beam of the spectrophotometer. The reaction was started by adding a small volume of the nitrite solution (typically 1 ml) to the other reagents. The solution was then thoroughly mixed and a sample was placed in an identical 1 cm silica cell and placed in the sample beam of the spectrophotometer. The absorbance change at a fixed wavelength was then measured as a function of time. The value of ko can then be obtained in a similar way to equation (7.2). A typical kinetic run is shown in Table (7.8)

Equilibrium measurements between alkyl nitrites and alcohols were carried out using the Perkin-Elmer lambda 3 spectrophotometer. The absorbance changes in the spectrum in the 280-410nm region were recorded as a function of the concentration of the reagents. Knowledge of the extinction coefficients of the alkyl nitrites enabled the concentrations of the alkyl nitrites to be calculated and hence the equilibrium constant could be obtained. This is shown below.

$$\underset{A}{\mathrm{RONO}} + \underset{B}{\mathrm{R'OH}} \rightleftharpoons \underset{C}{\mathrm{ROH}} + \underset{D}{\mathrm{R'ONO}}$$

If only A and D absorb at the wavelength then;

$$\mathrm{Abs} = [A]\varepsilon_A l + [D]\varepsilon_D l$$

$$\text{but } [A]_o = [A] + [D]$$

$$\text{so } [A] = \frac{\mathrm{Abs} - \varepsilon_D l [A]_o}{(\varepsilon_D l - \varepsilon_A l)}$$

So if [A]o (the concentration of A added), the value of [A] and hence [D] can be calculated and if [B] and [C] are such that they are constant through the experiment the value of K can be readily calculated. Typical results are shown in Table (7.9).

Table 7.9:

Typical results for equilibrium constant measurements between ^{i}PrONO and MeOH in acetonitrile

λ nm	$\varepsilon_{^{i}PrONO}$ (l mol^{-1} cm^{-1})	ε_{MeONO}
390	35.86	21.32
283	105.9	77.97

[MeOH] mol l^{-1}	[^{i}PrONO] mol l^{-1}	[^{i}PrONO]o mol l^{-1}	Abs 390nm	Abs 283nm	[^{i}PrONO]eq mol l^{-1} 390nm	[^{i}PrONO]eq mol l^{-1} 283nm	K
0.491	0.258	8.42×10^{-3}	0.192	0.698	8.6×10^{-4}	1.4×10^{-3}	3.26
0.491	0.515	8.37×10^{-3}	0.212	0.733	2.31×10^{-3}	2.89×10^{-3}	3.37
0.491	0.773	8.28×10^{-3}	0.224	0.748	3.27×10^{-3}	3.68×10^{-3}	3.75
0.246	0.515	8.30×10^{-3}	0.238	0.779	4.20×10^{-3}	4.72×10^{-3}	3.90

mean K = 3.56 ± 0.26

References

1. W.A.Noyes, Org. Synth., Coll. Vol. II, 1943, pp 108, 204, 363

2. G.J.Janz and R.P.T. Tompkins, in Non aqueous Electolytes Handbook, Vol 1., Academic Press, New York, 1972

APPENDIX

a) LECTURES AND SEMINARS ORGANISED BY THE DEPARTMENT OF CHEMISTRY DURING THE PERIOD 1985-1988
(* Denotes those attended)

17th October 1985

Dr C.J.Ludman (University of Durham)

'Some Thermochemical Aspects of Explosions'

24th October 1985*

Dr J Dewing (U.M.I.S.T.)

'Zeolites - Small Holes, Big Opportunities'

30th October 1985*

Dr S.N.Whittleton (University of Durham)

'An investigation of a Reaction Window'

31st October 1985*

Dr P.Timms (University of Bristol)

'Some Chemistry of Fireworks'

5th November 1985*

Prof.M.J.O'Donnell (Indiana - Purdue University)

'New Methodology for the Synthesis of Amino Acids'

7th November 1985*

Prof. G.Ertl (University of Munich)

'Heterogeneous Catalysis'

14th November 1985

Dr S.G.Davies (University of Oxford)

'Chirality Control and Molecular Recognition'

20th November 1985

Dr J.A.H.Macbride (Sunderland Polytechnic)

'A Heterocyclic Tour on a Distorted Tricycle - Biphenylene'

21st November 1985

Prof. K.H.Jack (University of Newcastle)

'Chemistry of Si-Al-O-N Engineering ceramics'

28th November 1985

Prof. D.J.Waddington (University of York)

'Resources for the Chemistry Teacher'

28th November 1985*

Dr B.A.J.Clark (Kodak Ltd)

'Chemistry and Principles of colour photography'

15th January 1986

Prof. N.Sheppard (University of East Anglia)

'Vibrational and Spectroscopic Determinations of the Structures of Molecules Chemisorbed on Metal Surfaces'

23rd January 1986*

Prof. Sir J.Lewis (University of Cambridge)

'Some More Recent Aspects in the Cluster Chemistry of Ruthenium and Osmium Carbonyls'

29th January 1986

Dr J.H.Clark (University of York)

'Novel Fluoride Ion Reagents'

30th January 1986*

Dr N.J.Phillips (University of Loughborough)

'Laser Holography'

12th February 1986*

Prof. O.S.Tee (University of Montreal)

'Bromination of Phenols'

12th February 1986

Dr J.Yarwood (University of Durham)

'The Structure of Water in Liquid Crystals'

13th February 1986

Prof. R.Grigg (University of Belfast)

'Thermal Generation of 1, 3-Dipoles'

19th February 1986*

Prof. G.Procter (University of Salford)

'Approaches to the Synthesis of some Natural Products'

20th February 1986*

Dr C.J.F.Barnard (Johnson Mathey Group)

'Platinum Anti-Cancer Drug Development'

26th February 1986

Miss C.Till (University of Durham)

'E.S.C.A. and Optical Emission Studies of the Plasma Polymerisation of Perfluoroaromatics'

27th February 1986*

Prof. R.K.Harris (University of Durham)

'The Magic of Solid State N.M.R.'

5th March 1986*

Dr D.Hathway (University of Durham)

'Herbicide Selectivity'

5th March 1986*

Dr M. Schroder (University of Edinburgh)

'Studies on Macrocycle Complexes'

6th March 1986*

Dr B.Iddon (University of Salford)

'The Magic of Chemistry'

12th February 1986

Dr J.H.Brown (University of Oxford)

'Chelate Control in Homogeneous Catalysis'

14th May 1986*

Dr P.R.R. Langridge-Smith (University of Edinburgh)

'Naked Metal Clusters - Synthesis, Characterisation and Chemistry'

9th June 1986

Prof. R.Schmutzler (Braunschweig, West Germany)

'Mixed Valance Diphosphorous Compounds'

23rd June 1986

Prof. R.E.Wilde (Texas Technical University, USA)

'Molecular Dynamic Processes from Vibrational Bandshapes'

16th October 1986*

Prof. N.N. Greenwood (University of Leeds)

'Glorious Gaffes in Chemistry'

23rd October 1986*

Prof. H.W.Kroto (University of Sussex)

'Chemistry in Stars, between Stars and in the Laboratory'

29th October 1986*

Prof. E.H.Wong (New Hampshire, USA)

'Coordination Chemistry of P-0-P Ligands'

5th November 1986*

Prof. D.Dopp (University of Duisburg)

'Cyclo-additions and cyclo-reversions involving Captodative Alkenes'

6th November 1986*

Dr R.M.Scrowston (University of Hull)

'From Myth and Magic to Modern Medicine'

13th November 1986*

Prof. Sir G. Allen (Unilever Research)

'Biotechnology and the future of the Chemical Industry'

20th November 1986*

Dr A.Milne/Mr S. Christie (International Paints)

'Chemical Serendipity - A Real Life Case Study'

26th November 1986

Dr N.D.S.Canning (University of Durham)

'Surface adsorbtion studies of Relevence to Heterogeneous Ammonia synthesis'

27th November 1986

Prof. R.N.Williams (Metropolitan Police Forensic Science)

'Science and Crime'

3rd December 1986*

Dr J.Miller (DuPont Central Research, USA)

'Molecular Ferromagnets;Chemistry and Physical Properties'

8th December 1986

Prof. T Dorfmuller (University of Bielefeld)

'Rotational Dynamics in Liquids and Polymers'

22nd January 1987*

Prof. R.H.Ottewill (University of Bristol)

'Colloid Science, A Challenging Subject'

28th January 1987

Dr W.Clegg (University of Newcastle)

'Carboxylate Complexes of Zinc; Charting a Structural Jungle'

4th February 1987

Prof. A.Thomson (University of East Anglia)

'Metallo Proteins and Magneto Optics'

5th February 1987*

Dr P. Hubberstey (University of Nottingham)

'Demonstration Lecture on various aspects of Alkali Metal Chemistry'

11th February 1987*

Dr D.T.Shepherd (University of Durham)

'Pteridine Natural Products; Synthesis and Use in Chemotherapy'

12th February 1987*

Dr P.J.Rodgers (ICI Billingham)

'Industrial Polymers from Bacteria'

17th February 1987*

Prof E.H.Wong (New Hampshire, USA)

'Symmetrical Shapes from Molecules to Art and Nature'

19th February 1987

Dr M. Jarman (Institute of Cancer Research)

'The design of Anti-Cancer Drugs'

4th March 1987

Dr R. Newman (University of Oxford)

'Change and Decay: A Carbon-13 CP/MAS N.M.R. Study of Humification and Coalification Processes'

5th March 1987

Prof. S.V. Ley (Imperial College)

'Fact and Fantasy in Organic Synthesis'

9th March 1987*

Prof. G.G. Bordwell (N.E. University,USA)

'Carbon Anions, Radicals, Radical Anions and Radical Cations'

11th March 1987

Dr R.D. Cannon (University of East Anglia)

'Electron Transfer in Polynuclear Complexes'

12th March 1987*

Dr E.M. Goodger (Cranfield Inst. of Tech.)

'Alternative fuels for transport'

17th March 1987

Prof. R.F. Hudson (University of Kent)

'Aspects of Organophosphorus Chemistry'

18th March 1987*

Prof. R.F. Hudson (University of Kent)

'Homolytic Rearrangement and Free Radical Stability'

6th May 1987

Dr R. Bartsch (University of Sussex)

'Low Coordinate Phosphorus Compounds'

7th May 1987*

Dr M. Harmer (ICI Chem and Polymer Group)

'The Role of Organometallics in Advanced Materials'

11th May 1987

Prof. S. Pasynkiewicz (Tech. Univ., Warsaw)

'Thermal Decomposition of Methyl Copper and its Reactions with Tri-alkyl Aluminium'

17th May 1987*

Dr M. Blackburn (University of Sheffield)

'Phosphonates as analogues of Biological Phosphate Esters'

24th June 1987*

Prof. S.M. Roberts (University of Exeter)

'Synthesis of Novel Antiviral Agents'

26th June 1987

Dr C. Krespan (E I DuPont de Nemours)

'Nickel (0) and Iron (0) as Reagents in Organofluorine Chemistry'

15th October 1987*

Dr M.J. Winter (University of Sheffield)

'Pyrotechnics'

22nd October 1987*

Prof. J.W. Gray (University of Hull)

'Liquid Crystals and their Applications'

12th October 1987*

Mrs S. van Rose (Geological Museum)

'Chemistry of Volcanoes'

5th November 1987*

Dr A.R. Butler (University of St. Andrews)

'Chinese Alchemy'

12th November 1987*

Prof. D. Seebach (E T H Zurich)

'From Synthetic Methods to Mechanistic Insight'

26th November 1987

Dr D.H. Williams (University of Cambridge)

'Molecular Recognition'

3rd December 1987*

Dr J. Howard (ICI Wilton)

'Chemistry of Non-equilibrium Processes'

10th December 1987*

Dr C.J. Ludman (University of Durham)

'Explosives'

16th December 1987

Mr R. M. Swart (ICI)

'The Interaction of Chemicals with Lipid Bilayers'

19th December 1987*

Prof. P.G. Sammes (Smith, Kline and French)

'Chemical Aspects of Drug Development'

21st January 1988*

Dr F. Palmer (University of Nottingham)

'Luminescence'

28th January 1988*

Dr A. Cairns-Smith (Glasgow University)

'Clay Minerals and the Origin of Life'

11th February 1988

Prof J.J. Turner (University of Nottingham)

'Catching Organometallic Intermediates'

18th February 1988*

Dr K Borer (University of Durham Industrial Research Labs.)

'The Brighton Bomb - A Forensic Science View'

25th February 1988*

Prof. A Underhill (University of Bangor)

'Molecular Electronics'

3rd March 1988

Prof. W.A.G.Graham (University of Alberta, Canada)

'Rhodium and Iridium Complexes in the Activation of Carbon-Hydrogen Bonds'

7th March 1988*

Prof. H.F. Koch (Ithaca College, USA)

'Does the E2 Mechanism Occur in Solution'

7th April 1988

Prof. M.P. Hartshorn (University of Canterbury, New Zealand)

'Aspects of Ipso Nitration'

18th April 1988

Prof. C.A. Nieto de Castro (University of Lisbon and Imperial College'

'Transport properties of Non-Polar Fluids'

19th April 1988*

Graduate Chemists (Northeast Polytechnics and Universities)

'R.S.C. Graduate Symposium'

25th April 1988*

Prof. D. Birchall (ICI Advanced Materials)

'Environmental Chemistry of Aluminium'

27th April 1988

Dr R Richardson (University of Bristol)

'X-ray Diffraction From Spread Monolayers'

27th April 1988*

Dr J.A. Robinson (University of Southampton'

'Aspects of Antibiotic Biosynthesis'

28th April 1988*

Prof. A. Pines (University of California, Berkeley, USA)

'Some Magnetic Moments'

11th May 1988*

Dr W.A. McDonald (ICI Wilton)

'Liquid Crystal Polymers'

8th June 1988

Dr J.P. Majoral (Universite Paul Sabatier)

'Stabilisation by Complexation of Short-lived Phosphorus Species'

29th June 1988*

Prof. G.A. Olah (University of Southern California)

'New Aspects of Hydrocarbon Chemistry'

b) First Year Induction Course (October-November 1985)

A series of one hour presentations on the services available in the Department

1) Departmental organisation
2) Safety matters
3) Electrical appliances and infra-red spectroscopy
4) Chromatography and Microanalysis
5) Atomic absorptiometry and inorganic analysis
6) Library facilities
7) Mass spectroscopy
8) Nuclear magnetic resonance spectroscopy
9) Glassblowing technique