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Nitration in Inert Fluids

by

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A Thesis submitted for the degree of Doctor
of Philosophy September 2000
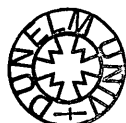
Abstract

Nitration in Inert Fluids

Traditional methods of nitration have several disadvantages including the environmental problem of disposal of the spent acid. A main aim of this work was to investigate alternative methods for nitration while minimising the amount of acid required.

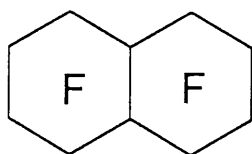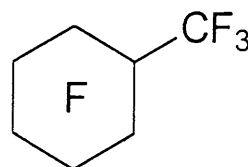Perfluorocompounds have been used as bulking agents to replace partially the acid solvent. They are chemically inert and may be reused without the need for purification.

(Perfluorodecalin)   (Perfluoromethylcyclohexane)

Mechanistic and synthetic studies of nitration reactions have been made. Toluene was successfully nitrated to trinitrotoluene using less sulfuric acid than in traditional methods. Benzene, styrene and *trans*-stilbene have been nitrated using nitric acid or dinitrogen pentoxide in perfluorocompounds.

Kinetic results have been obtained for the homogeneous nitrations by N_2O_5 in perfluorodecalin of substrates including 4-chloroanisole, 4-bromophenetole, 4-bromophenol and various chlorophenols. The rate constants have been determined and some mechanistic conclusions have been made.

The nitration of various amines using dinitrogen pentoxide or nitric acid in perfluorocarbons has been studied. Nitrated derivatives of morpholine, pyrrolidine, piperidine, oxazolidinone and pyrimidine were successfully obtained using *N*-'butoxycarbonyl, acetyl or silyl amines.

Declaration

The content of this thesis represents the work of the author unless indicated to the contrary or acknowledged by reference. The thesis describes the results of research carried out in the Department of Chemistry at the University of Durham between October 1997 and September 2000. This work has not been submitted for a higher degree in any other academic institution.

Statement of Copyright

Acknowledgements

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I would like to thank all my lab colleagues over the last three years. A special thanks goes to Darren who has proof read my thesis and has been a constant help, even if his jokes are a bit poor! I would also like to thank Andy (for showing me the pubs), Kathryn (for showing me the ropes), Lynsey (for teaching me to table dance), Dave (for his pen clicking), and Tony (for showing me how to be funny and sarcastic all at the same time) for their friendship and support. I would like to thank Paul for making me laugh and looking after me in Bressanone. Particular thanks goes to Colin Greenhalgh who has solved many of my technical problems.

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Most of all I would like to thank my parents for everything they have done for me; they are always there when I need them. Not forgetting my cats Harvey, Charlie and Maggie and my dogs Keisha and Jess.

To my Mam and Dad

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Abbreviations

UV	ultra violet
Vis	visible
IR	infra red
^{1}H NMR	proton nuclear magnetic resonance
^{13}C NMR	carbon nuclear magnetic resonance
s	singlet
d	doublet
dd	doublet of doublets
p	pentet
m	multiplet
GC	gas chromatography
MS	mass spectroscopy
CIMS	chemical ionisation mass spectroscopy
EIMS	electron ionisation mass spectroscopy
ESME	elctrospray mass spectroscopy
GCMS	gas chromatography mass spectroscopy
HPLC	high performance liquid chromatography
RBF	round bottomed flask
mmol	millimoles
μl	microlitres
M	mol dm^{-3}
wt	weight
s	seconds
min(s)	minutes
hr(s)	hour(s)
ppm	parts per million
Mpt	melting point
Bpt	boiling point
DNT	dinitrotoluene
TNT	trinitrotoluene
DNB	dinitrobenzene
TNB	trinitrobenzene
MCP	monochlorophenol
DCP	dichlorophenol
TCP	trichlorophenol
DCM	dichloromethane
THF	tetrahydrofuran
KHCO$_3$	potassium hydrogen carbonate
MgSO$_4$	magnesium sulphate
DMSO-d$_6$	(dimethylsulfoxide)-d$_6$
D$_2$O	deuterium oxide
CDCl$_3$	(chloroform)-d
Mr	molecular mass

Chapter One

1 Introduction

Nitration[1] is an important synthetic process. Introduction of the nitro group into organic compounds may lead to functionalisation on carbon (**1**), oxygen (**2**) or nitrogen (**3**).

$$R-\underset{\underset{R}{|}}{\overset{\overset{R}{|}}{C}}-NO_2 \qquad\qquad R-O-NO_2 \qquad\qquad \underset{R}{\overset{R}{>}}N-NO_2$$
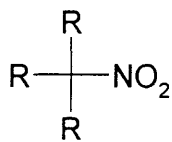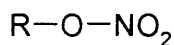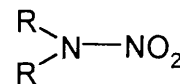
(**1**)   (**2**)   (**3**)

1.1 History of nitration

Faraday discovered benzene in 1825 and it is almost certain that he was the first to nitrate it. His diary for the 24th May 1825 records the experiment ('N.A.' being nitric acid, and the substance being benzene)[2] :

N.A. to substance – little action - reddening of acid-cold froze the substance which nearly colourless liquid became bright red solid-colour disappeared on thawing. Acid poured off, its smell very like almonds – no prussic compound detectable by iron, etc. – substance itself then smelling like almonds – washed became clear and then white on freezing.

Mitscherlich[3] in 1834 prepared nitrobenzene by treating benzene with fuming nitric acid and shortly after this mixed acid nitration was introduced.[4] It was Mansfield[5] who suggested that the sulfuric acid was a useful component because it removes water which would otherwise dilute the nitric acid. Mixed acid nitrations were first employed on an industrial scale by Mansfield in 1847.

The nitration of aliphatic compounds was first recorded by Beilstein and Kurbatov in 1880,[6] but only became important after inception of the petrochemical industry.

From these beginnings, nitration has grown to become an industrially important process, and the mechanisms of nitration have been the subject of continuous study.

1.1.1 Industrial use and research significance

Nitration has been an active area of industrial chemistry for more then a century,[7] which is testimony to its importance and accounts for the numerous products synthesised commercially. By far the most common industrial nitration is the reaction using sulfuric acid with nitric acid. This process is used in the manufacture of the vast majority of organic compounds produced today.

Some examples of organic compounds produced in bulk quantities include nitrated derivatives of toluene, benzene, phenol, chlorobenzene, alcohols, glycols, glycerin, aromatic amines and paraffins. Several of these are currently used as explosives including, trinitrotoluene (TNT) (4), trinitrophenol (picric acid) (5), cyclo-1,3,5-trimethylenetrinitramine (RDX) (6), cyclo-1,3,5,7-tetramethylenetetranitramine (HMX) (7), glyceryl trinitrate (nitroglycerin) (8) and cellulose trinitrate (9).
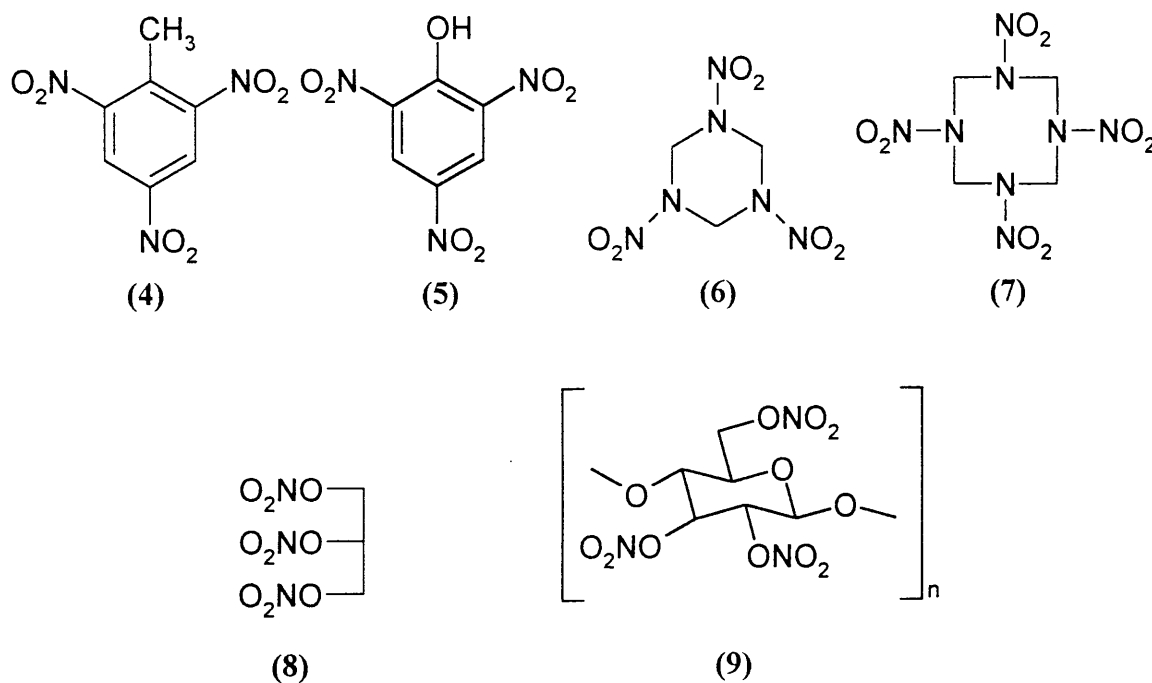
Nitrobenzenes are widely used in the manufacture of aniline. Dinitrobenzenes, nitrotoluenes and nitrochlorobenzenes are used as intermediates for dyes, pharmaceuticals, and perfumes.

Dinitrotoluene (DNT) is yet another nitrated product of major industrial importance. It is converted to toluene di-isocycanates that are then used to produce polyurethane foams, elastomers, fibres, and varnishes.[8]

Although nitration is considered to be a mature process, important changes and advances have occurred in the past twenty years. A plethora of new methods and procedures have become available recently which address contemporary issues such as selectivity, safety, economy, waste and the environment.[9]

1.2 Nitrating agents

There are numerous possibilities for effective nitration. Many nitrating agents are of the general formula NO_2-X. This serves as a source of the nitronium ion, NO_2^+, the effective nitrating agent.

Some nitration media and their properties are given in **Table 1.1** below: [9]

System	Application arom[a] nam[b] nest[c] sel[d]				By-products	Features
Pure HNO₃	+	+ +	+	-	Dilute HNO₃	Low nitrating strength, limited substrate choice, disposal/recycling problems
HNO₃-H₂SO₄	+ +	+ +	+ +	-	Dilute mixed acid	High nitrating strength, wide substrate choice, several disposal problems.
NO₂⁺BF₄⁻	+	+ +	(+)	-	H+BF₄⁻, acyl tetrafluoroborate	Very high nitrating strength, limited substrate choice, high expense & very corrosive by-products
HNO₃-Ac₂O	(+)	+ +	+ +	+	Acetyl nitrate (xs), AcOH	Moderate nitrating strength, limited substrate choice, high hazard – detonable.
N₂O₅/HNO₃	+ +	+ +	+ +	-	Strong HNO₃,	High nitrating strength, wide substrate choice, easy recyclability
N₂O₅/halogenated solvent	+	+ +	+ +	+	Potentially none (with ring-opening nitrations)	Moderate nitrating strength, wide substrate choice, by-product disposal problems virtually eliminated

arom[a] = aromatic nitrations; nam[b] = nitramine synthesis; nest[c] = nitrate ester synthesis; sel[d] = selective nitrations.

++ = highly suitable; + less suitable but possible; - = not possible.

Table 1.1 Selected nitration media and their properties.

1.2.1 Nitric acid (HNO₃)

Dilute nitric acid is useful for nitrating reactive substances such as phenols and other activated aromatic compounds but concentrated nitric acid can be disadvantageous because of its oxidising properties and environmental problems. The chief drawback of using 100 % nitric acid is that its reactivity diminishes substantially as water is produced during the reaction. Ridd has studied the nitration of a number of aromatic substances in aqueous nitric acid systems ranging from 64 % to 100 %.[10] At low acidities activated aromatics

such as phenol, anisole and mesitylene were nitrated, but higher acidities were required for the nitration of quarternary anilinium salts.

Nitro-aromatic compounds are often soluble in nitric acid making them difficult to recover on a practical scale due to the prohibitive cost of distillation. Carr *et al*[11] described a method for recovering nitroaromatics from the spent acid by decomposing it with nitric oxide (NO), to give nitrogen dioxide and water, (**Scheme 1.1**).

$$2HNO_3 + NO \rightleftharpoons 3NO_2 + H_2O$$
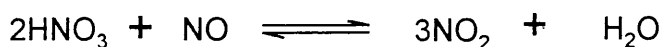
Scheme 1.1 Decomposition of nitric acid

Nitric acid is decomposed only to the extent necessary to cause the products to precipitate. The evolved gases are then reacted with oxygen to regenerate nitric acid.

1.2.2 Mixed acid

Solutions of nitric acid (or nitrates) in sulfuric acid (H_2SO_4) or oleum ($H_2SO_4.SO_3$) have the advantage that organic compounds may be soluble in them. One potential disadvantage in these media is the possibility of sulfonation competing with nitration.
Sulfuric acid aids the ionisation of nitric acid to the nitronium ion (**10**) as shown in **Scheme 1.2** and also binds water formed. A convenient way of altering the nitrating activity is by changing the concentration of sulfuric acid. Ingold[12a], Seidenfaden[12b] et al, Houben – Weyl[12c] have reviewed this in detail.

A general mechanism for the nitration of benzene is shown in **Scheme 1.3**. The first step involves slow reaction with the nitronium ion to give the Wheland intermediate (**12**) followed by fast loss of a proton, which is aided by HSO_4^-, to regenerate H_2SO_4.

$$HNO_3 + 2H_2SO_4 \rightleftharpoons NO_2^+ + H_3O^+ + 2HSO_4^-$$

(**10**)
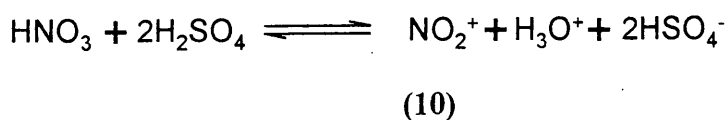
Scheme 1.2 Formation of the nitronium ion

(11)   (12)
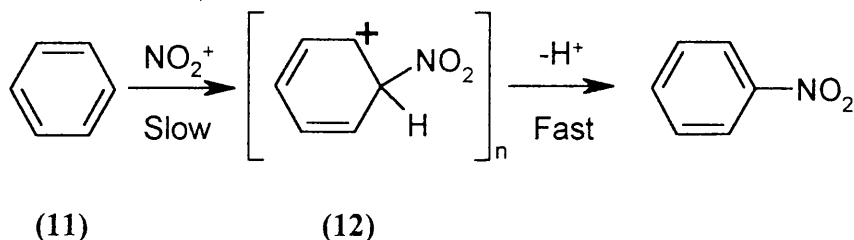
Scheme 1.3 Nitration of benzene

Manufacture of mononitrotoluenes on an industrial scale is conducted in 58 % H_2SO_4, with no detectable formation of dinitration, whereas dinitrated products are obtained in 65 % H_2SO_4. These reactions are heterogeneous in nature, as the aromatic precursor is only partially soluble in the mineral acid mixture.[13] The rate of nitration in commercial reactors is therefore often limited by diffusion of the aromatic compound into the acid phase or at least to the interface. Rys[14] has studied the regiochemistry of mixed acid nitrations and found it to be strongly influenced by mixing effects.

Solutions of nitric acid in other mineral acids such as phosphoric acid can give different isomer proportions from those in sulfuric acid. The regioselectivity of the nitration of toluene can be altered by using increasingly stronger H_3PO_4 resulting in decreasing *ortho* over *para* nitration as compared with reaction in H_2SO_4.[15] The reason may be the polymeric nature of H_3PO_4 at higher concentrations causing steric hindrance to *ortho* nitration.

The disposal of the spent acid represents a significant environmental problem with these mixed acid nitrations.

1.2.3 Nitronium Salts

Hydrocarbons are efficiently nitrated by nitronium salts under anhydrous conditions as shown by Olah *et al*,[16] (**Scheme 1.4**).

$$RH \ + \ NO_2^+MX_n^- \ \longrightarrow \ RNO_2 \ + \ HX \ + \ XM_{n-1}$$

Scheme 1.4 Nitration of hydrocarbons by nitronium salts

Nitronium tetrafluoroborate (**13**) is the most frequently used nitronium salt for nitrating aromatics, (**Scheme 1.5**).

$$ArH \ + \ NO_2^+BF_4^- \ \longrightarrow \ ArNO_2 \ + \ HF \ + \ BF_3$$
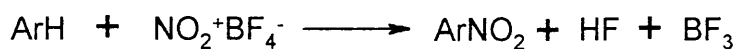
$$(13)$$

Scheme 1. 5

The side products obtained are HF and BF$_3$, which can be readily recycled on an industrial scale.

Nitronium tetrafluoroborate can be used to mono-nitrate benzene and toluene and other arenes, haloarenes and nitroarenes in good yield.[17] Nitronium tetrafluoroborate is useful for nitrating aromatics with acid sensitive functionality, such as aromatic nitriles, acid halides and esters. This is because it is not dependent on the presence of a strong acid.

The reactivity of nitronium salts is further enhanced by the use of strong acids such as FSO$_3$H. These reagent mixtures can even trinitrate benzene, [18,19,20] previously only reported in low yield. Thus 1,3,5-trinitrobenzene is usually prepared indirectly [21] but can be made in good yield by the reaction of *meta* dinitrobenzene with NO$_2$BF$_4$ and FSO$_3$H.[22] Nitrations using nitronium salts can also be used effectively with heterocyclic compounds such as pyridine.[23,24, 25] Reaction of pyridine (**14**) with NO$_2$BF$_4$ gives *N*-nitropyridinium ion and if

excess pyridine is present in the reaction mixture this may be followed by ring opening to give glutaconic aldehyde (**Scheme 1.6**).

(14) **(15)**
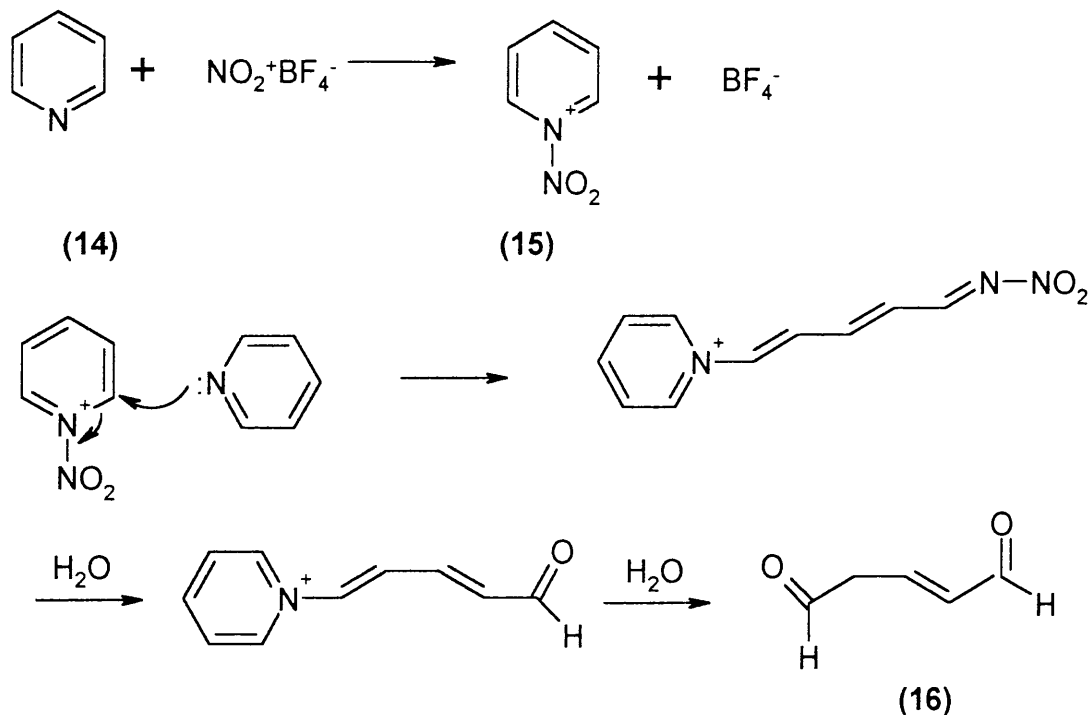
Scheme 1.6 Nitration of pyridine

The main synthetic disadvantage associated with the use of nitronium tetrafluoroborate is its poor solubility in commonly used organic solvents. Nitronium tetrafluoroborate is quite soluble in sulfolane (7 %), but in nitromethane its solubility is only 0.2 %. Other nitronium salts are more soluble; for example, nitronium hexafluorophopsphate ($NO_2^+PF_6^-$) has a solubility in nitromethane > 30 %. However the synthetic utility of nitronium hexafluorophopsphate is limited due to its poor synthetic accessibility and thermodynamic stability.

1.2.4 Acyl nitrates

Acyl nitrates are reactive nitrating agents. They are mixed anhydrides of nitric and carboxylic acids, with a general formula, $RC(O)ONO_2$. Aromatic nitration using acyl nitrates is shown in **Scheme 1.7**.

$$ArH + RC(O)ONO_2 \longrightarrow ArNO_2 + RCOOH$$
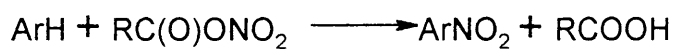
Scheme 1.7 Nitration using acyl nitrates

As isolated solids and at temperatures above 60°C in solution they are extremely unstable. However they are safely generated *in situ*, (**Scheme 1.8**).

$$(RCO)_2O + N_2O_5 \longrightarrow 2RC(O)ONO_2 \qquad \textbf{(a)}$$

$$RCOCl + AgNO_3 \longrightarrow RC(O)ONO_2 + AgCl \qquad \textbf{(b)}$$
$$\quad\ \textbf{(17)} \qquad \textbf{(18)}$$
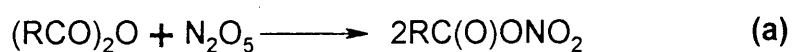
Scheme 1.8 Generation of acyl nitrates

Acetyl nitrate is the most widely used acyl nitrate. It may be prepared from N_2O_5 in Ac_2O, (**Scheme 1.8 a**), and can also be prepared more conveniently *in situ* by adding acetyl chloride (**17**) and silver nitrate (**18**)[26] (**Scheme 1.8 b**) to the aromatic compound.

Some specific examples of nitrations using acetyl nitrate are that of biphenyl to nitrobiphenyls in 87 % yield, giving 58 % of the 2- and 42% of the 4-nitro isomer, (**Scheme 1.9**).[27] Nitration of phenol with acetyl nitrate gives 52 % ortho and 48 % para nitrophenol. [28]
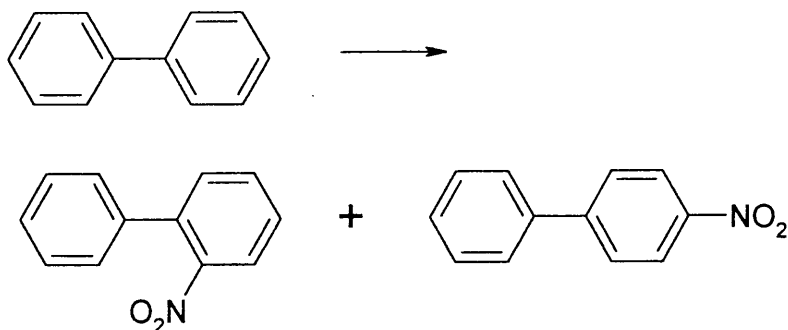
Scheme 1.9 Nitration of biphenyl using acetyl nitrate

1.2.5 Dinitrogen Pentoxide (N₂O₅)
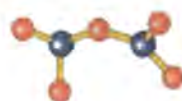
Red Oxygen
Blue Nitrogen

Figure 1.1 Structure of N₂O₅

Nitration reactions using dinitrogen pentoxide, the anhydride of nitric acid, are well known.[29] Most of the work has been carried out in the absence of a catalyst. Solid dinitrogen pentoxide at low temperature has been shown to exist as nitronium nitrate, $NO_2^+NO_3^-$, by Raman methods, [30] IR [31] and X-ray. [32] Studies of the kinetics and mechanism of reactions using dinitrogen pentoxide gave evidence that other carriers of the nitronium ion may also play a role. See **section 1.3** for a more in depth discussion of the mechanism involved.

Decomposition to N_2O_4 and oxygen should also be considered if the N_2O_5 used is not entirely pure. Feuer and Nielsen[33] have given a review of mechanistic studies using N_2O_5.

1.2.5.1 Nitration of aromatics by dinitrogen pentoxide

An early account of nitration by N_2O_5 is provided by Haines and Adkins.[34] Direct interaction of dinitrogen pentoxide with aromatic compounds is violent and often explosive, but dilute solutions of dinitrogen pentoxide, at low temperatures in carbon tetrachloride react readily with benzene and bromobenzene to give mono-nitrocompounds, (**Scheme 1.10**).

$$X = H \text{ or } Br$$
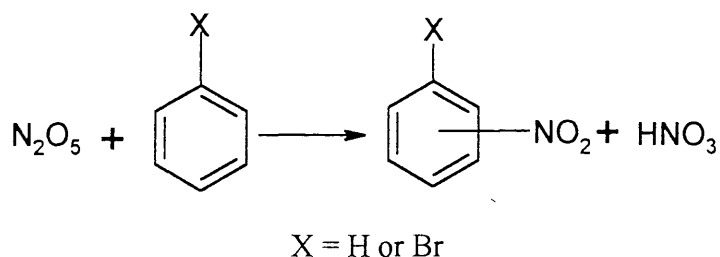
Scheme 1.10   Nitration of aromatics by N_2O_5

1.2.5.2 Dinitrogen pentoxide in sulfuric acid

Klemenz and Scholler[35] have shown that solutions of N_2O_5 in sulfuric acid, are extremely effective nitrating agents, having properties similar to those observed for solutions of nitric acid in sulfuric acid, (**Scheme 1.11**).

$$N_2O_5 + 3H_2SO_4 \rightleftharpoons 2NO_2^+ + 3HSO_4^- + H_3O^+$$
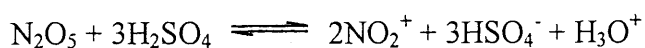
Scheme 1.11 Nitration using N_2O_5 in sulfuric acid

1.2.5.3 Dinitrogen pentoxide in the synthesis of nitramines

Recently dinitrogen pentoxide has successfully been used as a nitrating agent in the synthesis of nitramines and nitrate esters by nitrodesilylation reactions.[36] The substrate silylamines and silylalcohols were derived from the corresponding secondary amine or alcohol by reaction with trialkylsilylhalide. N_2O_5 cleaves the heteroatom-silicon bonds to yield the desired energetic groupings, (nitramines or nitrate esters), (**Scheme 1.12**). This occurs without the liberation of acids which would occur with conventional substrates, such as in mixed acid nitrations. These nitrodesilylation reactions proceed cleanly and in good yield, at low temperatures, and may be used to produce high energy compounds such as plasticisers.

$$RR'NH \xrightarrow{R_3''SiX} RR'NSiR_3'' \xrightarrow{N_2O_5} RR'NNO_2 + O_2NOSiR''_3$$
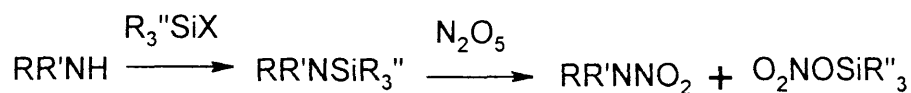
Scheme 1.12 Nitramine synthesis

Table 1.2 and **1.3** shows the reactions of silylamines and disilylamines with N_2O_5, and the reaction conditions and the yields recorded.

R^1	R^2	R^3	R^4	Rn. Time (hrs)	Yield (%)
-(CH$_2$)$_2$O(CH$_2$)$_2$-		CH$_3$	CH$_3$	2	80
-(CH$_2$)$_5$-		CH$_3$	CH$_3$	0.75	81
-(CH$_2$)$_4$-		CH$_3$	CH$_3$	0.5	76
CH$_3$	CH$_3$	CH$_3$	CH$_3$	0.75	78
C$_2$H$_5$	C$_2$H$_5$	CH$_3$	CH$_3$	0.75	84
i-C$_4$H$_9$	i-C$_4$H$_9$	CH$_3$	CH$_3$	0.75	87
-(CH$_2$)$_2$O(CH$_2$)$_2$-		CH$_3$	t-C$_4$H$_9$	2.25	37
-(CH$_2$)$_2$O(CH$_2$)$_2$-		n-C$_4$H$_9$	n-C$_4$H$_9$	1.5	39
-(CH$_2$)$_2$O(CH$_2$)$_2$-		C$_2$H$_5$	C$_2$H$_5$	0.75	61
i-C$_4$H$_9$	i-C$_4$H$_9$	C$_2$H$_5$	C$_2$H$_5$	1	70
-CH$_2$-CH(CH$_3$)-		CH$_3$	CH$_3$	10 min	Not isolated

General Formula: $R^1R^2N-Si(R^3)_2R^4$

Table 1.2 Reactions of silylamines with N_2O_5 in CH_2Cl_2 at 0°C to give the corresponding nitramines
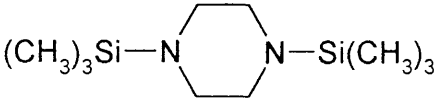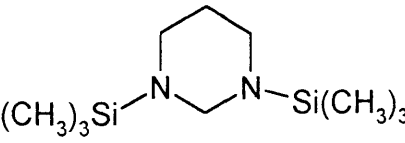
Disilylamines	Rn. time (hr)	Yield (%)
$(CH_3)_3Si-N$⬭$N-Si(CH_3)_3$	1	91
$(CH_3)_3Si-N$⬠$N-Si(CH_3)_3$	1	69

Table 1.3 Reactions of disilylamines with N_2O_5 in CH_2Cl_2 at 0°C to give the corresponding dinitramines

Silylamides were also investigated and were found to give the corresponding nitramide derivatives in good yields. An example of the reaction of a silyl amide with N_2O_5 is shown in **Scheme 1.13**. The yield was 79 %, which was a significant improvement from the previously reported yield (27%.was reported for compound shown in **Scheme 1.13**). [37]

Scheme 1.13 Reaction of silyl amide with N_2O_5

Nitrate esters were also successfully synthesized from corresponding silyl ethers giving the nitrate ester and silyl nitrate using the same conditions outlined above, (**Scheme 1.14**).

$$R-O-\underset{\underset{R''}{|}}{\overset{\overset{R''}{\diagup}}{Si}}-R'' \longrightarrow R-ONO_2 + O_2NOSiR''_3$$
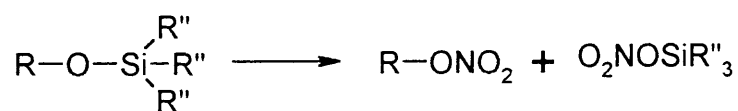
Scheme 1.14 Nitrate ester synthesis from silyl alcohols

1.2.5.4 Dinitrogen pentoxide in ring opening reactions

Dormer, Hylands and Moodie have carried out investigations of oxetane ring opening reactions using solutions of dinitrogen pentoxide dissolved in dichloromethane,[38] (**Scheme 1.15**).
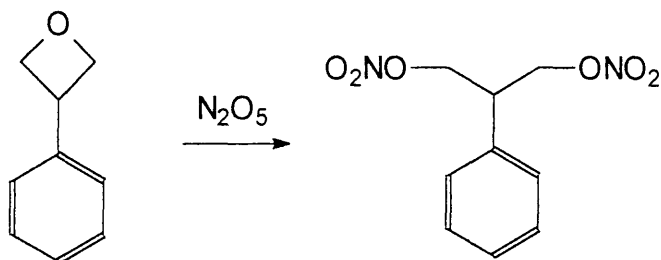
Scheme 1.15

The reaction of 7-oxabicyclo[2.2.1]heptane gave exclusively *trans*-cyclohexane-1,4-diol dinitrate, (**Scheme 1.16**). This reaction is approximately second order in dinitrogen pentoxide and has high negative entropy of activation, suggesting a cyclic transition state (**19**).

(19)
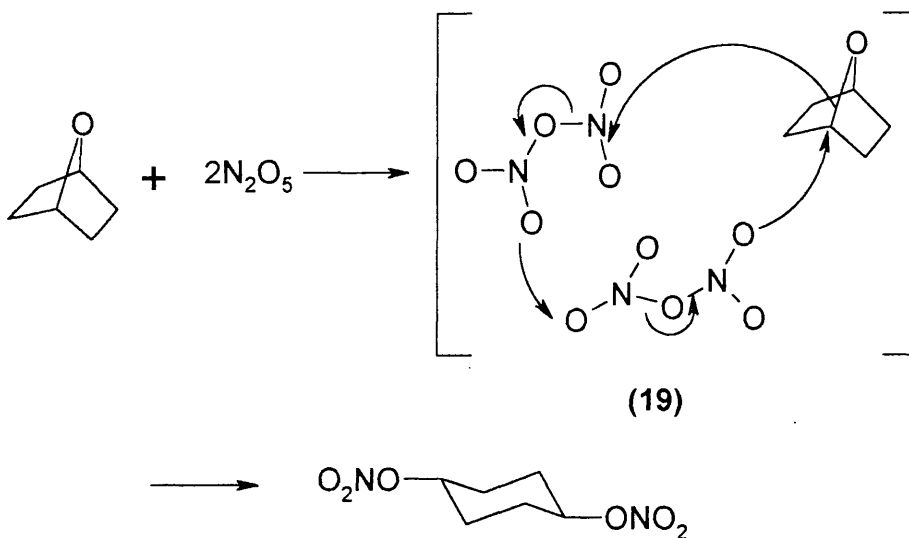
Scheme 1.16 Cyclic transition state of the nitration with N_2O_5

Golding, Millar, *et al*, [39] have reported the ring opening nitration, with solutions of N_2O_5 in CH_2Cl_2, of ten oxetane rings bearing various substituents. The products are the corresponding 1,3 dinitrate esters, (**Scheme 1.17**).

$$R', R'' = H, CH_3, -(CH_2)_5-$$
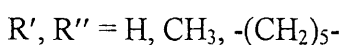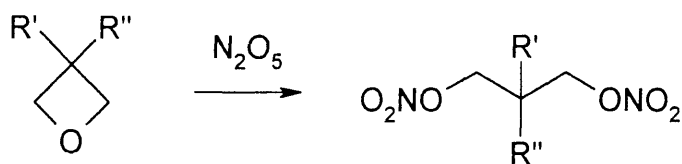
Scheme 1.17 Example of ring opening nitration in oxetanes

Ring strained epoxides have also been nitrated using N_2O_5 in chlorinated solvent to yield the corresponding dinitrates in excellent yield. [40]

$$R, R' = H, Me, Et, -(CH_2)_3-, -(CH_2)_4-, -(CH_2)_6-$$
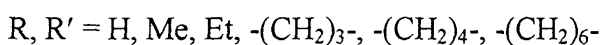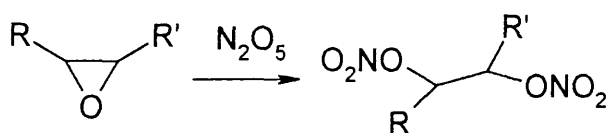
Scheme 1.18 Example of ring opening in epoxides at 0°C in CH_2Cl_2

Aziridines have also been successfully nitrated with N_2O_5. [41] A wide variety of aziridines underwent the reaction including *N*-alkyl (**Scheme 1.19a**), *N*-acyl (**Scheme 1.19b**) and *N*-imidyl (**Scheme 1.19c**) derivatives, yields were high (70-82 %).
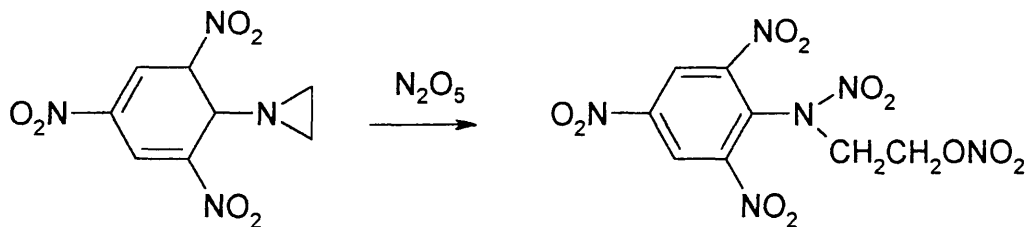
Scheme 1.19 a
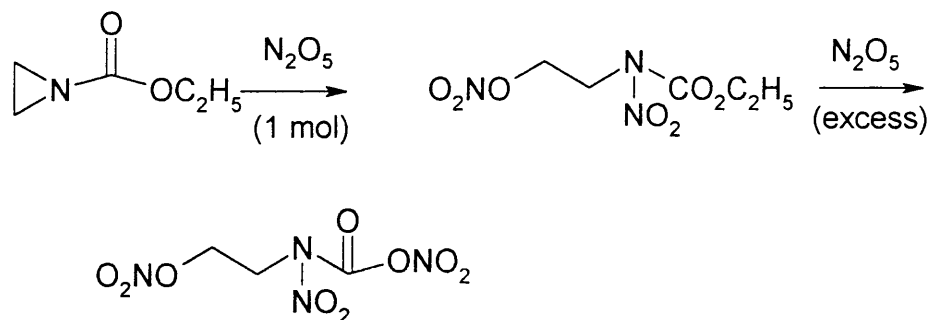
Scheme 1.19 b
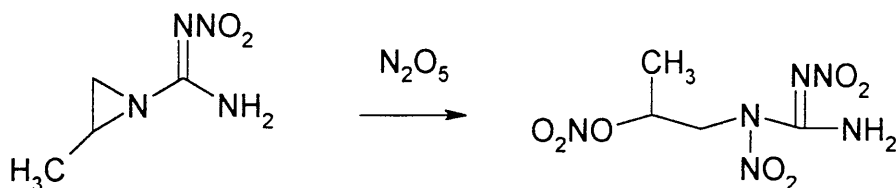
Scheme 1.19 c

Scheme 1.19 (a, b, and c) Example of ring opening in aziridines in chlorinated solvents at sub-ambient temperatures

In some cases azetidines have been found to react similarly to aziridines to form nitramine nitrates in ring opening reactions. This is shown in **Path A** in **Scheme 1.20**. However azetidines bearing *N*-acyl substituents underwent nitrolysis of the exocyclic substituent to form *N*-nitroazetidine; this is shown in **Path B** in **Scheme 1.20**. The reduced reactivity of the azetidines compared with aziridines can be rationalized in terms of the reduced strain in a four membered ring compared to the corresponding three membered system.[42]

R = Bu^n, (CH$_2$)$_2$CN, (CH$_2$)$_2$COEt, CO$_2$Et

R = COEt, CONMe$_2$, CONHPr^n, COPr^n, COMe,COCON
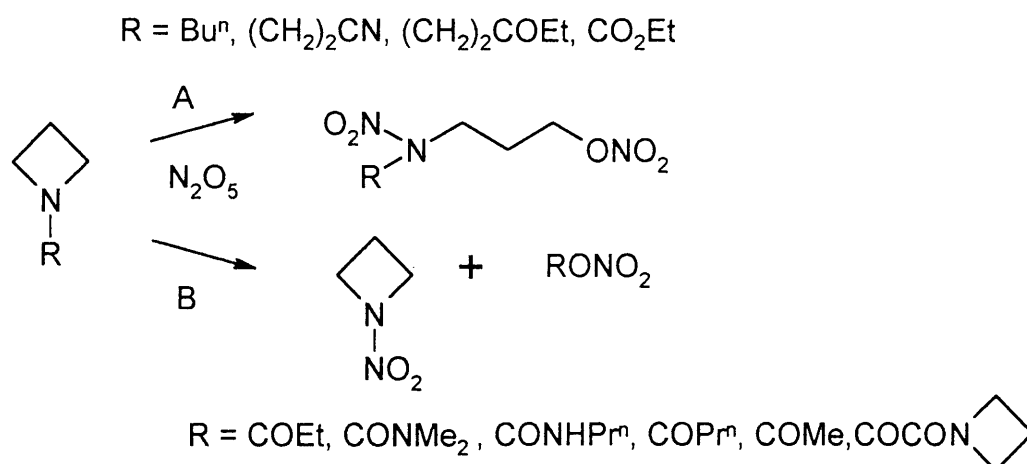
Scheme 1.20 Example of ring opening (**A**) in azetidines and *N*-nitration (**B**) in chlorinated solvents at sub-ambient temperatures.

1.2.5.5 Nitration of pyridine using dinitrogen pentoxide

Bakke et al have studied the sulfur dioxide mediated reaction of pyridine (**20**) with N$_2$O$_5$. The reaction may be carried out in liquid sulfur dioxide and also in organic solvents. [43,44,45,46] As shown in **Scheme 1.21** the eventual product is 3-nitropyridine, (**23**). It was proposed that initially a pyridine-SO$_2$-N$_2$O$_5$ complex (**21**) was formed. When this complex is added to water the dihydropyridine (**22**) was formed. Two possible mechanisms were proposed for the conversion of (**22**) into the eventual product. The first, shown in **Scheme 1.22**, involves intramolecular transfer of the NO$_2$ group via a six-membered transition state, followed be elimination of HNu. The second possibility, shown in **Scheme 1.23**, involved the formation of a nitronium ion which reacts in a solvent cage.[47] Again the final step is elimination of HNu.

(20)   (21)   (22)   (23)
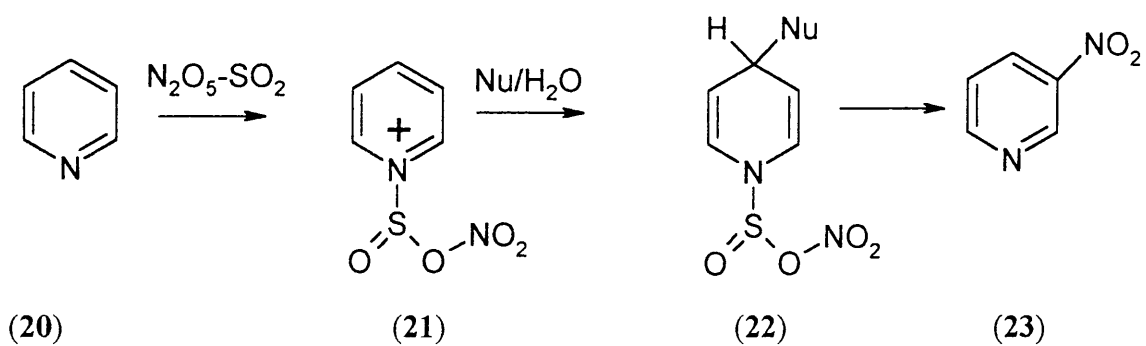
Scheme 1.21 Nitration of pyridine with SO_2/N_2O_5
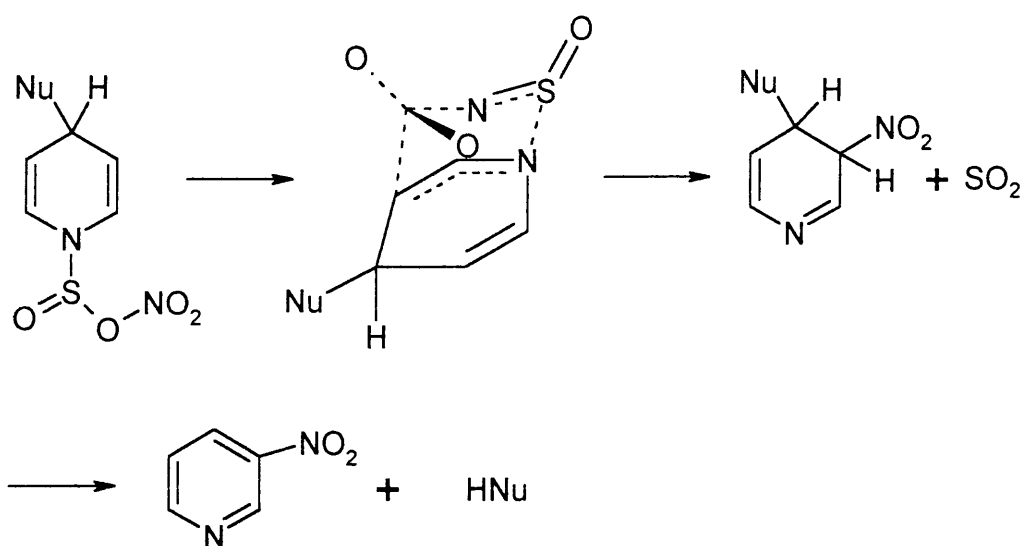
Scheme 1.22 First possible mechanism in the conversion of dihydropyridine into nitro-pyridine
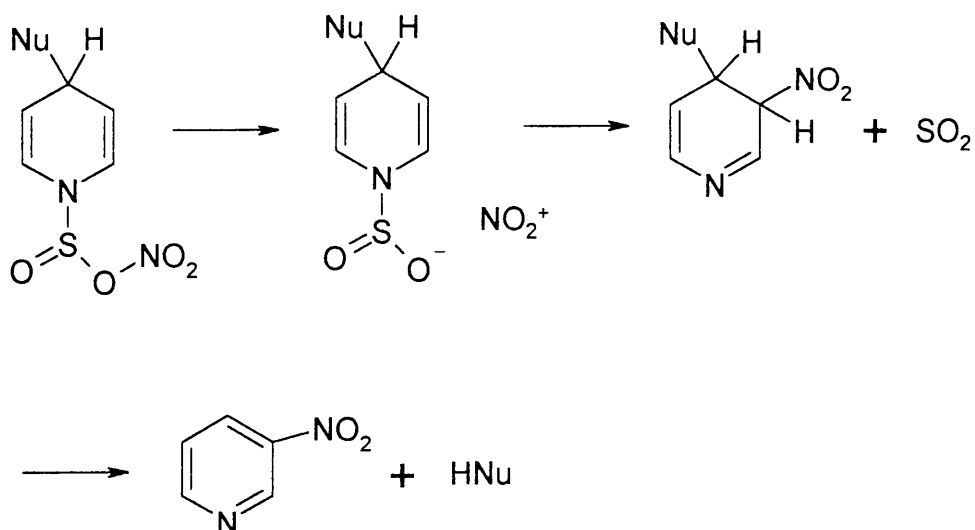
Scheme 1.23 Second possible mechanism in the conversion of dihydropyridine into nitro-pyridine

A further refinement of the reaction conditions by Bakke was to react pyridine with N_2O_5 in THF or CH_3NO_2 to give *N*-nitropyridinium nitrate. Reaction with an aqueous solution of sodium bisulfite nucleophile, e.g. SO_3^{2-}, HSO_3^- or $SO_2.xH_2O$, gave a 1,2-dihyropyridine derivative.[48] The results are in accord with the mechanism shown in **Scheme 1.24**. This involves a (1,5) sigmatropic shift of the nitro group followed be the further addition and elimination of bisulfite.
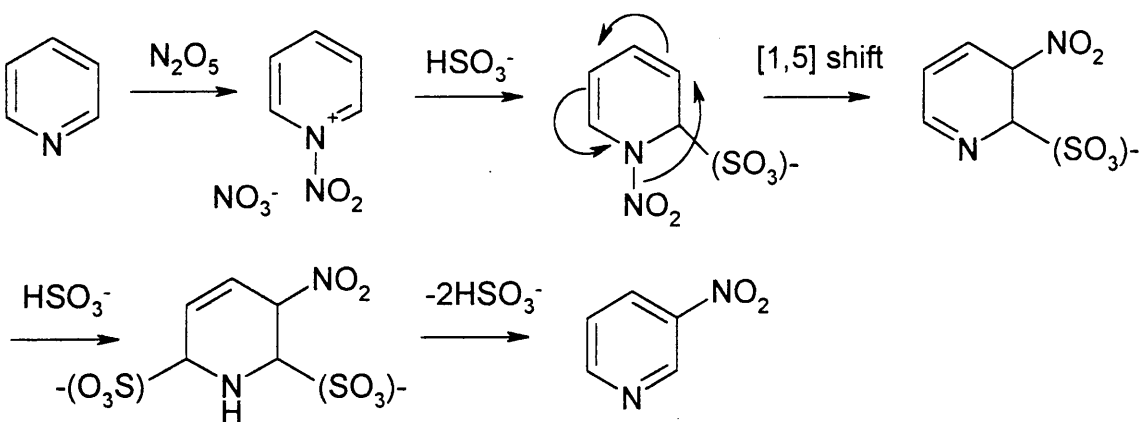
Scheme 1.24 Mechanism for the nitration of pyridine with N_2O_5 involving a (1,5) sigmatropic shift

1.2.5.6 Nitration of styrenes using dinitrogen pentoxide

The reaction of N_2O_5 with polymers containing oxirane units has been used in the preparation of explosive materials. These polymers may contain double-bonds in their back-bone structure. Hence study of the reactions of N_2O_5 with alkenes is of interest.

The reactions with alkenes are often complex, and may lead to the formation of nitro-nitrate addition products.

The reaction of 4-substituted styrenes (H, Me, Cl, CF_3, NO_2) with N_2O_5 has been studied by Lewis and Moodie.[49] Several products are formed, predominantly by radical pathways as shown by ^{15}N CIDNP studies. However there is also evidence for ionic pathways. One example of the possible radical pathway is shown in **Scheme 1.25**.
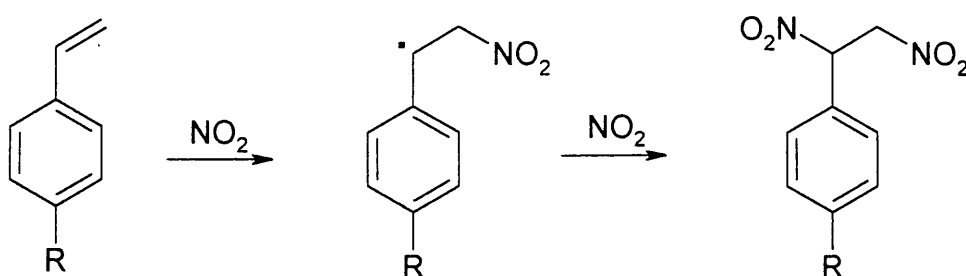
Scheme 1.25 Radical pathway in the nitration of styrene using N_2O_5

Nitration of the unsubstituted styrene resulted in at least ten different products and attempts to separate these were unsuccessful. Hence, the reaction was not investigated further. Four structures (**24-27**) were assigned to some of the products.

(24)   (25)   (26)   (27)

R= H, Me, Cl, CF and NO$_2$
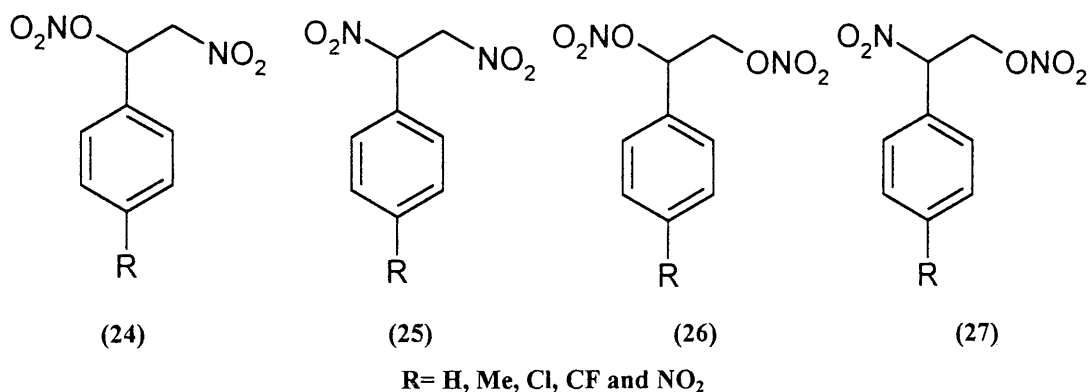
1.2.5.7 Indirect use of N$_2$O$_5$ in nitration

Recent work has been published on the use of vanadium (V) oxytrinitrate, (VO(NO$_3$)$_3$), as a powerful reagent for the nitration of aromatic compounds at room temperature under non acidic conditions.[50] Vanadium oxytrinitrate was produced from the reaction of vanadium pentoxide with dinitrogen pentoxide,[51] and was reported to nitrate successfully various aromatics, (**Scheme 1.26**), **Table 1.4**.
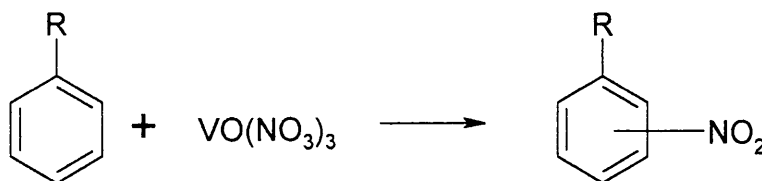
Scheme 1.26 Nitration of aromatic compounds with an equimolar quantity of VO(NO$_3$)$_3$ in CH$_2$Cl$_2$ at room temperature

R	*ortho* (%)	*meta* (%)	*para* (%)	2,4 disub. (%)	yield (%)
H	99				99
CH$_3$	35	2	41	19	99
Bu^t	11	6	77	6	99
OH	32		9	51	93
OMe	23		38		61
Br	48		52		99
Cl	43		57		99
I	35		62		97
NHAc	37		48		85
CO$_2$H	15	37	2		54
CO$_2$Me	29	67	4		99
CN					0

Table 1.4 The nitration of various aromatics with vanadium oxytrinitrate in dichloromethane.

1.3 Mechanisms of aromatic nitrations

1.3.1 The mechanism of electrophilic aromatic nitration

The foundations of the mechanism involved in electrophilic aromatic nitration stem from the preliminary work of Ingold and Hughes *et al.*[52] The essence of this is a four step process, outlined below (**Scheme 1.27**).

The Ingold Mechanism consists of 4 steps:

$$(1)\ HNO_3 + HA \rightleftharpoons H_2NO_3^+ + A^-$$

$$(2)\ H_2NO_3^+ \rightleftharpoons NO_2^+ + H_2O$$

$$(3)\ ArH + NO_2^+ \rightleftharpoons ArHNO_2^+$$

$$(4)\ ArHNO_2^+ + A^- \longrightarrow ArNO_2 + HA$$
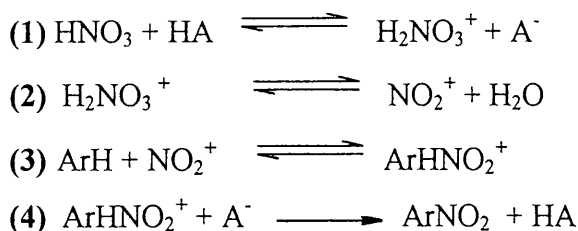
HA – general acid

ArH –general aromatic compound

Scheme 1.27 Ingold's proposed mechanism

Steps (1) and (2) show the formation of the nitronium ion from nitric acid and a general acid. Step (3) shows the addition of an aromatic substrate to give the 'Wheland Intermediate'. Step (4) shows the deprotonation of the 'Wheland Intermediate' to give the nitrated product, regenerating the aromaticity.

The Ingold group firmly established the nitronium ion as the nitrating agent in electrophilic nitration, and kinetic studies have demonstrated a zero order dependence on the substrate in the nitration of reactive aromatics such as benzene and toluene. This is best explained by the rate determining step being the formation of the nitronium ion followed by fast reaction with the aromatic compound.

The Ingold Mechanism has since been modified. Olah[53] and Schofield[54] have both proposed possible mechanisms. Olah's studies involved nitronium tetrafluorborate as the nitronium ion source. This eliminates the relatively slow acid catalysed transformation of HNO_3 into NO_2^+ and allows direct study of the reaction of NO_2^+ with aromatics. Olah argued that his data could only be explained if the substrate- and positional-selectivities are determined in two distinct steps separated by an intermediate. Olah suggested that reactive

alkyl aromatics and the NO_2^+ ion first form a π complex which transforms into the Wheland intermediate (σ complex) (**Scheme 1.28**).

π-complex   σ-complex
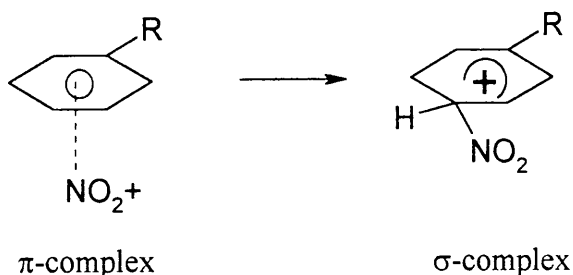
Scheme 1.28 Olah's proposed mechanism

Schofield agreed that there was evidence for an interaction between the reagent and the substrate before the formation of the Wheland intermediate but argued that it was not necessarily a chemical one. He proposed that the first intermediate was being formed at the encounter rate and the resulting product was in fact an encounter pair, with reagent and substrate contained in the solvent shell.

$$H^+ + HNO_3 \rightleftharpoons H_2NO_3^+$$

$$H_2NO_3^+ \rightleftharpoons H_2O + NO_2^+$$
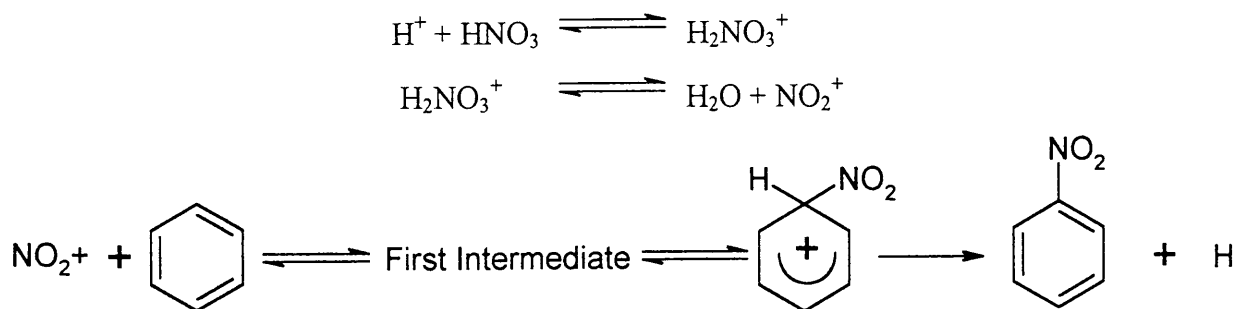
First Intermediate : π complex (Olah), or an encounter pair (Schofield).

Scheme 1.29 Mechanism for nitration of an aromatic compound by nitric acid via the nitronium ion.

1.3.2 Nitration at the encounter rate

1.3.2.1 Diffusion controlled reactions

Diffusion can influence the reaction rates in two ways:

i)   Macroscopic diffusion control – the rate is determined by the speed of mixing of solutions containing the reactants.

ii) Microscopic diffusion control – the rate depends on the speed of diffusion together of the reactants in homogenous solution.

1.3.2.2 The kinetic behaviour

Bimolecular reactions involve two steps. The reagents must approach each other before a chemical reaction can occur. When any limitations due to mixing are removed, then the maximum rate of a bimolecular reaction is determined by the rate of encounter of the two molecules; such reactions are called diffusion-controlled or encounter-controlled.

The rate of diffusion in solution depends on the viscosity of the solvent. For molecules of equal size the value of the second order rate constant for diffusion controlled reactions is given by **Equation 1.1**:

$$k = 8000RT/3\eta$$

Equation 1.1

where η is the coefficient of viscosity of the solvent.
Values of k (second order rate constant) at 25°C are typically around 10^9 $dm^3 mol^{-1} s^{-1}$.[5]

There is evidence that nitrations carried out in various media occur at a rate controlled by the diffusion together of the substrate and the nitronium ion. Values of the second order rate constant, defined by the **Equation 1.2**,

$$\text{Rate} = k_2\text{obs}[Ar][HNO_3]$$

Equation 1.2

are found to reach a maximum value as the reactivity of the aromatic substrate increases.

Compound	$k_2$obs $/\text{dm}^3\text{mol}^{-1}\text{s}^{-1}$	krel
Benzene	5.8×10^{-2}	1
Toluene	1.0	17
o-xylene (1,2-dimethylbenzene)	2.2	38
m-xylene (1,3-dimethyl benzene)	2.2	38
p-xylene (1,4-dimethylbenzene)	2.2	38
mesitylene (1,3,5-trimethylbenzene)	2.1	36

where $k_{rel} = k_{compound}/k_{benzene}$

Table 1.5   Rate constants for nitration in 68% sulfuric acid at 28°C. [55]

The data in **Table 1.5** show that as the substrate reactivity is increased, by increasing methyl substitution, (increasing electron density), the rate constant for nitration reaches a maximum value. This corresponds to reaction at the encounter rate. As a consequence, reactive aromatics appear to be less reactive than expected on the basis of the additivity of substituent effects.

In sulfuric acid media the reaction will involve the following processes;

$$HNO_3 + H^+ \xrightleftharpoons{K} NO_2^+ + H_2O$$

$$Ar + NO_2^+ \xrightarrow{k} \text{product}$$
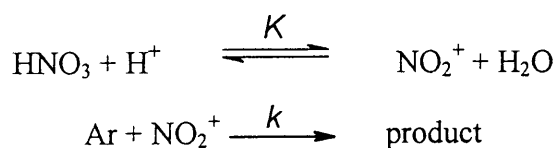
Scheme 1.30

Schofield has shown that values of k may be estimated using the relation in **Equation 1.3**, [56]

$$\text{rate} = k_2\text{obs}[Ar][HNO_3] = k[Ar][NO_2^+]$$

Equation 1.3

In solutions of greater than 89% sulfuric acid the nitric acid is completely ionised. This fact coupled with the known decrease of $k_2$obs with decreasing acidity allows the calculation that in 68% sulfuric acid,

$$[NO_2^+] \approx 10^{-8}\ [HNO_3].$$

Equation 1.4

Hence in 68% sulfuric acid $k \sim 10^8\ k_2$obs. Use of the data in **Table 1.5** leads to values for k of $\sim 6 \times 10^6\ dm^3 mol^{-1}s^{-1}$ for benzene and $\sim 2 \times 10^8\ dm^3 mol^{-1}s^{-1}$ for mesitylene. The latter value is close to that expected for a reaction controlled by diffusion together of mesitylene and the nitronium ions.

1.3.2.3 Apparent activation energies of encounter-controlled nitrations

The intrinsic activation energy of an encounter-controlled reaction must be small. However it is not generally negligible and may be sufficient to allow product-formation to manifest considerable selectivity.

For nitration reactions the experimental activation energy is made up from the viscosity of the medium and ΔH° for the pre-equilibrium in which nitronium ion is produced. The steady-state approximation applied to the following simplified kinetic **Scheme 1.31** represents an encounter-controlled nitration,

$$HNO_3 + H^+ \overset{K}{\rightleftharpoons} NO_2^+ + H_2O$$

$$Ar + NO_2^+ \xrightarrow{k} (E.p.)$$
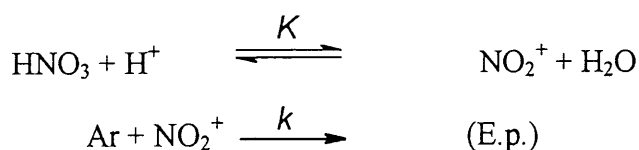
Scheme 1.31

And leads to **Equation 1.5**, where a_{H+} and a_{H2O} represent the activities of the proton and water respectively,

$$k_2 obs = kK a_H^+/a_{H2O}$$

Equation 1.5

Now,

$$E_a = RT^2 d(\ln k_2 obs)/dT$$

Equation 1.6

So that if the dependence of the viscosity of the medium upon temperature can be represented by an exponential relationship as shown in **Equation 1.7**,

$$\eta = be^{B/RT}, \text{ also } k = 8000RT/3\eta$$

Equation 1.7

Then combining 5 and 6,

$$E_a = RT + B + \Delta H^o + RT^2 d[\ln(a_{H+}/a_{H2O})]/dT.$$

Equation 1.8

For the nitration of mesitylene in 67% sulfuric acid, the experimental activation energy, E_a, has a value of 75.3 kJmol^{-1}. For this medium at 25°C it is known that RT + B has the value 24 kJ mol^{-1} whilst ΔH^o has been estimated as 43 kJ mol^{-1}.[56] The final term in **Equation 1.8** is expected to be small. Hence the value of E_a calculated for a diffusion-controlled reaction is close to the experimental value. This provides further evidence for reaction at the encounter rate.

1.3.2.4 Microscopic and macroscopic diffusion in nitration.

Most nitrations are carried out in such a way so that the nitronium ion is formed in very small concentrations. Hence, although with sufficiently reactive aromatics the reaction with nitronium ion may become microscopically diffusion controlled, the experimentally determined rate coefficient (Rate = k_2obs [Ar][HNO$_3$]) may more often than not be measured by conventional methods. If those nitrations which show the phenomenon of a rate limiting coefficient are correctly regarded as being microscopically diffusion-controlled, or encounter-controlled, then they, and even some nitrations of less reactive aromatics must be macroscopically diffusion-controlled when bulk concentrations of nitronium ion are used. This is the case for nitrations in which nitronium salts in organic solvents are used.

1.3.2.5 The pre-association mechanism

The comparison of observed rate coefficients with those calculated for encounter-controlled reactions suggest that certain weak bases are nitrated in sulfuric acid through the small concentration of unprotonated base present in the solutions.[57] The most thoroughly discussed members of this group are *p*-nitroaniline and 2-chloro-4-nitroaniline.

A serious difficulty arises if these reactions are seen as conventional diffusion controlled processes. Under these conditions the half-life of each unprotonated amine is probably shorter (ca10^{-9} s) than the lifetime of the encounter pair (10^{-8}-10^{-10} s). The two steps of the reaction, loss of proton and diffusion together of the amine molecule and the nitronium ion cannot be regarded as discrete process. Here in strongly acidic solutions the compounds will exist very largely in the protonated form, (**Equation 1.9**).

$$ArNH_2 + H^+ \rightleftharpoons ArNH_3^+$$

Equation 1.9

In strongly acidic solutions most of the nitric acid will be present as NO_2^+. Hence the situation is the reverse of the usual one, in that the electrophile is readily formed while the aromatic substrate is generated in very small concentration from the cation.

The amine complex must be generated in an encounter complex already containing the nitronium ion. A mechanism, (**Scheme 1.32**), has been proposed in which the nitronium ion facilitates proton loss from the anilinium ion, whilst in the rate determining step the nitronium ion attacks a hydrogen bonded complex of the free amine and the protonated base.[58] There is no diffusion together of the amine and the nitronium ion.

$$Ar\ NH_3+ + NO_2^+ \rightleftharpoons O_2N^+ ---ArNH_3^+ \underset{}{\overset{B}{\rightleftharpoons}} O_2N^+ ---ArNH_2 + HB^+$$

Rate determining

↓
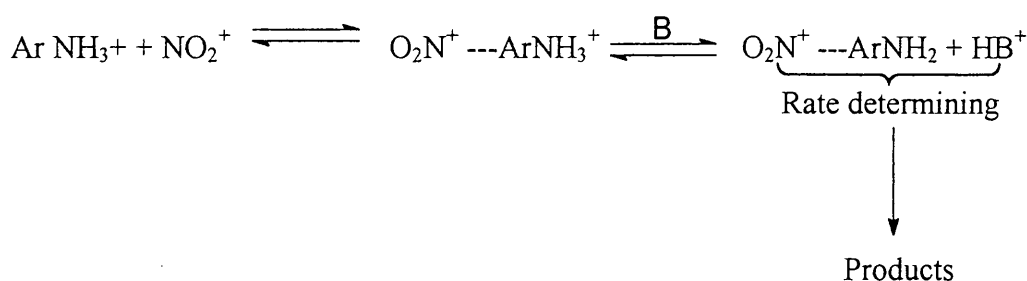
Products

Scheme 1.32

A more general discussion of cases of electrophilic substitutions in which one of the reactants is produced in low concentration from an inactive precursor, suggests that if the half life of a reactant is $<10^{-10}$ s a pre-association mechanism of above type will by-pass the conventional diffusion process as the means of generating the encounter complex.[58] For the nitration of the aniline derivatives a more generalised mechanism was proposed, having no implications about the order in which the encounter triplet is assembled, (**Scheme 1.33**).

$$NO_2^+ + ArNH_3^+ + B \rightleftharpoons NO_2^+.ArNH_3^+.B$$
$$NO_2^+.ArNH_3^+.B \rightleftharpoons NO_2^+.ArNH_2.HB^+$$
$$NO_2^+.ArNH_2.HB^+ \longrightarrow products$$
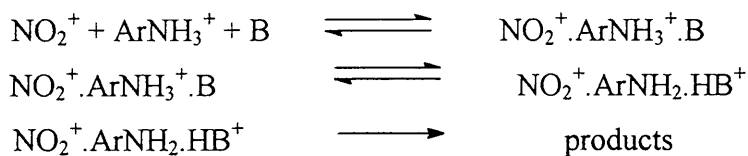
Scheme 1.33

1.3.2.6 Encounter rate nitration and positional selectivity

In solution molecules are closely packed, and when two reactant molecules become nearest neighbours they remain so for some time. This event is called an encounter and the two reactant molecules an encounter pair. During the lifetime of the encounter the reactant molecules collide a number of times, and in one of these collisions they may react. When the probability of the reaction is near to unity, the reaction becomes diffusion controlled and the rate of reaction is limited by the rate of encounter.

The identification of circumstances in which a reaction becomes microscopically diffusion-controlled introduces the encounter pair into the mechanism of that reaction as a kinetically discrete entity. For substrates reacting under these circumstances, substrate selectivity is lost. In nitration, it is found that such loss of substrate selectivity is not accompanied by loss of positional selectivity within the molecules of each substrate.

1.3.2.7   Partial rate factors

In reactions which occur at rates which are below the diffusion controlled limit, it is useful to compare quantitatively reactivities of different substrates and at different ring positions. This may be done by the use of partial rate factors. [29] These compare the rates of reaction at a single ring position of the substrate with the rate of a single ring-position of benzene. In order to determine these values it is necessary to compare the overall rate of reaction with that of benzene and to know accurately the relative amounts of isomer formed. For example, [29] it was found that toluene is *ca* 25 times more reactive than benzene in nitration reactions using nitric acid, and that the isomer proportion are *ca o:m:p*, 58:4:38. Hence it is possible to calculate partial rate factors for *ortho, meta,* and *para* positions of 44, 3, and 57 respectively.

Studies of the nitration of monohalobenzenes in sulfuric acid have yielded values for the *ortho*, *meta* and *para* positions of chlorobenzenes of 0.067, 0.0018 and 0.246 respectively. [59] While partial rate factors give general indications of reactivity some variations occur depending on the nitrating medium and reaction conditions.

When substitution occurs in compounds containing two or more substituents, partial rate factors may be used to estimate reactivities of the various ring positions. This approach assumes that the effects of substituents are additive. This may not always be the case due to the intrusion of steric effects and by resonance interactions between groups.

1.3.3 The mechanism involved in dinitrogen pentoxide nitration

The mechanism of aromatic nitration by N_2O_5 was studied in detail by Ingold *et al.*[60] Benzene and toluene were too fast to study by their method. Therefore, they used reactants containing deactivating halogens (from 1 to 3) or carboxyl substituents (up to 2). The solvents used varied in polarity with the main solvent systems being tetrachloromethane and a nitromethane : tetrachloromethane mixture (1:9). The addition of the nitromethane had little effect on the kinetics but improved substrate and product solubility. Temperatures were in the range 248-298 K.

The kinetic studies were carried out using dilatometry under pseudo first order conditions, using mainly excess aromatic substrate, and were generally found to be complex in nature. The kinetic results (dilatometer readings) showed three broad classes, exponential, linear and sigmoidal depending on the reaction conditions.

This suggested that when the aromatic compound was in constant concentration there might be first order kinetics, zeroth order kinetics and an autocatalytic reaction, separately or in superposition. However, more careful studies of the curves showed two possible pathways:

1   Non-catalysed first order reactions which are favoured at higher temperatures and lower initial concentrations of reagent. These showed exponential form.

2   Autocatalytic reaction which was favoured at lower temperatures and higher concentrations and showed sigmoidal kinetic form.

1.3.3.1   Non-catalytic Reaction

The observation that nitration follows an exponential law when either aromatic compound is in excess over N_2O_5 or the latter is in excess over the former, can evidently be correlated by the following rate equation:

$$Rate = k_2[ArH][N_2O_5]$$

Equation 1.10 Rate correlation for non-catalytic reaction.

It was also proposed that the nitration was not occurring via the nitronium ion. Instead molecular N_2O_5 was thought to be the nitrating agent, involving the direct attack by the non-ionised N_2O_5.
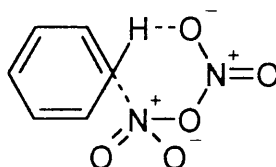
Figure 1.2 The Ingold intermediate in aromatic nitration with N_2O_5

This conclusion was supported by two pieces of experimental data. The first was that increased solvent polarity generated only a small increase in the rate of reaction. The second was that the addition of salts including nitrates gave an increased rate of nitration. This result is not consistent with nitronium ion nitration where the concentration would be diminished by the common ion effect.

$$N_2O_5 \rightleftharpoons NO_2^+ + NO_3^-$$
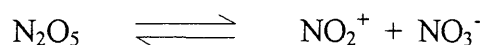
Scheme 1.34 Nitronium ion nitration

1.3.3.2 Autocatalytic reaction

Nitric acid was found to catalyse the nitration reaction dominating the kinetic profile of the process. Addition of sulfuric acid gave a similar result although more pronounced. As nitration proceeds, nitric acid is formed, therefore under certain circumstances the reaction becomes autocatalytic.

The rate law of the catalytic route is written:

$$\text{Rate} = k_2'[\text{ArH}][\text{N}_2\text{O}_5][\text{HNO}_3]^n$$

Equation 1.11

The value of n was found experimentally to be 2, 3 or 4 depending on the amount of nitric acid present. The catalytic nitration route was considered to occur via the nitronium ion. Ingold argued that the minimum value of n=2 arises from the need for at least one molecule of nitric acid to solvate each of the nitronium and nitrate ions formed by dissociation of N_2O_5. If the nitronium ion aggregates with more than one nitric acid molecule, then the rate is proportional to the concentration of the nitric acid raised to a power greater than one, (**Scheme 1.35**).
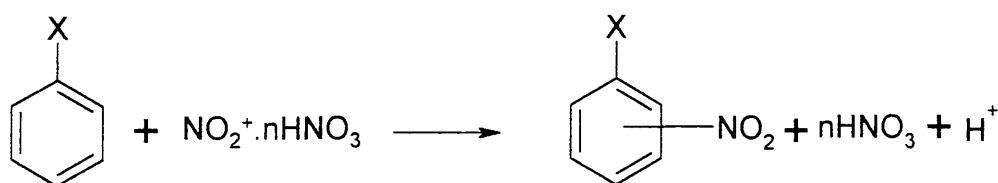
Scheme 1.35 The nitronium ion route

The initial non-catalytic route can combine with the auto catalytic route to give the rate law shown. This accounts for both possible mechanisms for nitration with N_2O_5, **Equation 1.12**.

$$\text{Rate} = k_2[\text{ArH}][\text{N}_2\text{O}_5] + k_2{}'[\text{ArH}][\text{N}_2\text{O}_5][\text{HNO}_3]^n$$

Equation 1.12

This combination of routes may give rise to the near linear dependence of dilatometer readings on time

1.4 Nitration via nitrosation.[61]

The direct nitrosation of carbon atoms in an aromatic ring is another important process for introducing the nitro functionality, all be it indirectly. This nitrosating agent can either be NO^+ or a carrier of NO^+ in the form NOX. The nature of X will depend on the experimental conditions.[62]

Other common reactions are *N*-nitrosation and *O*-nitrosation. *N*-Nitrosation leads to diazotization, deamination or nitrosamine formation. *O*-nitrosation is involved in the formation and hydrolysis of alkyl nitrites and in the exchange of ^{18}O between nitrous acid and water. The mechanisms of *N*-nitrosation and *O*-nitrosation have been investigated in detail,[63] but mechanistic studies on *C*-nitrosation are mainly limited to the kinetics of nitrations via nitrous acid.

C-Nitroso-compounds initially can be rapidly oxidised to nitro-compounds, so that the rate determining step is the initial nitrosation. In the oxidation, a molecule of nitric acid is reduced to a nitrous acid, agreeing with the experimental observation that in the absence of side reactions the concentration of nitrous acid remains constant throughout the reaction. For the reactions of 4-nitrophenol and 4-chloroanisole with nitric acid in acetic acid it has been noted that the nitration is accelerated in the presence of nitrous acid, **Equation 1.13**.

$$\text{rate} \propto [\text{ArH}]^1[\text{HNO}_2]^1$$

Equation 1.13

With 4-chloroanisole there was evidence for nitration both by nitric and nitrous acids. However, with phenols the nitrous acid pathway was dominant.[64]

The question why only reactive aromatics such as phenols show catalysis of their nitration by HNO_2, can be answered by first remembering that these aromatics are highly reactive towards electrophilic reagents in general. Thus to carry out mononitration relatively free of dinitration, it is necessary to choose conditions that render the NO_2^+ ion not easily available, allowing the much less reactive, but more plentiful carriers of the NO^+ ion to react with aromatics.

The mechanism in **Scheme 1.36** shows nitrosation followed by oxidation. The first step involves the fast reaction or the aromatic with NO^+ followed by the slow, rate determining step for the loss of H^+. The final step involves the oxidation of the ArNO intermediate generating the nitrated aromatic and nitrous acid.

$$ArH + NO^+ \xrightarrow{\text{FAST}} ArHNO^+$$

$$ArHNO^+ \xrightarrow{\text{SLOW}} ArNO + H^+$$

$$ArNO + HNO_3 \xrightarrow{\text{FAST}} ArNO_2 + HNO_2$$

$$HNO_2 + H^+ \xrightarrow{\text{FAST}} NO^+ + H_2O$$
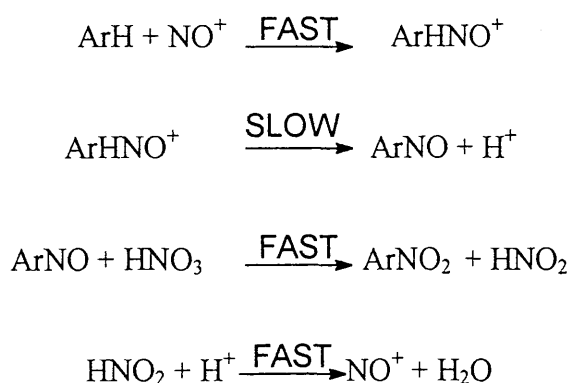
Scheme 1.36

1.5 Free radical Nitration

Nitration by a free radical process is also possible, and has been discussed in detail by Titov.[65] With this mechanism the radical adds to the aromatic π sextet to form the nitrocyclohexadienyl radical and this is followed by dehydrogenation.
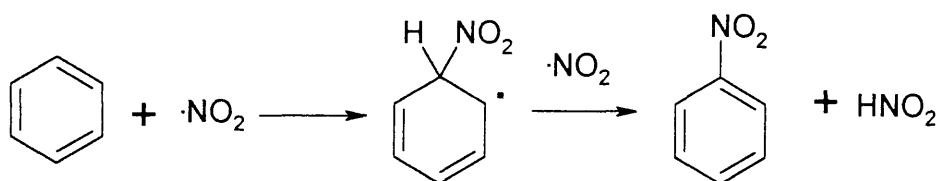
Scheme 1.37

This mechanism of nitration explains the presence of anomalous products such as polynitrobenzenes, carboxylates and phenols which are generally not observed with electrophilic nitration. The isomer ratios that this mechanism of nitration yields are very different also from other methods of nitration. Thus, it has been observed that distributions for toluene (40 % *ortho*, 40 % *meta*, 20 % *para*), contain far more of the *meta* isomer where the usual yield for the *meta* isomer is in the region of 3-4 %.

Free radical nitrations can occur via nitrogen oxides present in dilute nitric acid and are promoted by raising the temperature. [66] Dinitrogen pentoxide dissociates to radicals homolytically, (**Scheme 1.38**), allowing the possibility of radical reactions.

$$N_2O_5 \rightleftharpoons NO_2\cdot + NO_3\cdot$$
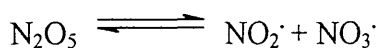
Scheme 1.38 N_2O_5 dissociates to radicals with heat in CCl_4

1.6 Nitration using solid acid catalysts

The use of solid acid catalyst or a supported catalyst is a relatively recent technology.[67] The advantages are that the solids are generally easy to handle; they hold the acid internally, they are readily separable from the products and are recyclable. Another advantage is that they require milder conditions, use minimal amounts of acid and generally increase selectivity.

Nitration of toluene was studied using these catalysts in attempts to produce *p*-nitrotoluene which has a higher commercial value than *o*-nitrotoluene. [68]

1.6.1 Zeolites

Zeolites have well-defined pore structures and channels that are derived from networking SiO_2 and Al_2O_3 making them attractive candidates for shape selective catalysis.[69] In most cases zeolites are found to have both Lewis and Bronsted acidic sites throughout the inner and outer surfaces so that they can function as a solid acid (**Figures 1.3 and 1.4**).[70]
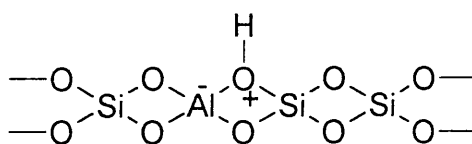
Figure 1.3   Bronsted acidic sites
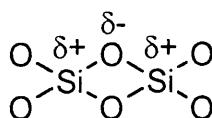
Figure 1.4   Lewis acidic sites

Kwok *et al* recently reported the application of H-ZSM-5 zeolite for the regioselective mononitration of toluene.[71] The paper reports remarkable selectivity.
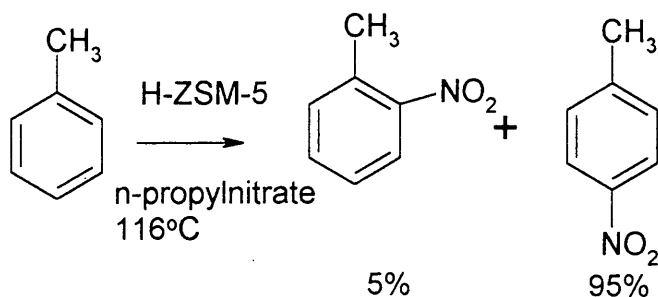
Scheme 1.39 Mononitration of toluene

The increased selectivity could be due to how toluene sits in the pores with only the para position available for nitration. Various conditions have been shown to have varying effects on the selectivity. These include the order of addition of reagents and the silica/aluminium ratio.[72]

1.6.2 Clays

Laszlo *et al* have reported novel methods involving clays for the nitration of aromatic compounds.[72-75] The most common clay (doped with ferric nitrate) used in nitration is montmorillonite (clayfen), which has been used to mononitrate toluene with good selectivity.

Laszlo and co-workers have developed the reagent known as claycop, which is $Cu(NO_3)_2$ supported on acidic monomorillonite clay. This selectively nitrates toluene under Manke conditions (use of acetic anhydride as co-reagent). The yield of isomers of *ortho, meta, para* was 23:1:76 respectively.

Recent work published on the nitration of toluene using claycop reports that using acetic anhydride in CCl_4 is catalytic and shows regioselectivity in the mononitration of toluene but not with 2-nitrotoluene. [76]

1.6.3 Silica gel

Silica gel has also been used as a solid support in nitration.[77] The material is inexpensive and easier to prepare than claycop and clayfen. The reactivity can be modified in accordance with the aromatic substrate and most aromatics were successfully nitrated with 70% nitric acid, which is the suggested concentration for industrial requirements.

Nitric acid absorbed on silica gel has also been reported to be an effective nitrating agent for activated aromatics such as phenols and aryl ethers. [78]

1.6.4 Polymers

Polymeric acids have been used in nitrations of aromatics; for a brief summary see Olah.[79] Kameo *et al*[80] reported the use of polystyrene sulfonic acid with nitric acid and Wright *et al*[81] reported the nitration of toluene with 90% HNO_3 over dried sulfonated polystyrene

resin. These methods are limited because the catalyst tends to degrade in the reaction mixture and therefore can be difficult to separate and recycle. Olah *et al* studied superacidic Nafion-H perfluorosulfonic acid resin catalysed nitrations of aromatic compounds with HNO_3 and with azeotropic removal of water.[82] Nitrations are carried out by heating the reaction mixture to reflux and by azeotropically removing the water –aromatic mixture until no HNO_3 was left in the mixture.

In the nitration of toluene by nitric acid the *o/p* ratio is 1:4 which is comparable to mixed acid nitration. The advantage of this system is that the acid catalyst can be recovered and reused with ease.

1.7 Perfluorocarbons as traditional solvent replacements[81]

Perfluorocarbons (PFC) are defined as saturated fluids made up of solely carbon and fluorine (perfluoroalkane), or carbon, fluorine and oxygen (perfluoroethers) or carbon, fluorine and nitrogen (perfluoroamines).

Some commonly used systems are perfluorohexane, (PP1), (**28**), perfluorodecalin (PP6), (**29**), perfluoroperhydrophenanthrene (PP11), (**30**), perfluoromethylcyclohexane (PP2), (**31**), and HT135 perfluoroether (PFE), (**32**), shown below.

$CF_3\!-\!CF_2\!-\!CF_2\!-\!CF_2\!-\!CF_2\!-\!CF_3$

(28)

(29)

(30)

(31)

$CF_3\!-\!\left[\ (O\!-\!CF\!-\!CF_2)n\!-\!(O\!-\!CF_2)m\ \right]\!-\!O\!-\!CF_3$
$\qquad\qquad\qquad\ \ CF_3$
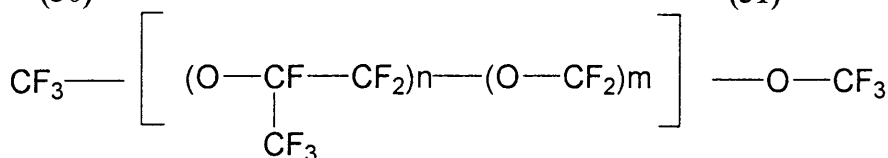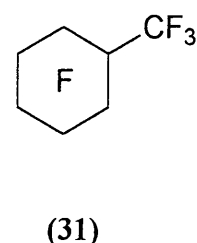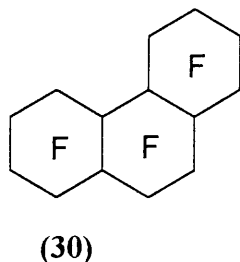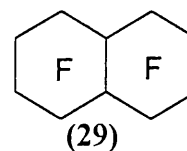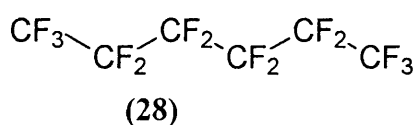
(32)

PFC's are chemically inert and may be reused without purification. They are immiscible with most organic solvents and water which allows the easy recover of catalysts and reagents which are selectivity soluble in perfluorocarbons. Miscibility with 1,1,2-trichlorotrifluoroethane ($CFCl_2CF_2Cl$) and some low molecular weight hydrocarbons has been recorded, together with their ability to solubilise gases.[84] PFC's are good solvents for gases and readily dissolve large amounts of oxygen, nitrogen, hydrogen and carbon dioxide. In contrast to halofluorocarbons, PFC's are not ozone depleting compounds and have replaced the former in some technological applications.[85]

Some of the advantages in using PFC's as inert media in established synthetic procedures have been pointed out by Zhu.[86] He reports that reactions containing unstable reagents, or which require vigorous conditions, or when low boiling products must be separated from the bulk can be conveniently carried out in PFC's. Zhu substantiated his claims by showing that in reactions such as transesterification of sensitive compounds or enamine formation, rates are enhanced, products are cleaner and are more easily isolated when PFC's replace common organic media. PFC's have also been reported as replacement solvents for many reactions such as bromination of alkenes, where PFC's have been used to replace toxic and

ozone depleting CCl$_4$.[87] Because of the high oxygen solubility of PFC's they have found wide spread application in oxygenation reactions.[88, 89, 90, 91, 92]

Many important chemical processes can be conveniently be carried out in liquid multiphasic systems.[93] The fluorous biphasic system consists of a fluorous phase (PFC phase) containing a preferentially fluorous soluble reagent or catalyst and a second product phase, which may be any organic or nonorganic solvent with limited solubility in the fluorous phase. These reactions can be carried out using phase transfer catalysts.[94]

Perfluorocarbons have been used to replace the solvent sulpholan in various fluorine-chlorine exchange reactions reported by Chambers and Edwards.[95] The reaction of alkyl and aryl chlorides with potassium fluoride in sulpholan is operated on the industrial scale to produce various fluorinated products. Perfluoroperhydrophenanthrene (**30**) can be used as a bulking agent to minimise the problem of solvent recovery in halogen exchange ('Halex') reactions for the preparation of octafluorocyclopentene, chlorofluoropyridine, pyrimidine, and benzene derivatives. New 'one-pot' procedures for the synthesis of hexafluorobut-2-yne, octafluorobut-2-ene and hexafluorocyclobutene have been discovered.

1.8 Scope of work

The work presented in this thesis concerns the nitration of aromatics and amines using inert solvents. Perfluorocarbons have been used to partially replace the acid solvent thus reducing disposal problems. Highly nitrated products are needed for the use as energetic materials.

Chapter two covers the nitration of aromatic compounds using nitric acid, nitric and sulfuric acid and N_2O_5 in perfluorocarbons. Synthetic results for the nitration of toluene, and benzene have been obtained.

Chapter three covers the nitration of aromatic compounds using nitric acid, nitric and sulfuric acid and N_2O_5 in perfluorocarbons. Synthetic results for the nitration of styrene, and *trans*-stilbene have been obtained.

Chapter four concerns the mechanistic studies of aromatic nitration with dinitrogen pentoxide in perfluorocarbons. The kinetic results relate to homogeneous nitrations of substrates including 4-chloroanisole, 4-bromophenetole, 4-bromophenol and various chlorophenols. The rates have been determined and some mechanistic conclusions have been made.

Chapter five describes the nitration of various amines with dinitrogen pentoxide and nitric acid in perfluorocarbons. Synthetic results for amines relating to morpholine, pyrrolidine, piperidine, oxazolidinone and pyrimidine have been obtained.

Chapter six details experimental procedures and methods.

Chapter seven details the conferences and colloquia attended

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Chapter Two

2 Nitration of toluene and benzene

This chapter will explore the nitration of toluene (33) and benzene (38) using nitric acid, mixed acid and dinitrogen pentoxide in perfluorocarbon solvents.

2.1 Introduction

There are many methods available for the nitration of toluene and benzene, some of which have been discussed in chapter one. There are three main types of nitration systems, one using oleum and nitric acid, one using concentrated sulfuric and nitric acid, and the use of concentrated nitric acid alone (**see chapter one**).[1]

Oleum based nitrations produce a spent acid by-product which is typically between 70-80 % H_2SO_4, contaminated with nitric and nitrous species and other organics. Mixed acid nitrations typically use sulfuric acid (86-96 %) in the nitration mix and produce similar spent acid by-products. Nitric acid nitrations use large excesses of 99 % nitric acid resulting in a dilute spent nitric acid stream contaminated with other organics. Increasing environmental pressures mean that new methods are being actively sought to decrease the amount of spent acid by-products.[2]

This chapter investigates the use of perfluorocarbons as bulking liquids to partially replace the acid solvent, and also at nitration using N_2O_5 in perfluorocarbons to eliminate mixed acids.

2.2 Determining the characteristics of the nitration system

2.2.1 Solubility of toluene and nitrated toluene derivatives in various perfluorocarbons

Before attempting the nitration of toluene in perfluorocarbons its solubility needed to be determined.

Various known concentrations of solutions of toluene were prepared in methanol and the UV/Vis spectra were recorded. The extinction coefficient was found to be 240 $dm^3\,mol^{-1}$ cm^{-1} at 260 nm. The spectra were recorded of saturated solutions of toluene in the following perfluorocarbons allowing the solubilities to be calculated (**Table 2.1**). This was done using the Beer Lambert law (**Equation 2.1**) based on the assumption that the extinction coefficient of toluene in methanol will be unchanged in PP6.

$$Absorbance = \varepsilon cl$$

$$therefore,\ c = Absorbance/\varepsilon l$$

Where ε is extinction coefficient, c is concentration and l is path length.

Equation 2.1 Beer Lambert law

Solvent	Solubility / mol dm^{-3}
PP11	0.11
PP1	0.25
PP6	0.29
PP2	0.39
PFE (HT135)	0.18

Table 2.1 Solubility of toluene in various perfluorocarbons

The solubilities of toluene and its nitrated derivatives were also determined using an analogous method to that above but in PP11, (**Table 2.2**).

Substrate	λ_{max} in methanol / nm	ε in methanol / $dm^3\ mol^{-1}\ cm^{-1}$	Solubility in PP11 / $mol\ dm^{-3}$
toluene	260	240	0.112
4-nitrotoluene	274	1.0×10^4	0.012
2,4-dinitrotoluene	243	4.5×10^4	4.5×10^{-4}

Table 2.2 Solubility of toluene and derivatives in PP11

From the **Tables 2.1** and **2.2** we can see that toluene was most soluble in PP2 and PP6 and as toluene is nitrated it becomes less soluble in perfluorocarbons. Presumably as the dipole increases its solubility decreases in these non-polar media.

2.2.2 Determining the miscibilities of various solvents with the perfluorocarbons.

A potential method for the nitration of toluene in perfluorocarbons was to use a mixed solvent system. In order to determine the miscibilities of various solvents with the perfluorocarbons a few drops of the perfluorocarbons were added to the following solvents (5 cm^3), (**Table 2.3**). The miscibilities were determined by eye, and therefore this was only a crude experiment.

Compound (5 cm³)	1-2 drops PP6	2-3 drops PP6	1-2 drops PP1	2-3 drops PP1	3-5 drops PP1
Acetonitrile	Miscible	Immiscible	Miscible	Miscible	Immiscible
Nitromethane	Immiscible		Miscible	Immiscible	
Sulfolane	Immiscible		Immiscible		
DMSO	Immiscible		Immiscible		

Table 2.3 Miscilibilities of perfluorocarbons with common nitrating solvents

Perfluorocarbons are generally immiscible with most other common nitrating solvents. Similarly various solvents were tested for their solubility in the perfluorocarbons. A few drops of solvent were added to the perfluorocarbons (5 cm³). Acetonitrile, nitromethane and sulfolane were found to be only slightly soluble in perfluorocarbons. Therefore we decided not to investigate mixed solvent systems any further.

2.2.3 Solubility of acid in perfluorocarbons

Nitric and sulfuric acid were tested for their solubility in the perfluorocarbons by adding a few drops of acid to each perfluorocarbon (5 cm³). They were both almost totally insoluble in the perfluorocarbons. Therefore we concluded that nitration with mixed acid using perfluorocarbons would be a heterogeneous system.

2.2.4 Checking for solubility of water in perfluorocarbons

In order to determine the water content of PP6, ^{1}H NMR spectra were recorded on PP6 and a sample of PP6 that had been dried overnight with silica gel. Toluene was dissolved in two samples of PP6, giving a concentration of toluene in PP6 of 0.1 mol dm^{-3}.

The two ^{1}H NMR spectra were identical giving signals at δ 1.9 ppm and δ 6.8 ppm, due to toluene, but no observable signal due to water. Therefore it can be concluded that the PP6 sample contains very little if any water. Dr A. Joel (F2 Chemicals) provided information

that the solubility of water in PP6 is < 10 ppm, which corresponds to a concentration of ca. 5×10^{-4} mol dm^{-3}.

2.2.5 Checking for decomposition/nitration of perfluoroether (HT135) with nitric acid

On addition of nitric acid to the perfluoroether (HT135) the solution became turbid. IR spectra were recorded on the perfluoroether (HT135) before (**Figure 2.1**) and after (**Figure 2.2**) the nitration experiment involving the addition of nitric acid. If perfluoroether was nitrated we would expect to see NO$_2$ stretches in the spectrum, symmetric stretches are typically in the region of 1385-1350 cm^{-1} and asymmetric stretches are typically 1555-1540 cm^{-1}.
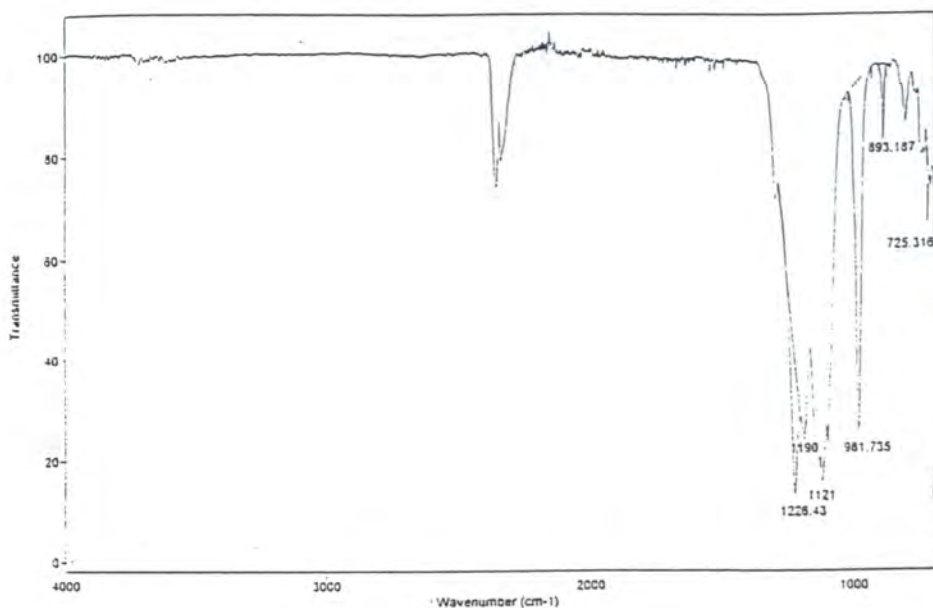

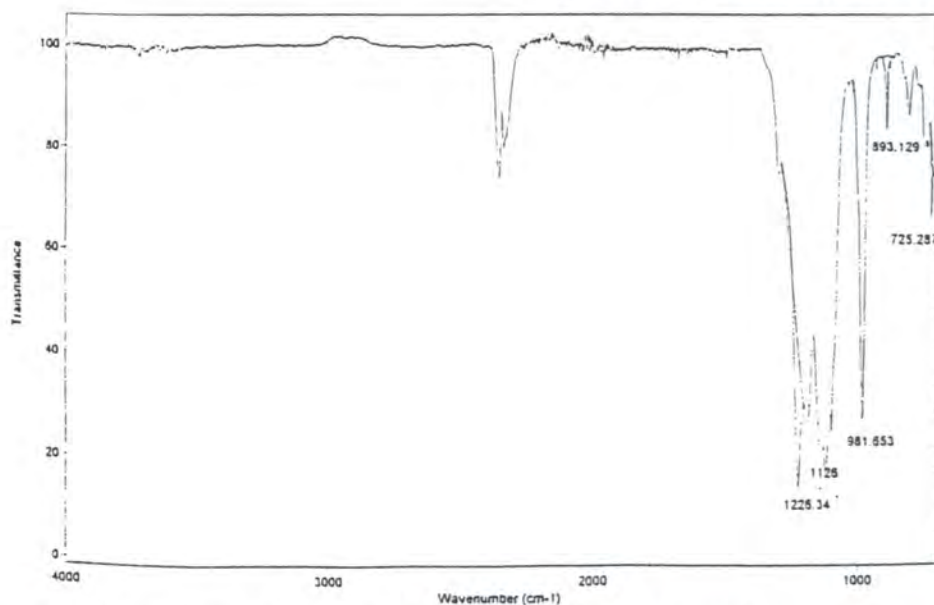**Figure 2.1** IR spectrum of perfluoroether (HT135)

Figure 2.2 IR spectrum of perfluoroether (HT135) after nitration

The spectra were identical, (no bands due to NO_2 stretches, nitration of perfluoroether) - therefore it can be concluded that there was no decomposition or nitration of the solvent with the addition of nitric acid.

2.3 Nitration of toluene (33) using nitric acid
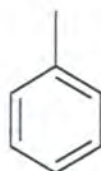
(33)

Experiment 1 in PP11

For experimental details see **chapter six, section 6.4**.

Toluene (**33**) was dissolved in PP11 and 100 % concentrated nitric acid, (for synthesis of 100 % nitric acid see **chapter six, section 6.3**), (8 molar equivalents) was added. The solution was heated to 75 °C for 2 hours. The reaction mixture had two layers, the top layer being the acidic layer and the bottom layer PP11. Distilled water was added to the solution and this formed a larger top layer. The top layer was separated and neutralised, yielding a

solid. The solid was filtered and dried (yield 60 %). A ^{1}H NMR spectrum was recorded on the product, (**Figure 2.3**).

The bottom layer was washed with distilled water and then diethyl ether in order to remove any product in the perfluorocarbon. The diethylether was evaporated off and no product was left. Therefore the product was situated in the top acidic layer.
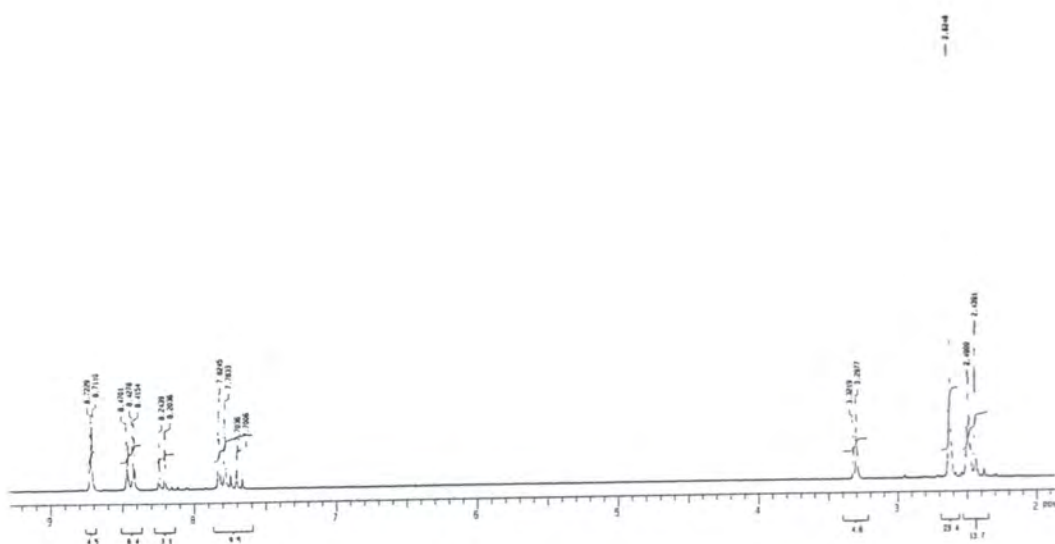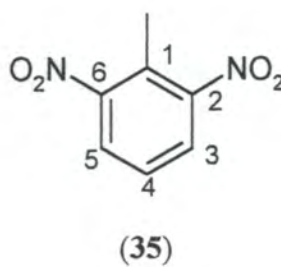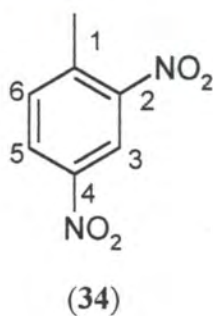

Figure 2.3 ^{1}H NMR spectrum of nitrated toluene

(34)   (35)

Shift / ppm	Multiplicity	Coupling constant J / Hz	Inference
2.44	s		$C\underline{H}_3$ (2,6-DNT)
2.49	p		DMSO (solvent)
2.63	s		$C\underline{H}_3$ (2,4-DNT)
3.30	s		H_2O
7.70	t	$J_{43\ 45} = 8.1$	H4 (2,6-DNT)
7.80	d	$J_{65} = 8.3$	H6 (2,4-DNT)
8.22	d	$J_{34\ 54} = 8.1$	H3, H5 (2,6-DNT)
8.45	dd	$J_{56} = 8.3\ J_{53} = 2.4$	H5 (2,4-DNT)
8.72	d	$J_{35} = 2.4$	H3 (2,4-DNT)

Where 2,4-DNT is 2,4-dinitrotoluene and 2,6-DNT is 2,6-dinitrotoluene

Table 2.4 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated toluene (**Figure 2.3**)

The ^{1}H NMR spectrum of the product (**Figure 2.3**) was used to estimate the composition of the product, which was determined to be 2,4-dinitrotoluene (**34**) (80 %) and 2,6-dinitrotoluene (**35**) (20 %).

Experiment 2 in perfluoroether (HT135)

Toluene was dissolved in perfluoroether (HT135) and 100 % concentrated nitric acid (5 molar equivalents) was added. The solution was heated to 70 °C for a total of 6 hours. Aliquots were removed from the top acidic layer at 2 hour intervals. The product (yield 43 %) was separated as in previous experiments. ^{1}H NMR spectra were recorded on each sample.

The resulting spectra gave signals corresponding to mainly 2,4-dinitrotoluene with traces of 2,6-dinitrotoluene and 4-nitrotoluene. The spectrum after 6 hours was very similar to the spectra after 2 hours and 4 hours.

Two experiments were performed using nitric acid alone. Neither gave 2,4,6-trinitrotoluene as a product. The ^{1}H NMR spectrum of 2,4,6-trinitrotoluene would give a singlet in the region of δ 9 ppm. This was not seen in the ^{1}H NMR spectra from either of these two experiments. Therefore it can be concluded that only dinitration can occur in this system using nitric acid alone, (**Scheme 2.1**). The major product in the dinitration of toluene is 2,4-dinitroluene. Therefore it was decided to investigate other nitration systems using stronger nitration conditions, i.e. using sulfuric acid as a co-solvent.
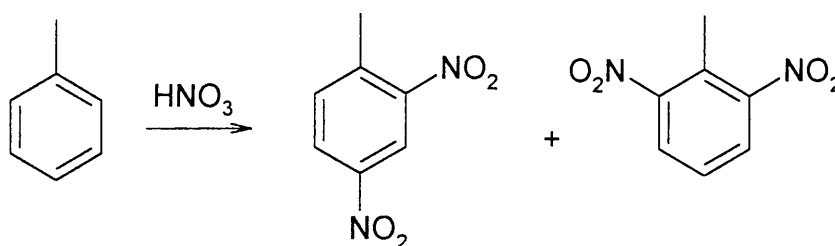
Scheme 2.1 Nitration of toluene with nitric acid

2.4 Nitration of toluene using nitric and sulfuric acid

Experiment 1 in PP11

Toluene was dissolved in PP11 and 100 % concentrated nitric acid (9 molar equivalents) and 98 % concentrated sulfuric acid (7 molar equivalents) were added. The solution was heated to 75 °C for 2 hours. The product (yield 83 %) was separated as in previous experiments. The solvent layer was reused in the following experiment. The resulting product mixture was established by ^{1}H NMR spectroscopy, (**Figure 2.4**).
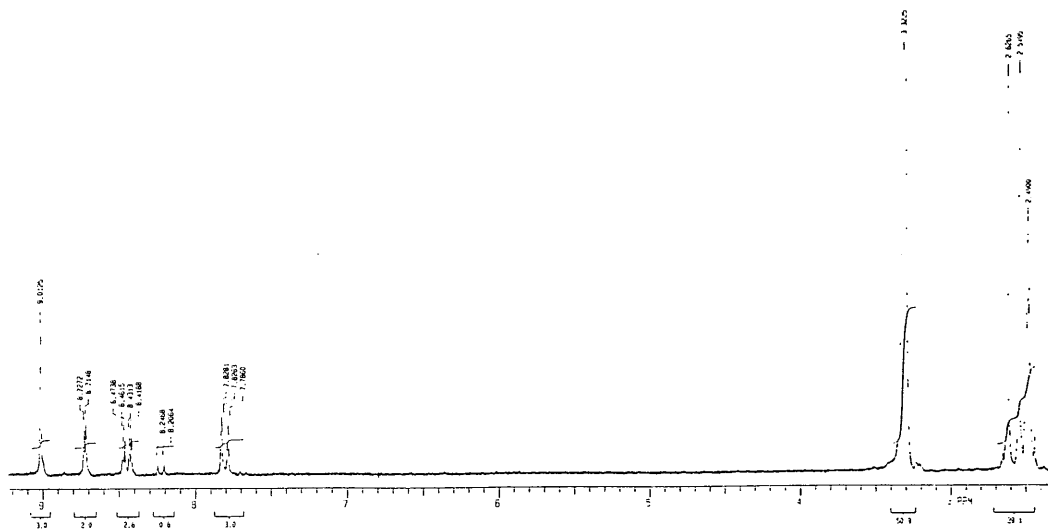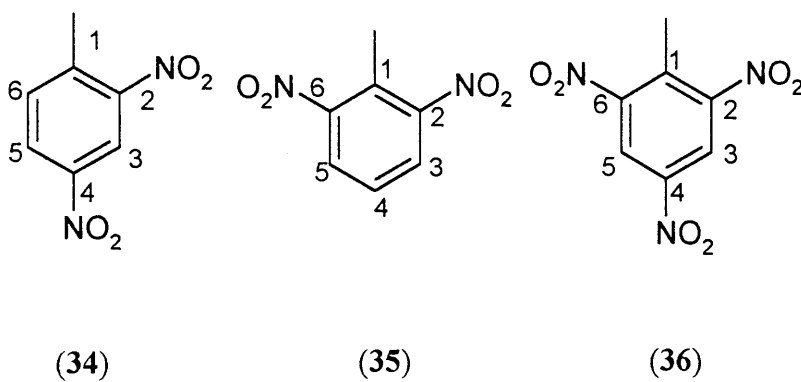
Figure 2.4 ^{1}H NMR spectrum of nitrated toluene

(34)   (35)   (36)

Shift / ppm	Multiplicity	Coupling constant / Hz	Inference
2.49	p		DMSO (solvent)
2.54	s		C$\underline{H}_3$ (2,4,6-TNT)
2.62	s		C$\underline{H}_3$ (2,4-DNT)
3.30	s		H_2O
7.71	t		H4 (2,6-DNT)
7.81	d	J_{65} = 8.3	H6 (2,4-DNT)
8.22	d	$J_{34\ 54}$ = 8.3	H3, H5 (2,6-DNT)
8.45	dd	J_{56} = 8.5 J_{53} = 2.5	H5 (2,4-DNT)
8.72	d	J_{35} = 2.5	H3 (2,4-DNT)
9.01	s		H3, H5 (2,4,6-TNT)

Where 2,4-DNT is 2,4-dinitrotoluene and 2,6-DNT is 2,6-dinitrotoluene and 2,4,6-TNT is 2,4,6-trinitrotoluene

Table 2.5 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated toluene **(Figure 2.4)**

The ^{1}H NMR spectrum of the product (**Figure 2.4**) showed signals due to 2,4-dinitrotoluene (57 %) 2,6-dinitrotoluene (8 %) and 2,4,6-trinitrotoluene (**36**) (35 %), (**Scheme 2.2**). Therefore it can be concluded that trinitration of toluene can occur within 2 hours using mixed acid nitration in this system but it was necessary to carry out further experiments to investigate the possibility of 100 % conversion into 2,4,6-trinitrotoluene.
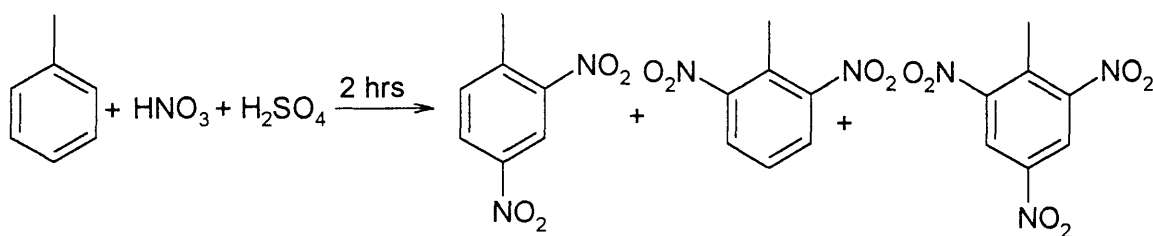
Scheme 2.2 Nitration of toluene with mixed acid.

Experiment 2 further nitration in PP11 and recycling solvent

Toluene was dissolved in PP11 and 100% concentrated nitric acid (13 molar equivalents) and 98% concentrated sulfuric acid (10 molar equivalents) were added. The solution was heated to 75 °C for a total of 6 hours and aliquots were taken at 2 hour intervals. The product (yield 63 %) was separated as in previous experiments and the solvent was reused from the previous experiment. The composition of the resulting mixture was established by ^{1}H NMR spectroscopy (**Figure 2.5**).
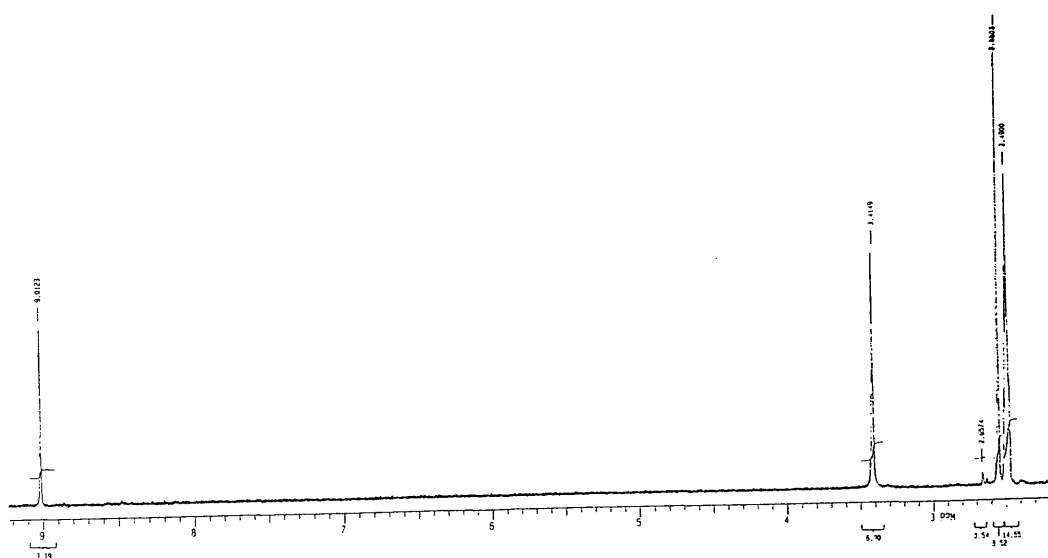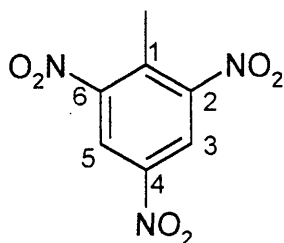

Figure 2.5 ^{1}H NMR spectrum of nitrated toluene

(**36**)

Shift /ppm	Multiplicity	Inference
2.49	p	DMSO (solvent)
2.55	s	C$\underline{H}_3$ (2,4,6-TNT)
2.66	s	C$\underline{H}_3$ (2,4-DNT)
3.41	s	H_2O
9.01	s	H3, H5 (2,4,6-TNT)

Where 2,4-DNT is 2,4-dinitrotoluene and 2,4,6-TNT is 2,4,6-trinitrotoluene

Table 2.6 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated toluene (**Figure 2.5**)

The ^{1}H NMR spectrum of nitrated toluene after six hours shows that the product composition contained more than 95 % 2,4,6-trinitrotoluene (**36**). Only aliphatic peaks could be seen for 2,4-dinitrotoluene because the amount present was so small. An aliquot was taken from the experiment at 2 hour intervals and the composition was determined using ^{1}H NMR spectroscopy, the results are shown in **Table 2.7**.

Nitrated toluene formed	2hrs, 75°C % composition	4hrs, 75°C % composition	6hrs, 75°C % composition
2,4-dinitrotoluene	40	15	5
2,6-dinitrotoluene	0	0	0
2,4,6-trinitrotoluene	60	85	95

Table 2.7 % Composition of nitrated toluene after certain time periods

The results shown in **Table 2.7** show that after 6 hours the composition of the product contained 95 % 2,4,6-trinitrotoluene, therefore it was concluded that trinitration of toluene can be achieved within 6 hours using mixed acid in this system using PP11 as the solvent. Other perfluorocarbons were examined to see if similar results could be achieved.

Experiment 3 in PP6

Toluene was dissolved in PP6 and 100 % concentrated nitric acid (5 molar equivalents) and 98 % concentrated sulfuric acid (5 molar equivalents) were added together and heated to 80 °C for a total of six hours, aliquots were taken at 2 hour intervals. The product (yield 22 %) was separated as in previous experiments.

Nitrated toluene formed	2 hrs, 80 °C % composition	4 hrs, 80 °C % composition	6 hrs, 80 °C % composition
2,4-dinitrotoluene	30	10	3
2,6-dinitrotoluene	0	0	0
2,4,6-trinitrotoluene	70	90	97

Table 2.8 % Composition of nitrated toluene after certain time periods

From the results (**Table 2.8**) it can be seen that 97 % conversion to 2,4,6-trinitrotoluene occurs using this system, using only 5 molar equivalents of each acid.

Experiment 4 in PP2

Toluene was dissolved in PP2 and 100 % concentrated nitric acid (5 molar equivalents) and 98 % concentrated sulfuric acid (5 molar equivalents) were added and heated the mixture to 70 °C for a total of six hours. Aliquots were taken at 2 hour intervals. The product (yield 85 %) was separated as in previous experiments. The composition of the resulting mixture was established by ^{1}H NMR spectroscopy (**Table 2.9**).

Nitrated toluene formed	2hrs , 70°C % conversion	4hrs, 70°C % conversion	6hrs, 70°C % conversion
2,4-dinitrotoluene	69	49	3
2,6-dinitrotoluene	6	8	0
trinitrotoluene	25	43	97

Table 2.9 % Composition of nitrated toluene after certain time periods

From the results (**Table 2.9**) it can be seen that 97 % conversion to 2,4,6-trinitrotoluene can be achieved using this system.

Experiment 5 in perfluoroether (HT135)

Toluene was dissolved in perfluoroether (HT135) and 100 % concentrated nitric acid (5 molar equivalents) and 98 % concentrated sulfuric acid (5 molar equivalents) were added and the mixture was heated to 70 °C for a total of six hours. Aliquots were taken at 2 hour intervals. The product (yield 60 %) was separated as in previous experiments. The composition of the resulting mixture was confirmed by ^{1}H NMR spectroscopy (**Table 2.10**).

Nitrated toluene formed	2hrs , 70°C % conversion	4hrs, 70°C % conversion	6hrs, 70°C % conversion
2,4-dinitrotoluene	71	68	68
2,6-dinitrotoluene	12	0	0
trinitrotoluene	17	32	32

Table 2.10 % Composition of nitrated toluene after certain time periods

From the results (**Table 2.10**) it can be seen that only a 32 % conversion to 2,4,6-trinitrotoluene can be achieved using this system. Therefore it was concluded that the perfluoroether (HT135) was inferior to PP6 and PP2 for the trinitration of toluene under these conditions. In addition the solubility of toluene in PFE (HT135), 0.18 mol dm^{-3}, is

lower than in perfluorocarbons. A larger excess of acid may be required for the conversion to be successful. Therefore this was therefore investigated further.

Experiment 6 in perfluoroether (HT135) using larger excess of mixed acid

The above experiment was repeated using a larger excess of nitric and sulfuric acids (10 molar equivalents) and the composition of the product was determined as >95 % 2,4,6-trinitrotoluene after 2 hours using ^{1}H NMR spectroscopy, (**Figure 2.6**).
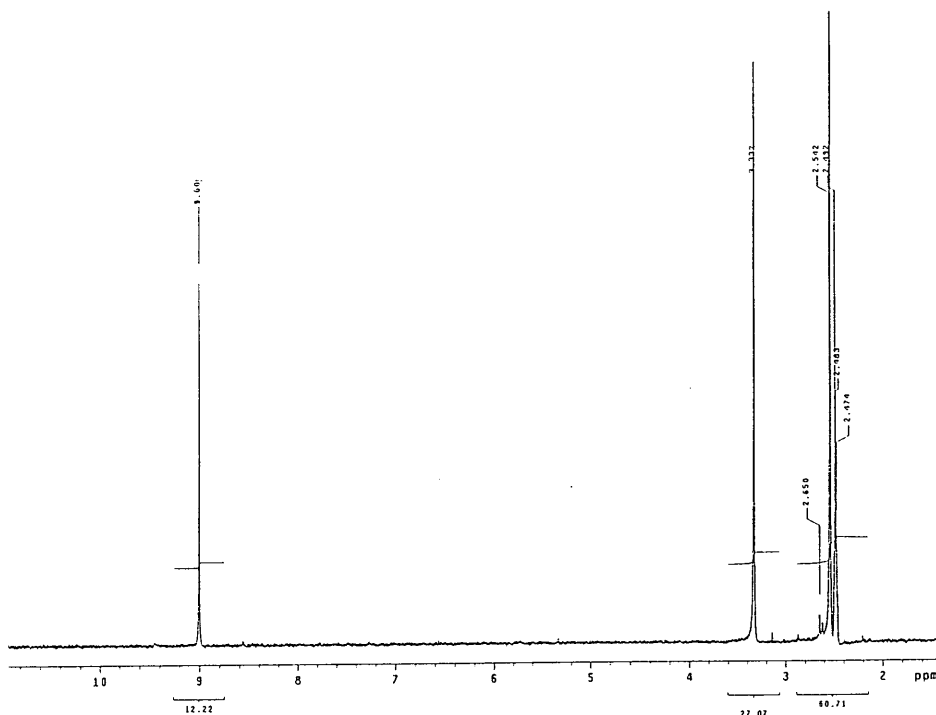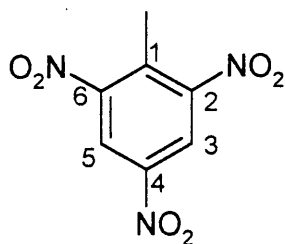

Figure 2.6 ^{1}H NMR spectrum of trinitrated toluene

(**36**)

Shift /ppm	Multiplicity	Inference
2.49	p	DMSO (solvent)
2.55	s	C$\underline{H}_3$ (2,4,6-TNT)
2.66	s	C$\underline{H}_3$ (2,4-DNT)
3.33	s	H_2O
9.01	s	H3, H5 (2,4,6-TNT)

Where 2,4-DNT is 2,4-dinitrotoluene and 2,4,6-TNT is 2,4,6-trinitrotoluene

Table 2.11 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated toluene (**Figure 2.6**)

From the ^{1}H NMR (**Figure 2.6**) it could be seen that toluene was trinitrated (>95 %). Therefore we can conclude that trinitration of toluene can occur in 2 hours using perfluoroether (HT135) but larger excess of acids were needed in comparison to PP6 and PP2.

2.5 Nitration of toluene using nafion –H (37)

Nafion is a perfluorinated ion-exchange membrane prepared from polytetrafluoroethylene and perfluorinated monomers containing sulfonic acid groups. Its general formula is shown below (**37**). [3]

$$[(CF_2CF_2)_n\text{-}CFCF_2]_x$$
$$|$$
$$(O\ CF_2CF)_mOCF_2CF_2SO_3H$$
$$|$$
$$CF_3$$

(**37**)
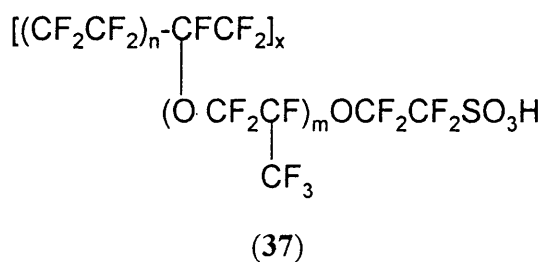
It has been used previously in aromatic nitrations shown in **Scheme 2.3**. [4]
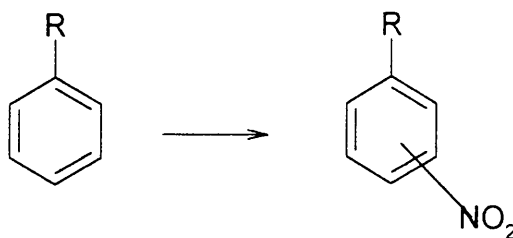
Reagents : Nafion-H/Hg(NO$_3$)$_2$ and HNO$_3$ at 100°C
Yield 48-77%

Scheme 2.3 Nitration of aromatics using nafion-H as catalyst

The rationale for using nafion-H in the reaction was the elimination of the sulfuric acid in the trinitration of toluene. Nafion-H can be supplied as beads or as a membrane. The membrane was used in the following experiment.

Toluene was dissolved in PP2 and 100 % nitric acid (10 molar equivalents) was added. Nafion-H membrane was added to the reaction mixture. The reaction was stirred for 6 hours at 70 °C and the product (yield 65 %) was separated as in previous experiments.

The signals in the ^{1}H NMR spectrum were assigned to a mixture of 2,4-dinitrotoluene (75 %) and 2,6-dinitrotoluene (25 %). No signals could be seen at δ 9 ppm, which would correspond to 2,4,6-trinitrotoluene. Therefore it was concluded that nafion-H was not seen to assist the conversion of toluene into 2,4,6-trinitrotoluene significantly.

2.6 Nitration of toluene using N$_2$O$_5$

N$_2$O$_5$ was carefully dissolved in PP6 and this was added to a solution of toluene in PP6 at either 0 °C or ambient temperature and left to stir overnight. The resulting solution was homogeneous as N$_2$O$_5$ is soluble in perfluorocarbons (**see chapter six**). On the addition of distilled water to the solution a solid was formed and was filtered. ^{1}H NMR spectroscopy was used to establish the composition of the product mixture.

Molar Ratio		Temperature	% Composition			Yield / %
Toluene	N₂O₅	on addition / °C	2,4 DNT	2,6 DNT	2,4,6 TNT	
1	3	0	78	15.5	6.5	37
1	5	0	73	16	11	56
1	5	ambient	90	10	<1	54

Table 2.12 Nitration of toluene with N_2O_5

From the results in **Table 2.12** it can be seen that only an 11 % conversion of toluene into trinitrotoluene could be achieved with N_2O_5 using 5 molar excess. Adding N_2O_5 at ambient temperature gives a lower conversion of toluene into trinitrotoluene. This is presumably because there is some decomposition of N_2O_5 at higher temperatures

2.7 Summary of reactions for the nitration of toluene

| PFC	Molar equivalent			Temp / °C	Time /hrs	% Composition			Yield / %
	HNO_3	H_2SO_4	N_2O_5			2,4-DNT	2,6-DNT	2,4,6-TNT	
PP11	8	-	-	75	2	80	20	-	60
PFE	5	-	-	70	6	95	5	-	43
PP11	9	7	-	75	2	57	8	35	83
PP11	13	10	-	75	2	40	-	60	63
					4	15	-	85	
					6	5	-	95	
PP6	5	5	-	80	2	30	-	70	22
					4	10	-	90	
					6	3	-	97	
PP2	5	5	-	70	2	69	6	25	85
					4	49	8	43	
					6	3	-	97	
PFE	5	5	-	70	2	71	12	17	60
					4	68	-	32	
					6	68	-	32	
PFE	10	10	-	70	2	3	-	97	43
PP2	10*	-	-	70	6	75	25	-	65
PP6	-	-	3	0	12	78	16	7	37
PP6	-	-	5	0	12	73	16	11	56
PP6	-	-	5	ambient	12	90	10	-	54

*Nafion-H membrane was added as catalyst

Table 2.13 Summary of the reactions carried out for the study of nitration of toluene

Toluene can be converted to 2,4,6-trinitrotoluene successfully in perfluorocarbons (**Scheme 2.4**) with the only contaminant being < 5 % 2,4-dinitrotoluene. The highest yield was achieved using PP2 (85 %) with 5 molar equivalents of nitric and sulfuric acid in 6 hours at 70 °C. Nitration using nafion-H or N_2O_5 was inferior to the mixed acid system in terms of conversion into 2,4,6-trinitrotoluene but both systems can be successfully used to dinitrate

toluene giving 2,4-dinitrotoluene as the major product. 11 % conversion to 2,4,6-trinitrotoluene was achieved using N_2O_5 (5 molar equivalents) in PP6.

Overall the use of perfluorocarbons in the nitration of toluene has been proven to be very successful, the product was easily separated and the solvent was recycled. A smaller amount of acid was needed than is used in traditional methods,[5] which was the primary aim of this work. In traditional methods the acid is used as the solvent as well as assisting the nitration.
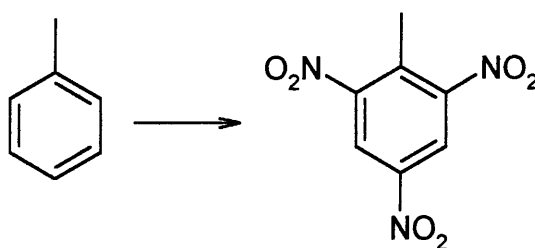

Scheme 2.4 Trinitration of toluene in PP2 using 5 molar equivalents of nitric and sulfuric acid at 70°C in 6 hours giving a yield of 85 %.

2.8 Nitration of benzene (38) using nitric and sulfuric acid
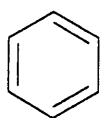
(38)

It is difficult to trinitrate benzene (38) directly (chapter one) and one possible indirect route is shown in Scheme 2.6. Oxidation of 2,4,6-trinitrotoluene with sodium dichromate and sulfuric acid, followed by decarboxylation in aqueous solution yields 1,3,5-trinitrobenzene.[5]
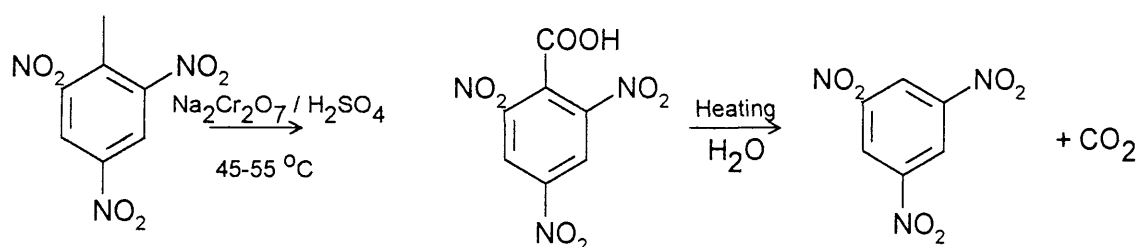
Scheme 2.6 Synthesis of 1,3,5-trinitrobenzene

Therefore it was decided to investigate the possibility of directly trinitrating benzene using the perfluorocarbon system.

Experiment 1 in PP6

Benzene was dissolved in PP6 and 100 % nitric acid (10 molar equivalents) followed by 98 % concentrated sulfuric acid (5 molar equivalents) were added. The solution was heated for a total of 20 hours at 70 °C, aliquots were taken after 6 hours and 12 hours. The mixture was again a biphasic system, the top layer being the acidic layer and the bottom layer the perfluorocarbon. Distilled water was added to the solution and this formed a larger top layer. The top layer was separated and neutralised, yielding a solid. The solid was filtered and dried (yield 62 %). A ^{1}H NMR spectrum was recorded on the product, (Figure 2.7).

Figure 2.7 ^{1}H NMR of nitrated benzene in PP6

Shift / ppm	Multiplicity	Coupling constant / Hz	Inference
2.49	p		DMSO (solvent)
3.37	s		H_2O
7.96	t	$J_{54\,56} = 8.08$	H5 in 1,3-DNB and H4, H5 in 1,2-DNB
8.22	m		H2, H6 in 1,2-DNB
8.45	s		H2,H3,H5,H6 in 1,4-DNB
8.65	dd	$J_{45\,65} = 8.16$ $J_{46} = 3.00$	H4, H6 in 1,3-DNB
8.82	s		H2 in 1,3-DNB

Where 1,2-DNB is 1,2-dinitrobenezene, 1,3-DNB is 1,3-dinitrobenzene and 1,4-DNB is 1,4-dinitrobenzene

Table 2.14 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated benzene (**Figure 2.7**)

1,3-dinitrobenzene (**40**) is the most likely product because NO_2 groups are *meta* directing towards electrophiles. 1,2-Dinitrobenzene (**39**) and 1,4-dinitrobenzene (**41**) are possible products to explain the signals in the ^{1}H NMR spectrum at δ 8.22 and δ 8.45 ppm. 1,3,5-Trinitrobenzene (**42**) would give a signal around δ 9 ppm, which was not seen in the spectrum from this reaction.

Experiment 2 in perfluoroether (HT135)

The above experiment was repeated but a different solvent was used, perfluoroether (HT 135). Benzene was dissolved in perfluoroether (HT 135) and 100 % nitric acid (10 molar equivalents) and 98 % sulfuric acid (10 molar equivalents) were added. The solution was heated for 6 hours at 70 °C. The product (yield 55 %) was separated as in previous experiments and was characterised using ^{1}H NMR spectroscopy. The ^{1}H NMR showed the major product to be 1,3-dinitrobenzene and a trace of 1,3,5-trinitrobenzene could be seen.

The perfluoroether (HT135) can be used as a solvent to dinitrate successfully benzene. There was no significant difference seen in the nitration of benzene using the perfluorcarbons compared to the perfluoroether as the solvent.

2.9 Nitration of benzene using oleum and nitric acid

In order to attempt to trinitrate benzene it was decided to use oleum ($H_2SO_4.SO_3$). Nitric acid-oleum is an extremely active nitrating agent. 1,3-Dinitrobenzene is nitrated to 1,3,5-trinitrobenzene at 110 °C during prolonged heating with anhydrous nitric acid and 60 % oleum in 71 % yield.[6]

Experiment 1 in PP6

Benzene was dissolved in PP6 and 100 % nitric acid (10 molar equivalents) followed by oleum (12-17% free SO_3, 10 molar equivalents) was added. The solution was heated to 70 °C for a total of 20 hours, (after 6 hours and 12 hours aliquots were taken from the top acidic layer). The product (yield 60 %) was separated as in previous experiments and the ^{1}H NMR spectrum was recorded (**Figure 2.7**).
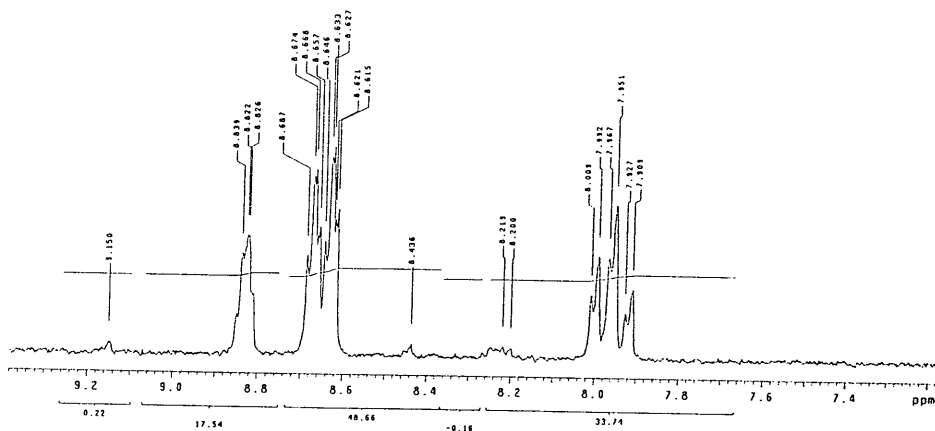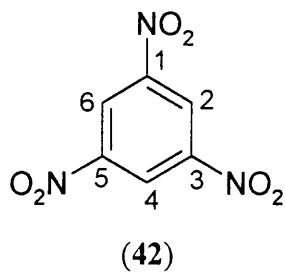
Figure 2.8 ^{1}H NMR of nitrated benzene

(**42**)

Shift / ppm	Multiplicity	Coupling constant / Hz	Inference
2.49	p		d_6.DMSO
3.32	s		H_2O
7.95	t	$J_{54\,56} = 8.2$	H5 in 1,3-DNB and H4, H5 in 1,2-DNB
8.22	m		H2, H6 in 1,2-DNB
8.44	s		H2, H3, H5, H6 in 1,4-DNB
8.65	dd	$J_{45\,65} = 8.2$ $J_{46} = 3.8$	H4, H6 in 1,3-DNB
8.82	s		H2 in 1,3-DNB
9.15	s		1,3,5-TNB

Where 1,2-DNB is 1,2-dinitrobenezene, 1,3-DNB is 1,3-dinitrobenzene and 1,4-DNB is 1,4-dinitrobenzene and 1,3,5-TNB is 1,3,5-trinitrobenzene

Table 2.15 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of nitrated benzene (**Figure 2.8**)

The ^{1}H NMR showed that the composition of the product was mainly 1,3-dinitrobenzene. Only a 1 % conversion to 1,3,5-trinitrobenzene was achieved even after leaving the reaction for 20 hours at 70 °C.

Experiment 2 using nitric acid, oleum and nafion-H beads

Benzene was dissolved in PP6, 100 % nitric acid (20 molar equivalents) followed by oleum (12-17% free SO_3, 20 molar equivalents) was added. Nafion-H beads were added and the solution was heated for a total of 12 hours, (after 6 hours a sample was taken from the top acid layer). The product (yield 40 %) was separated as in previous experiments and ^{1}H NMR spectrum was recorded.

The ^{1}H NMR spectrum after six hours and twelve hours showed the product contained over 90 % 1,3-dinitrobenzene with traces of 1,4 and 1,2-dinitrobenzene. There was not a signal

corresponding to 1,3,5-trinitrobenzene. Therefore it was concluded that even under forcing conditions trinitration of benzene could not be achieved with this system.

2.10 Nitration of benzene with N_2O_5.

Experiment 1 using N_2O_5

Benzene was dissolved in PP6 and N_2O_5 in PP6 (5 molar equivalents) was added. The solution was homogeneous as N_2O_5 is soluble in perfluorocarbons (**chapter six**). The solution was stirred for 6 hours at ambient temperature. The yellow solid (yield 40 %) was separated as in previous experiments and was characterised using ^{1}H NMR spectroscopy.

The ^{1}H NMR spectrum gave signals corresponding to mainly 1,3-dinitrobenzene with traces of 1,4 and 1,2-dinitrobenzene and benzene. There was not a signal that would correspond to 1,3,5-trinitrobenzene. Therefore it was concluded that benzene can easily be nitrated to 1,3-dinitrobenzene using 5 molar equivalents N_2O_5 at ambient temperature in 6 hours.

Experiment 2 using N_2O_5 and extraction using dichloromethane

Nitration of benzene with N_2O_5 was repeated using extraction with dichloromethane in order to determine why the yield from previous experiment was only 40 %.
Benzene was dissolved in PP6 and N_2O_5 in PP6 (5 molar equivalents) was added. The solution was stirred for 6 hours at ambient temperature. Dichloromethane was added forming a layer on the top of the perfluorocarbon. The solution was shaken and separated, this was repeated 3 times. The organic extracts were collected and neutralised, the dichloromethane was removed yielding the product (yield 85 %). The product was characterised using ^{1}H NMR spectroscopy.

The signals in the ^{1}H NMR spectrum could be assigned to a product containing 85 % 1,3-dinitrobenzene, 3 % 1,4- dinitrobenzene and 12 % 1,2-dinitrobenzene. Therefore it was

assumed that extracting the product with dichloromethane may result in higher yields but not improved product ratios.

Experiment 3 using N_2O_5, nitric acid, and nafion-H beads

Benzene was dissolved in PP6 and N_2O_5 in PP6 (3 molar equivalents) was added, followed by 100 % nitric acid (10 molar equivalents). Nafion-H beads were added and the reaction was stirred for 3 hours at ambient temperature then for a further 6 hours at 70 °C. An aliquot was taken after 3 hours, distilled water was added. The remainder of the mixture was left for 6 hours before distilled water was added. The yellow solid (yield 56 %) was separated as in previous experiments and characterised using ^{1}H NMR spectroscopy.

After a further 6 hrs (at 70°C) the composition of the product did not change. The ^{1}H NMR spectrum after 3 hours showed signals due to 1,3-dinitrobenzene. Therefore it can be concluded that benzene can be nitrated to 1,3-dinitrobenzene using a mixture of nitric acid, N_2O_5 and nafion-H at ambient temperature in 3 hours. Heating the reaction mixture for 6 hours does not change the composition of the product.

Experiment 4 using nitric acid, N_2O_5 and nafion-H membrane

Benzene was dissolved in PP6 and N_2O_5 in PP6 (3 molar equivalents) was added followed by the addition of 100 % nitric acid (7 molar equivalents) and nafion-H membrane. The solution was heated to 70 °C for 6 hours. The product (yield 46 %) was separated as in previous experiments. The signals in the ^{1}H NMR spectrum could be assigned to 1,3-dinitrobenzene (100 %).

2.11 Summary of reactions for the nitration of benzene

PFC	Molar equivalent				Temp / °C	Time /hrs	% Composition				Yield /%
	HNO₃	H₂SO₄	H₂S₂O₇	N₂O₅			1,2-DNB	1,3-DNB	1,4-DNB	TNB	
PP6	10	5	-	-	70	6	-	100	-	-	62
						12	10	87	3	-	
						20	10	87	3	-	
PFE	10	10	-	-	70	6	-	99	-	1	55
PP6	10	-	10	-	70	6	7	91	2	-	60
						12	8	90	1.5	0.5	
						20	8	89.5	1.5	1	
PP6	20*	-	20	-	70	6	-	100	-	-	40
						12	4	92	4	-	
PP6	-	-	-	5	ambient	6	-	100	-	-	4
PP6	-	-	-	5	ambient	6	12	85	3	-	85**
PP6	10*	-	-	3	3@ambient	3	-	100	-	-	56
					6@70	9	-	100	-	-	
PP6	7***	-	-	3	70	3	-	100	-	-	46

*Nafion-H beads **Dichloromethane used in extraction ***Nafion-H membrane

Table 2.16 Summary of the reactions in the study of the nitration of benzene

From the results in **Table 2.16** it can be seen that benzene can easily be dinitrated into 1,3-dinitrobenzene (**Scheme 2.7**). Even under forced conditions using nitric/oleum mixture, conversion into 1,3,5-trinitrobenzene cannot be achieved. Only a 1 % conversion was achieved with 10 molar equivalents of nitric acid and oleum.
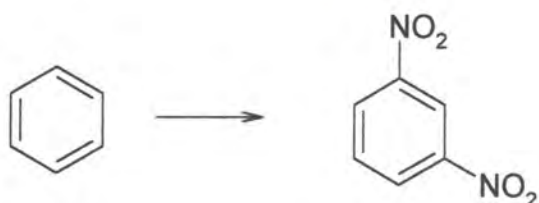
Scheme 2.7 Dinitration of benzene

2.12 Conclusion

The results in this chapter have shown that nitration of toluene to give 2,4,6-trinitrotoluene can be successfully achieved in perfluorocarbon solvents. The toluene is initially dissolved in the perfluorocarbon, in which the nitric acid is largely insoluble. It seems likely that the function of the perfluorocarbon is mainly that of a 'bulking agent' and that the nitration reaction occurs at the interface between the compounds of the heterogeneous system. The nitration probably involves a chemical 'nitronium ion' mechanism since the isomer distribution is similar to that observed in homogeneous nitrations. Nevertheless the trinitration occurs with far less sulfuric acid present than in classical 'mixed acid' nitrations, where sulfuric acid is the solvent. Further the perfluorocarbon solvent may be recycled.

Nitration of benzene gave very largely 1,3-dinitrobenzene and unfortunately it was not possible to achieve direct trinitration using the current systems.

The conclusion is that the system using perfluorocarbons is not a 'stronger' nitrating medium than mixed acid, but does allow equivalent nitrations with the requirement of far less sulfuric acid.

2.13 References

1. Olah, G.A., Malhotra, R., Narang, S.C., *Nitration Methods and Mechanisms*, VCH, New York, **1991**, 11.

2. Evans, C.M., *Industrial and Laboratory Nitrations*, Albright L. F., Carr, R.V.C., Schmitt, R.J., Ed., ACS Symposium series 623 Washington, DC, **1996,** ch. 22.

3. Olah, G.A., Iyer, P.S., Prakash, G.K.S., *Synthesis,* **1986,** 513.

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5. Streitwieser, A., Heathcock, C. H., Kosower, E. M., *Introduction to organic chemistry* 4th Ed. Macmillan Publishing company, **1992,** 780.

6. Desvergnes, L., *Chim. Ind.* (Paris), **1931,** 23, 291.

Chapter Three

3 Nitration of styrene and stilbene

This chapter will explore the nitration of styrene and stilbene using nitric acid, mixed acid and dinitrogen pentoxide in perfluorocarbon solvents.

3.1 Introduction

The nitration of styrenes using N_2O_5 has already been discussed in chapter 1, page 19. The reactions of 4-substituted styrenes (H, Me, Cl, CF_3, NO_2) with N_2O_5 in dichloromethane were studied by Lewis and Moodie.[1] Several products were formed, predominantly by radical pathways. However there was also evidence for ionic pathways. One example of the possible radical pathway is shown in **Scheme 3.1**.
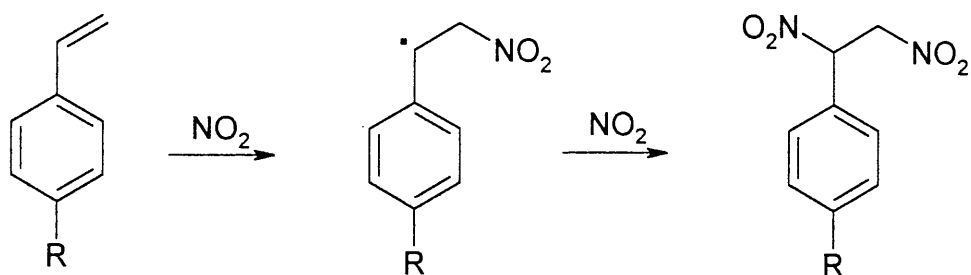
Scheme 3.1 Radical pathway for the nitration of styrene

Nitration of the unsubstituted styrene resulted in at least 10 different products and attempts to separate these were unsuccessful, so that the reaction was not investigated further. However reactions of the 4-substituted derivatives yielded four main products whose structures are given below.

(24)   (25)   (26)   (27)
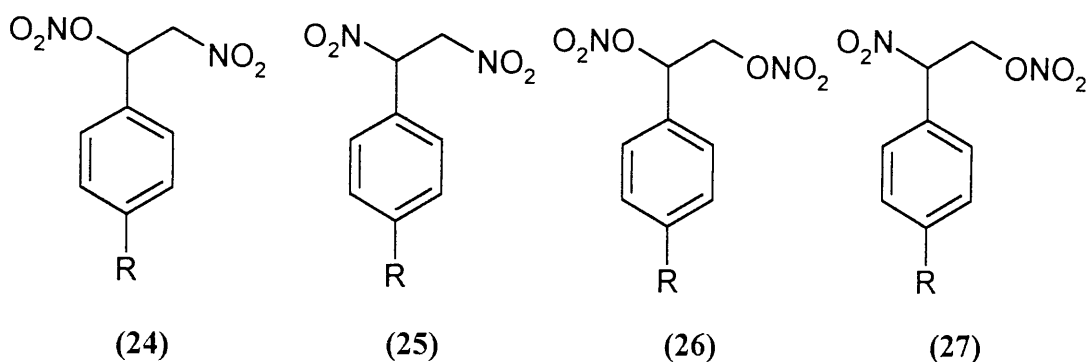
R= H, Me, Cl, CF and NO$_2$

There is evidence from ^{15}N CIDNP studies that radical pathways are involved in the formation of these products. However there is also evidence for ionic pathways involving the nitronium ion, since the addition of tetrabutylammounium nitrate inhibited reaction. The inhibition presumably derives from reduction in the ionisation of N$_2$O$_5$, **Scheme 3.2**.

$$NO_2^+ + NO_3^- \rightleftharpoons N_2O_5 \rightleftharpoons NO_2 + NO_3$$
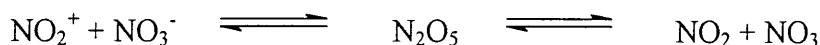
Scheme 3.2 Ionisation of N$_2$O$_5$

The kinetics and products of the reaction of 4-substituted styrenes (H, Me, Cl, CF$_3$, NO$_2$) with nitric acid in dichloromethane have also been reported.[2] The reaction was reported to occur in the alkene group and aromatic nitration was insignificant. One major product was seen that was not seen in the reaction of styrene and N$_2$O$_5$. This was 1-arylethylnitrate (46).

(46)
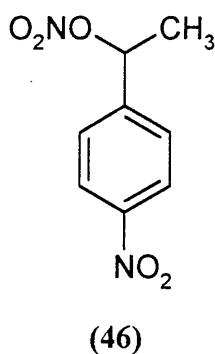
The reactions of alkenes are often complex, giving predominantly the nitro nitrate addition products across the double bond.

In the present work the nitrations of styrene and stilbene have been attempted using perfluorocarbon media. Both mixed acid, nitric and sulfuric, and N_2O_5 have been used as nitrating agents.

Stilbene is of interest since the hexanitroderivative (**47**) has been used as a thermally stable explosive for specialist uses.[3]
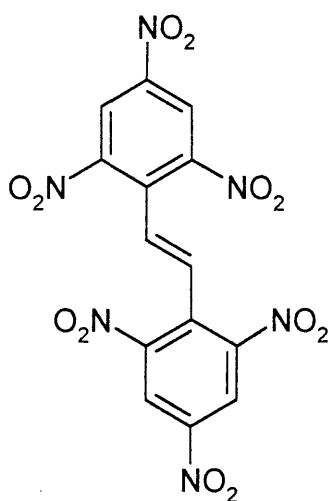
(**47**)

3.2 Nitration of styrene (48) using nitric and sulfuric acid
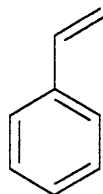
(**48**)

Experiment 1 using ten molar equivalents of each acid

Styrene (**48**) was dissolved in PP6 and nitric acid was added followed by sulfuric acid. The solution was heated for 6 hours at 70 °C and dichloromethane was used to extract the product. The dichloromethane layer was neutralised and evaporated yielding a yellow liquid (0.3126 g). A ^{1}H NMR spectrum in d_6-DMSO, (**Figure 3.1**) and EI mass spectrum (**Figure 3.2**) were recorded on the product.
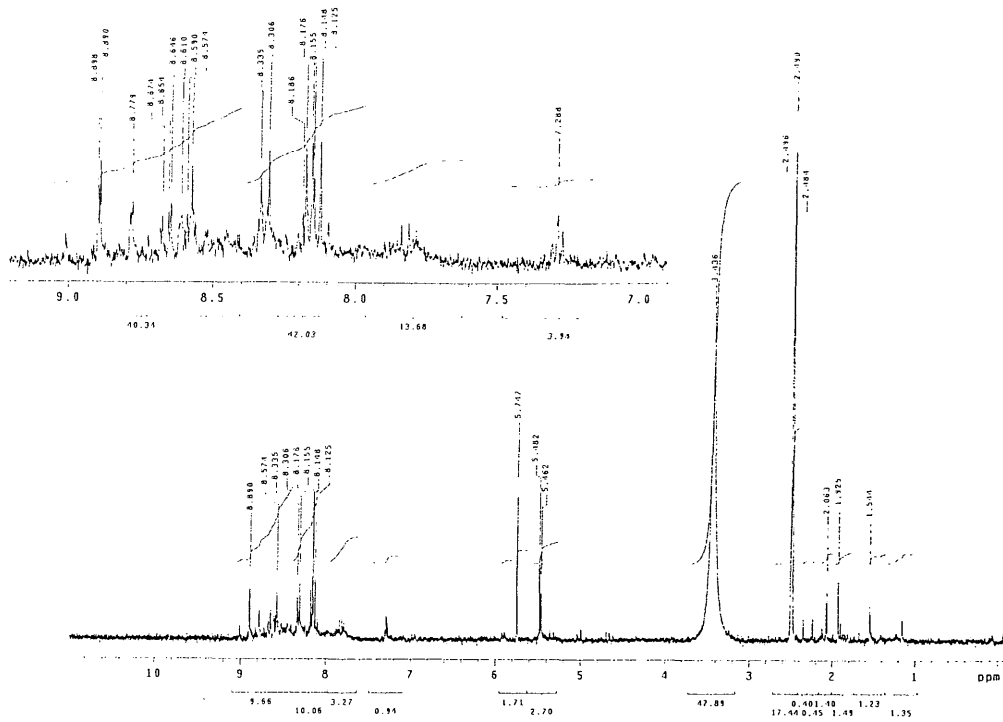
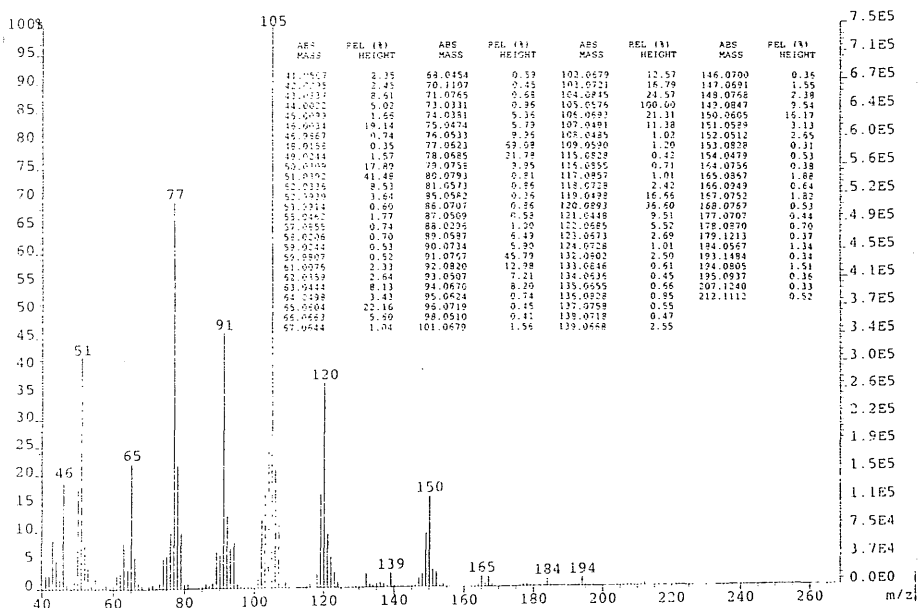**Figure 3.1** ¹H NMR spectrum of nitrated styrene

Figure 3.2 EI mass spectrum of nitrated styrene

The ^{1}H NMR spectrum of nitrated styrene (**Figure 3.1**) shows that various compounds are present. There are various possibilities of the structure of these compounds because aliphatic and aromatic nitration can occur. Lewis and Moodie reported that the major compound they observed when nitrating styrene with nitric acid in dichloromethane was 1-arylethyl nitrate (**46**).[2] This compound has a molecular mass of 167 and if one nitro group is added this gives a molecular mass of 212. Species with molecular mass of 167 and 212 were present in the EI mass spectrum recorded on the product (**Figure 3.2**). The ^{1}H NMR spectrum of 1-arylethyl nitrate was reported to give aliphatic signals at δ 1.6 ppm (d) and δ 5.9 ppm (q) with an aromatic signal at δ 7.3 ppm (m) in CDCl$_3$. The ^{1}H NMR spectrum above (**Figure 3.1**) contains small signals at δ 1.5 ppm, δ 5.7 ppm and δ 7.3 ppm in d$_6$-DMSO, which could correspond to 1-arylethyl nitrate (**46**). There were no signals in the spectrum above that would correspond to unreacted styrene (δ 5.24 ppm (d), δ 5.81 ppm (d), δ 6.71 ppm (dd), δ 7.27 ppm (t), δ 7.32 ppm (t), δ 7.45 ppm (d) in d$_6$-DMSO).

There are various signals in the region of δ8-9 ppm, which are likely due to aromatic nitration. If we compare the signals to nitrobenzene derivatives we can estimate the shifts of the signals in a ^{1}H NMR spectrum. In 1,3-dinitrobenzene (**see chapter two**) the hydrogen between the two nitro groups has a shift of δ 8.8 ppm (s) and the hydrogen *ortho* to one nitro group has a shift of δ 8.6 ppm (dd). The hydrogen *meta* to both nitro groups has a shift of δ 8.0 ppm (t). In the spectrum above (**Figure 3.1**) relatively intense signals can be seen at δ 8.15 ppm (t), δ 8.57 ppm (m) and δ 8.89 ppm (s), which are likely due to *ortho* and *para* aromatic dinitration of styrene. The other signals in this region may be due to aromatic mono-nitro compounds in *ortho* or *para* positions. It is also possible that both aromatic and aliphatic nitration have occurred together.

The experiment was repeated using a smaller excess of acid to see if the product composition could be more successfully determined.

Experiment 2 using one and a half molar equivalents of acid

The above experiment was repeated using 1.5 equivalents of nitric and sulfuric acid. The product was again extracted with dichloromethane yielding a yellow/orange liquid (0.0681 g). A ^{1}H NMR spectrum was recorded on the product.

The ^{1}H NMR spectrum was similar to the spectrum from the previous experiment indicating a complex mixture of products and the bands could not be assigned accurately. Therefore nitration of styrene with mixed acid was not investigated further and nitration of styrene using N_2O_5 was examined.

3.3 Nitration of styrene using N_2O_5

Experiment 1 using three molar equivalents of N_2O_5

Styrene was dissolved in PP6 and N_2O_5 in PP6 was added. The solution was stirred for 3 hours at ambient temperature. Dichloromethane was used to extract the product. The dichloromethane layer was neutralised and left to evaporate yielding a red liquid (0.2019 g). A ^{1}H NMR spectrum and was recorded on the product.
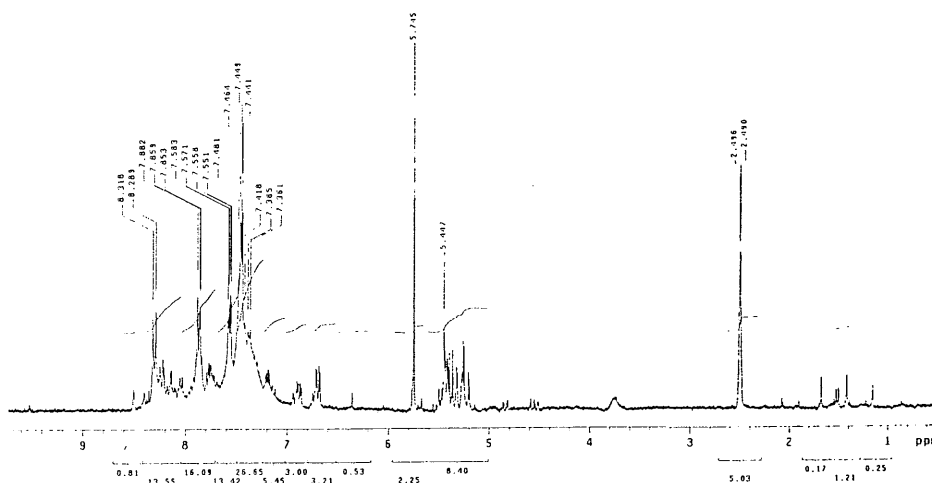
Figure 3.3 ^{1}H NMR spectrum of nitrated styrene

The ^{1}H NMR spectrum (**Figure 3.3**) in d_6-DMSO shows that the product contained various compounds. The major difference in the ^{1}H NMR spectrum of the compound nitrated using N_2O_5 in comparison to the ^{1}H NMR spectrum of the compound nitrated using nitric acid was bands present in the region of δ 5-6 ppm. These bands are most likely to be due to the compounds reported by Lewis and Moodie to be produced in the nitration of styrene with N_2O_5.[1] The structures of these compounds are shown earlier, Lewis and Moodie refer to them as β-nitro nitrate (**24**), the dinitro (**25**), the dinitrate (**26**) and the α-nitrate (**27**). The aromatic protons in these compounds would give a signal at δ 7.45 ppm which can be seen the above spectrum (**Figure 3.3**) as a major band. The product may also contain derivatives of 4-nitrostyrene, which has been reported to give δ 5.75 ppm (d), δ 6.75 ppm (dd), δ 7.50 ppm (d), δ 8.15 ppm (d) in $CDCl_3$.[1] The ^{1}H NMR spectrum (**Figure 3.3**) shows doublets at δ 7.8 and δ 8.3 ppm in d_6-DMSO. These are characteristic of a *para*-disubstituted benzene

-87-

derivative. The bands are at higher frequencies than those for 4-nitrostyrene itself, suggesting that nitration has occurred in the sidechain.

However no bands are observed which are attributable to a dinitrobenzene derivative in this case.

The experiment was repeated using a smaller molar excess of N_2O_5 to see if the product composition could be more successfully determined.

Experiment 2 using one and a half molar equivalents of N_2O_5

The above experiment was repeated using one and a half molar equivalents of N_2O_5. The product was extracted using dichloromethane yielding a red liquid (0.1199 g). A ^1H NMR spectrum and was recorded on the product. The products were separated by column chromatography

^1H NMR spectrum of the first fraction showed bands which are attributable to 4-nitrostyrene (δ 7.8 and δ 8.3 ppm) and another compound.

The GC mass spectrum found signals at 1055s with m/z 148, 1090s with m/z 194 and 1096s with m/z 194, which shows that there was one mononitrostyrene (Mr 148 g) and two dinitrostyrene (Mr 194 g) compounds present.

The ^1H NMR spectrum from the second fraction showed a band at δ 7.45 ppm which is due to the ring protons from a aliphatic nitrated styrene compound but the ^1H NMR spectrum was not clear enough to show which compounds were present.

The results for the nitration of styrene indicate that in PP6, as found previously [1,2] in dichloromethane, mixtures of products are produced. The present result indicate that there is a tendency for ring-nitrations to be favoured using mixed acid, so that dinitration is observed in the aromatic ring. Dinitration in the ring is not observed with N_2O_5 and ^1H NMR bands due to the products of side-chain nitration are present.

3.4 Nitration of *trans*-stilbene (49) using nitric and sulfuric acid
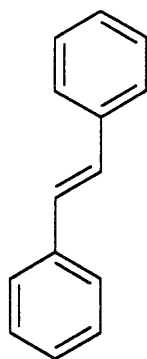
(49)

Experiment 1 using ten equivalents of nitric and sulfuric acid

trans-Stilbene (49) was dissolved in PP6 and nitric acid followed by sulfuric acid was added. The solution was heated for 6 hours at 75 °C. The PP6 was left to evaporate and the resulting product was washed with water to remove excess acid and filtered yielding a yellow solid (0.3126 g). A ^1H NMR spectrum was recorded on the product but the bands could not be assigned accurately to one specific compound therefore a HPLC spectrum (**Figure 3.4**) was recorded on the sample. The compound with the major signal in the HPLC spectrum was purified and separated and a ^1H NMR spectrum (**Figure 3.5**) was taken. A CI mass spectrum (**Figure 3.6**) was also recorded on the product. The melting point of the solid was 127 °C.
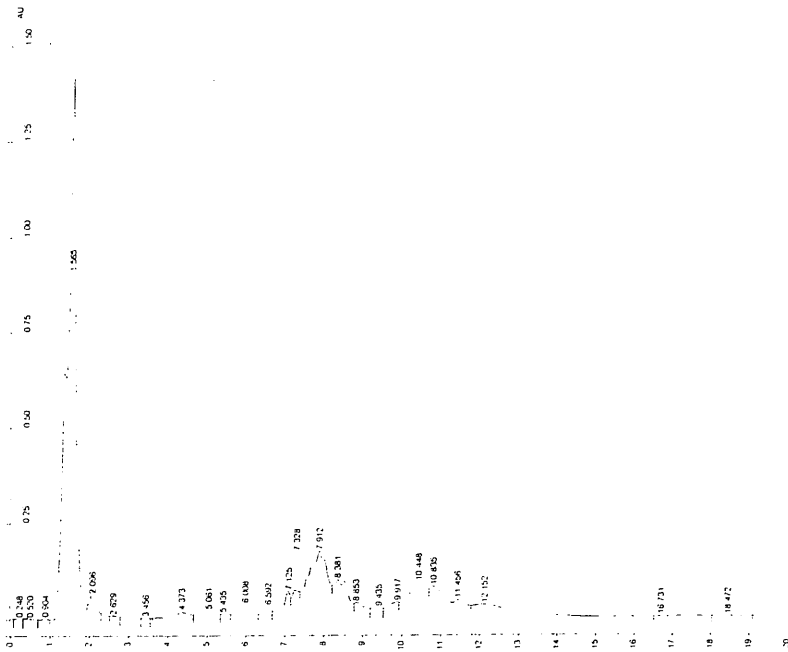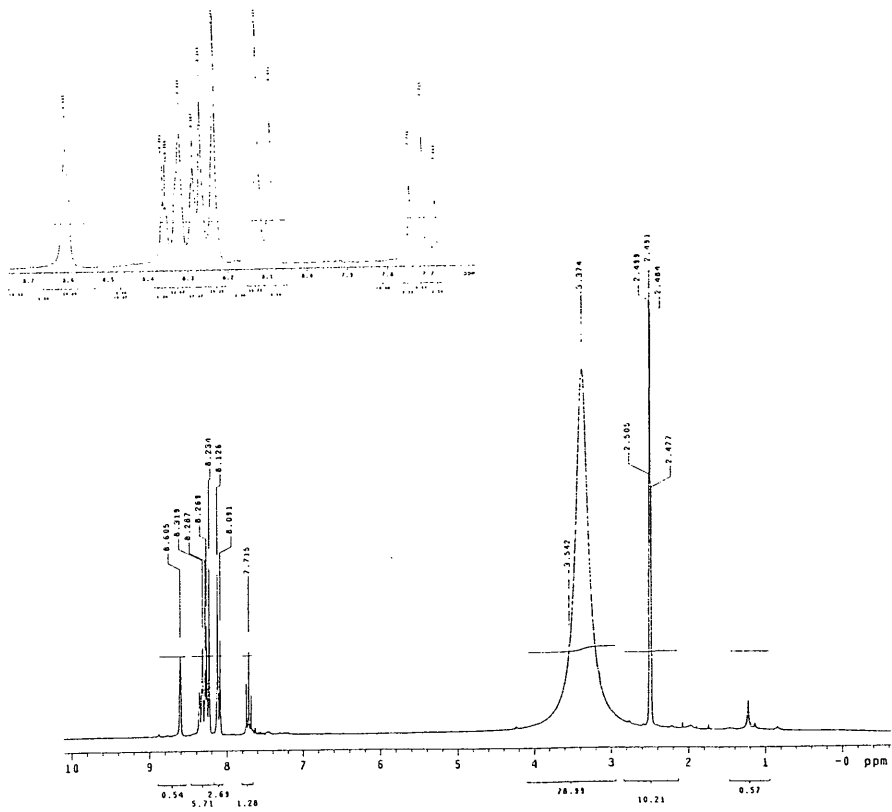
Figure 3.4 HPLC spectrum of nitrated *trans*-stilbene

Figure 3.5 ^{1}H NMR spectrum of nitrated *trans*-stilbene separated using HPLC
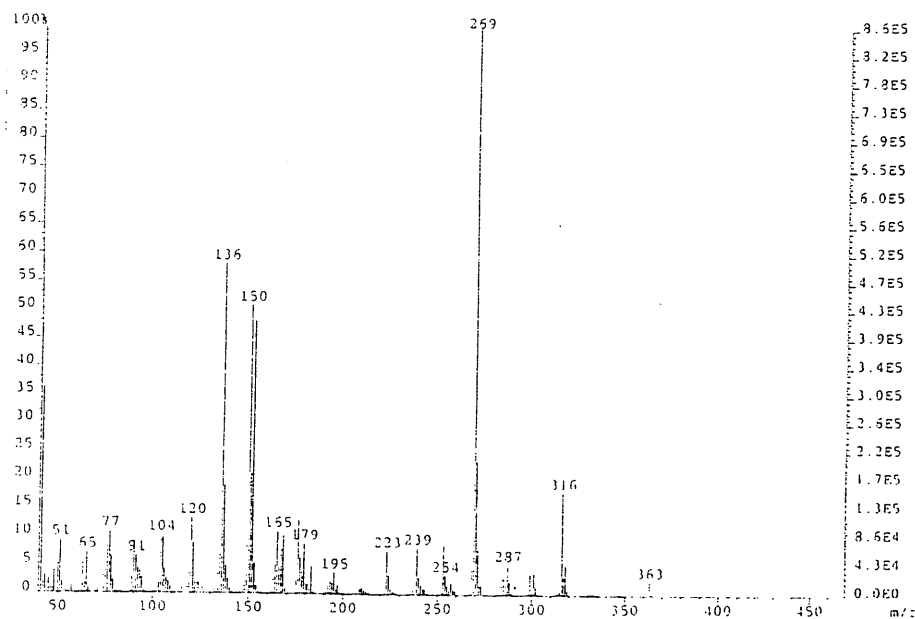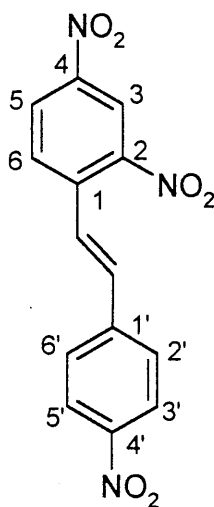
Figure 3.6 CI mass spectrum of nitrated *trans*-stilbene

The HPLC spectrum (**Figure 3.4**) found the major signal at 1.57 minutes. This component was separated. The ^{1}H NMR spectrum (**Figure 3.5**) gave signals that could be assigned to the following compound;


(**50**)

The distinctive AB quartet in the ^{1}H NMR spectrum (**Figure 3.5**) centred at δ 8.2 ppm could be due to protons in positions H2′, H3′, H5′, and H6′. The signals at δ 8.3 ppm could be due to protons in positions H5, H6 and the singlet at δ 8.6 ppm could be due to protons in position H3. The signals at δ 7.71 ppm could be assigned to the two CH groups. The CI mass spectrum (**Figure 3.6**) confirms the possibility of the presence of a trinitrated derivative and also shows the possibility of formation of a tetra-nitro derivative.

The CI mass spectrum (**Figure 3.6**) gave the following signals shown in **Table 3.1**.

m/z	Mr / g	Structure
363	362	(51)
316	315	(50)
269	268	(52)
150	149	(53)
136	135	(54)

Table 3.1 CI mass spectrum assignments

(51)   (50)   (52)   (53)   (54)
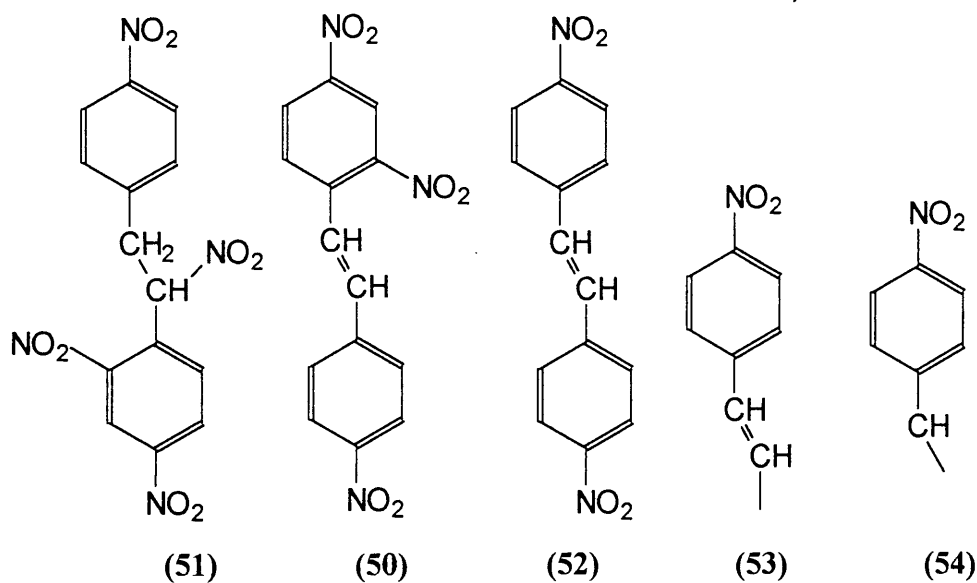
The bands could correspond to the structures above or a similar structure with an equivalent molecular mass.

From all the results we can conclude that a major product is probably 2,4,4'-trinitrostilbene (**50**) with a small amount of various other nitrated stilbene derivatives.

3.5 Unusual loss of 15 m/z in the GC mass spectrum of *trans*-stilbene

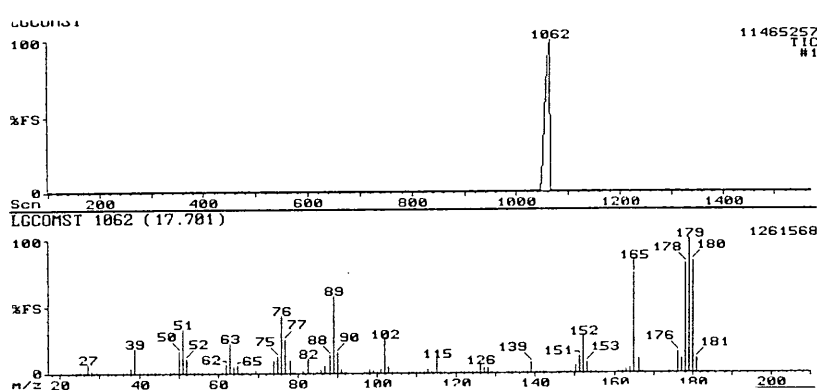The GC mass spectrum (**Figure 3.7**) of *trans*-stilbene was recorded while investigating the nitration of *trans*-stilbene.
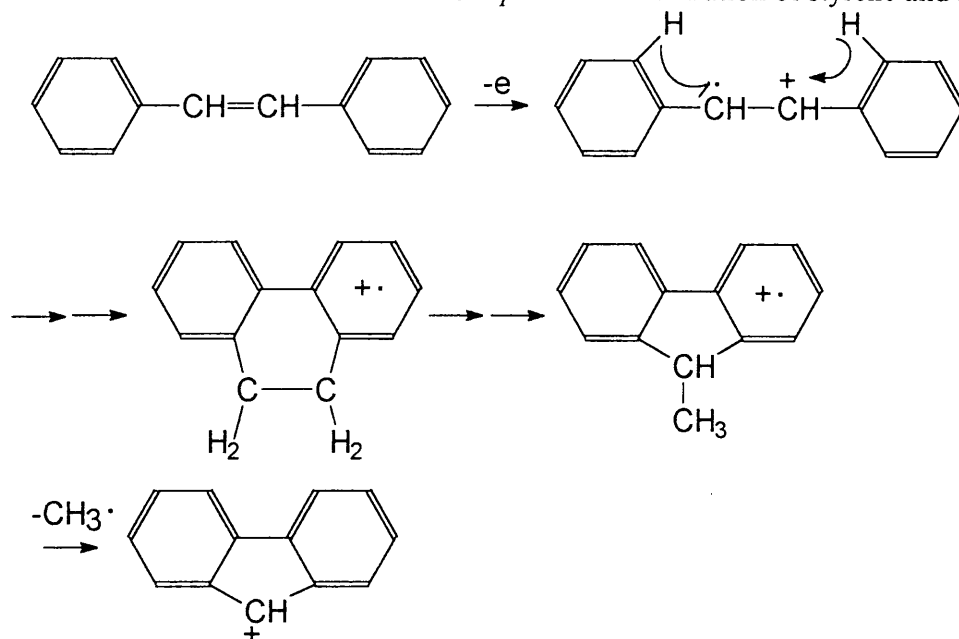

Figure 3.7 GC mass spectrum of *trans*-stilbene

The major chromatograph band at 1062s corresponds to a molecular mass of 180 g. The molecular mass of *trans*-stilbene is 180 g. The band at 165 shows a loss of 15 m/z, which is unusual in mass spectroscopy. The following mechanism has been proposed in the literature.[4]

Scheme 3.2 Loss of CH_3 radical in *trans*-stilbene

The loss of 15 m/z corresponds to the loss of CH_3 radical. Deuterium labelling has shown evidence for this process.[4]

3.6 Nitration of *trans*-stilbene using N_2O_5

The experiment below was repeated using three different molar equivalents of N_2O_5.

trans-Stilbene was dissolved in either PP6 or PP2 and N_2O_5 was added. The solution was stirred for 3 hours at ambient temperature. Distilled water was added to the reaction followed by neutralisation. The yellow solids formed were filtered off and dried. HPLC spectra were obtained for the three products and the product with the major signal was purified. A ^{1}H NMR spectrum and EI mass spectrum were recorded on the purified products.

Experiment 1 using one molar equivalent of N₂O₅

The HPLC spectrum of the product nitrated using one molar equivalent of N_2O_5 gave the same spectrum to that of the starting material (band at 11 minutes), *trans*-stilbene. Therefore it was concluded that *trans*-stilbene was not significantly nitrated using one molar equivalent of N_2O_5 under these conditions.

Experiment 2 using three molar equivalent of N₂O₅

In this case the HPLC spectrum of the product was different to commercial *trans*-stilbene. *trans*-Stilbene was present in the spectrum (11 minutes) but the major signal was at 8.3 minutes with a smaller signal 1.4 minutes. The compound corresponds to the signal at 8.3 minutes was separated and a ^{1}H NMR spectrum and EI mass spectrum were recorded, the ^{1}H NMR spectrum was inconclusive but the EI mass spectrum gave a signal at 315 m/z which could correspond to trinitrostilbene (Mr 315 g).

Experiment 3 using six molar equivalent of N₂O₅

The HPLC spectrum of the product showed bands in addition to that due to *trans*-stilbene. Surprisingly, *trans*-stilbene was present in the spectrum (11 minutes) but the major signal was at 8.3 minutes with smaller signals at 1.4 minutes and at 4.3 minutes. The product corresponding to the signal at 8.3 minutes was separated and a ^{1}H NMR spectrum and EI mass spectrum were recorded. The ^{1}H NMR spectrum was again inconclusive but the EI mass spectrum gave a signal at 315 m/z, which could correspond to trinitrostilbene (Mr 315 g).

Therefore it can be concluded that nitration of *trans*-stilbene is possible with N_2O_5 using more than one equivalent of N_2O_5. Identification of the products is difficult because there are several possibilities in the position of nitration.

3.7 Conclusions

It should be stated that the nitrations of styrene and stilbene did not form a major part of the work reported in the thesis.

The nitrations were attempted in the hope that multiple nitrations might be achieved and that relatively pure products might be easily obtained. The results show that mixtures are produced which are not easily separated.

It is interesting that mixtures of stilbene apparently produces the ring trinitrated derivative as a major product. It is not likely that it will be possible to achieve hexanitroderivative using perfluorocarbon solvents and mixed acid, or N_2O_5 as the nitrating agent.

3.8 References

1. Lewis, R. and Moodie, R. B., *J. Chem. Soc., Perkin Trans. II,* **1996,** 1315.
2. Lewis, R. and Moodie, R. B., *J.Chem.Soc., Perkin Trans. II,* **1997,** 563.
3. Crampton, M. R., and Routledge, P. J, *J. Chem. Soc., Perkin Trans II,* **1984,** 1785.
4. H. Budzikiewicz, C. Djerassi and D. H. Williams, 'Mass spectrometry of organic compounds', Holden-Day Inc, 89.

Chapter Four

4 Mechanistic studies of nitration using dinitrogen pentoxide

This chapter will explore the nitration of chloroanisole, bromophenetole and various other halogenated phenols using dinitrogen pentoxide in perfluorocarbons solvents. The rate constants have been determined and some mechanistic conclusions have been deduced.

4.1 Introduction

There has been little previous work on the kinetics of the nitration of aromatic compounds with N_2O_5 in halocarbon solvents. However in an early study Ingold *et al*[1] proposed that when the aromatic compound was in constant excess two possible mechanistic pathways are possible for the nitration when using dinitrogen pentoxide;

1   Non catalysed first order reactions are favoured at higher temperatures (*ca* 15 °C) and lower initial concentrations of reagent (0.04 M), showing exponential kinetic form.

2   An autocatalytic reaction was favoured at lower temperatures (-10 °C) and higher concentrations of reagent (1 M), showing sigmoidal kinetic form.

Ingold's work focused mainly on halobenzenes and alkyl benzoates in tetrachloromethane and nitromethane mixtures. Therefore it was decided to investigate the mechanism involved in the nitration of aromatics using dinitrogen pentoxide in perfluorocarbon solvents measurements were made in PP6 and also in perfluoroether (HT135).

Initially the solubility of reagents was investigated in the perfluorocarbons. The results in **chapter six, section 6.3**, show that N_2O_5 is soluble, *ca* 1 mol dm^{-3}, in the solvents used. The aromatic substrates varied with structure but were ≥ 0.01 mol dm^{-3}.

It is relevant to note that the solubility of water in PP6 is extremely low. The quoted value, see chapter two, section 2.2.4, is < 10 ppm, giving a concentration of *ca* 10^{-4} mol dm^{-3}. Similarly the solubility of nitric acid in PP6 is immeasurably small.

4.2 Spectral studies of substrates and their nitrated products

In order to measure the kinetics of nitration of aromatic compounds with dinitrogen pentoxide in perfluorocarbons it was necessary to find substrates where nitration resulted in a significant change in the UV/Vis spectrum. Therefore, the UV/Vis spectra were recorded for some substrates and their corresponding nitrated products. The aim was to follow kinetically the reaction of N_2O_5 with substrate that had significant change in absorption spectrum..

Various substrates and their corresponding nitrated products were dissolved in PP6 giving a final concentration of 1×10^{-3} mol dm^{-3}, (substrates and nitrated products were commercial materials purchased from Aldrich). The UV/Vis spectra were recorded and the extinction coefficients were calculated, (**Table 4.1**).

Starting material	λ_{max} / nm	ε / dm^3 mol^{-1} cm^{-1}	Nitrated product	λ_{max} / nm	ε / dm^3 mol^{-1} cm^{-1}
nitrobenzene	246	5000	1,3 dinitrobenzene	239	9200
1-chloro-4-nitro-benzene	258	9700	1-chloro-2,4-dinitrobenzene	253	10000
			1-chloro-2,6- dinitrobenzene	286	990
4-chloroanisole	278	1200	4-chloro-3-nitroanisole	314	1800
			4-chloro-2,6-dinitroanisole	309	2200

Table 4.1 Examination of absorption maxima and extinction coefficients of various substrates and their corresponding nitrated products

4-Chloroanisole was found to give a significant change in UV/Vis absorbance when compared to its nitrated products. Hence this was chosen as the initial substrate for closer examination of the nitration reaction.

Kinetic measurements were made with the concentration of N_2O_5 in excess of the concentration of N_2O_5 in excess of the concentration of aromatic substrate. Under this condition, reactions were found to be first order in the aromatic compound, as shown in **Equation 4.1**.

$$vel = -d[Ar]/dt = k_{obs}[Ar]$$

Equation 4.1

4.3 4-Chloroanisole (56)

(56)
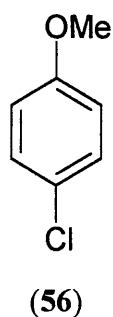
4-Chloroanisole (**56**) was dissolved in PP6 and the UV/Vis spectrum was recorded, (**Figure 4.1**, blue trace). N_2O_5 in PP6 was added to the solution of 4-chloroanisole in PP6, and the UV/Vis spectrum was recorded after 10 minutes, (**Figure 4.1**, red trace).
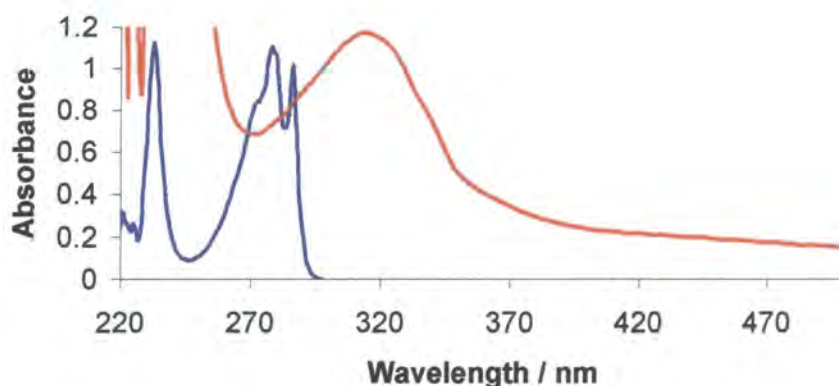
Figure 4.1 UV/Vis spectrum of 4-chloroanisole with and without N_2O_5 in PP6 at 25°C

The absorbance of 4-chloroanisole, with the addition of various concentrations of N_2O_5 (always in excess) in PP6, was measured over time at 316nm. **Figure 4.2** shows an example of the change in absorbance over 15 minutes. The curves obtained gave acceptable fits with an exponential function with correlation coefficients 0.998.
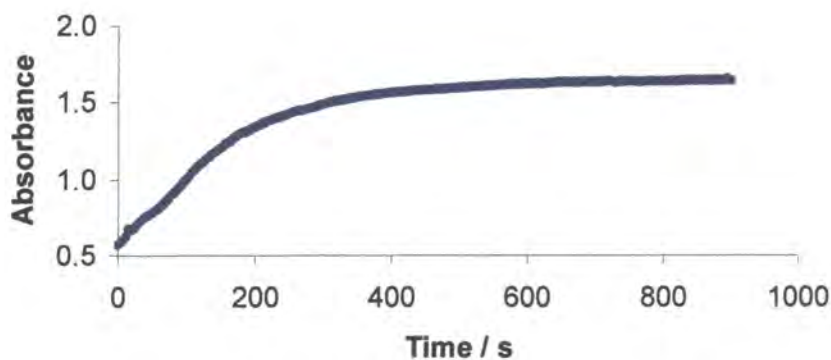

Figure 4.2 Reaction profile for the nitration of 4-chloroanisole using N_2O_5

Exponential fits for kinetic runs were calculated using a graphical method to give the best correlation of data. See chapter six for the methods of calculation. The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5 and by the

concentrations squared, (**Table 4.2**). This was done to determine whether the reaction was first or second order in N_2O_5.

[4-chloroanisole] / 10^{-4} mol dm^{-3}	[N_2O_5] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ / dm^{3}mol^{-1}s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]^2}$ / dm^{6}mol^{-2}s^{-1}
9.76	0.0031	0.0023	0.73	240
	0.0062	0.0045	0.72	120
	0.0124	0.0075	0.61	49
	0.0186	0.0108	0.58	31
	0.0248	0.0124	0.50	20
	0.0310	0.0141	0.45	15

Table 4.2 k_{obs} values for the nitration of 4-chloroanisole using N_2O_5 in PP6 at 25 °C

In order to determine k_2, the second order rate constant, k_{obs} versus concentration of N_2O_5 was plotted, (**Figure 4.3**) and k_{obs} versus concentration squared of N_2O_5 was plotted for a comparison, (**Figure 4.4**).
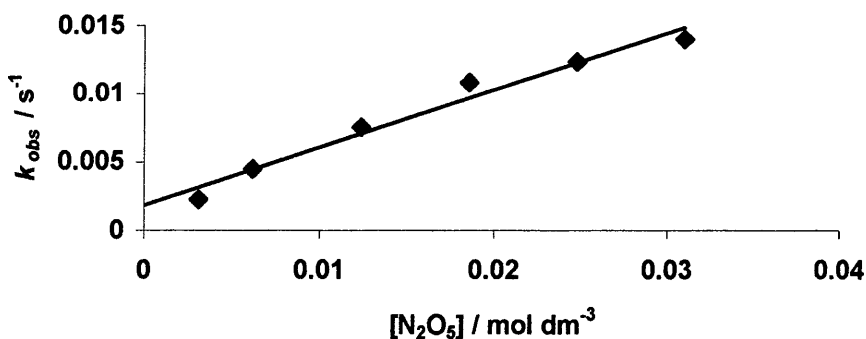
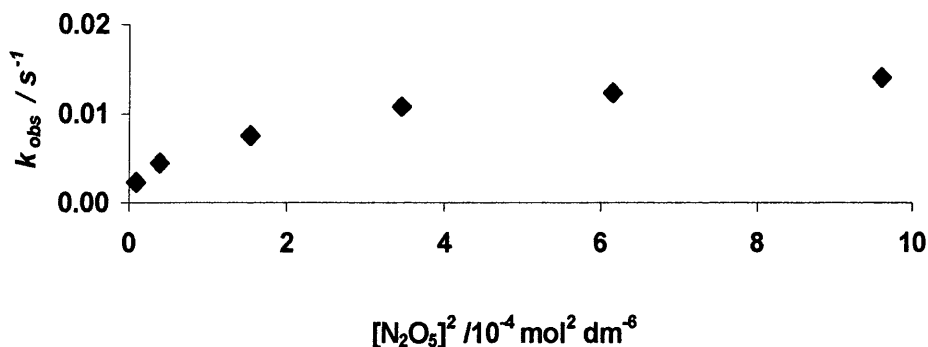**Figure 4.3** Correlation between k_{obs} and concentration of N_2O_5 for the nitration of 4-chloroanisole with N_2O_5 in PP6.

Figure 4.4 Correlation between k_{obs} and concentration of $N_2O_5{}^2$ for the nitration of 4-chloroanisole with N_2O_5 in PP6.

It can be seen that there is a good correlation between k_{obs} and the concentration of N_2O_5, (**Figure 4.3**). Therefore we can express the rate equation as first order in N_2O_5, with k_2 equal to 0.5 ± 0.2 s^{-1} mol^{-1} dm^3 as shown in **Equation 4.2 and 4.3**.

$$\text{Rate} = k_2 \, [N_2O_5] \, [\text{4-chloroanisole}]$$

Equation 4.2

where $k_{obs} = k_2$ [N$_2$O$_5$] when [N$_2$O$_5$] >> [4-chloroanisole]

Equation 4.3

It should be noted that in the first two data points in **Table 4.2** the condition [N$_2$O$_5$] >> [4-chloroanisole] is not initially obeyed. Hence the rate constants for these two points are less reliable than these obtained at higher concentrations of N$_2$O$_5$.

The plot shown in **Figure 4.3** has a small positive intercept in the y-axis. In general this might indicate that the reaction studied is reversible. However this explanation is unlikely in the present case since nitration is expected to be irreversible.

It was necessary to carry out a synthetic experiment to check the nature of the product, that is the position of nitration.

4.3.1 Synthetic experiment for the nitration of 4-chloroanisole

Nitration of 4-chloroanisole using N$_2$O$_5$ was carried out in order to determine the nature of the product from the kinetic experiment (vide supra). Two reactions were performed, one for three hours and one for two minutes.

Nitration after three hours

N$_2$O$_5$ in PP6 (0.17 mol dm^{-3}) was reacted with 4-chloroanisole in PP6 (0.05 mol dm^{-3}) and with stirring at ambient temperature for 3 hours. On the addition of distilled water to the solution a solid formed, which was collected by filtration.

The composition of the resulting mixture was determined by ^{1}H NMR spectroscopy giving a product ratio of 4-chloro-2-nitroanisole (46 %) and 4-chloro-2,6-dinitroanisole (54 %), with an isolated yield of 48 %. As the kinetics were measured in the first few minutes of the reaction a synthetic experiment was carried out in a shorter time frame.

Nitration after 2 minutes

The above experiment was repeated but the solution was allowed to stir for only two minutes before quenching with distilled water.

The composition of the resulting product mixture was determined by ^{1}H NMR spectroscopy as 4-chloro-2-nitroanisole (67 %) and 4-chloro-2,6-dinitroanisole (33 %).

The nature of the product was also investigated by UV/Vis spectroscopy. A UV/Vis spectrum was recorded for the product in PP6 gave λ_{max} =316 nm, ε = 1913 dm^{3}mol^{-1}cm^{-1}. The λ_{max} value for the commercial sample of 4-chloro-3-nitroanisole is 314 nm, ε = 1773 dm^{3}mol^{-1}cm^{-1}, shown in **Table 4.1**.

The synthetic experiment showed the major product formed in the required time frame was 4-chloro-2-nitroanisole. Nevertheless it is likely that under the conditions of the kinetic experiments there will be some further reaction to produce 4-chloro-2,6-dinitroanisole. However kinetic measurements were made spectrophotometrically at 316 nm where the extinction coefficients of the mono-nitro and di-nitro derivatives were very similar. Hence distinction would not result in a detectable change in absorbance.

The conclusion is that the reaction being measured is that shown in **Scheme 4.1**. The results indicate that the reaction is first order in N_2O_5 with k_2 = 0.5 ± 0.2 s^{-1} mol^{-1} dm^3.
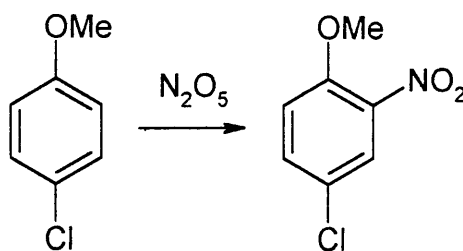
Scheme 4.1 Nitration of 4-chloroanisole with N_2O_5

4.4 4-Bromophenetole (56)

OEt

Br

(56)
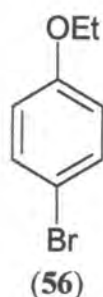
4-Bromophenetole (**56**) was also studied so that the kinetic results could be compared with those of 4-chloroanisole.

4-Bromophenetole was dissolved in PP6 and the UV/Vis spectrum recorded, (**Figure 4.5**, blue trace). N_2O_5 in PP6 was added to the solution of 4-bromphenetole in PP6, and the UV/Vis spectrum recorded after 10 minutes, (**Figure 4.5**, red trace), showing a change in absorbance and a shift in wavelength.
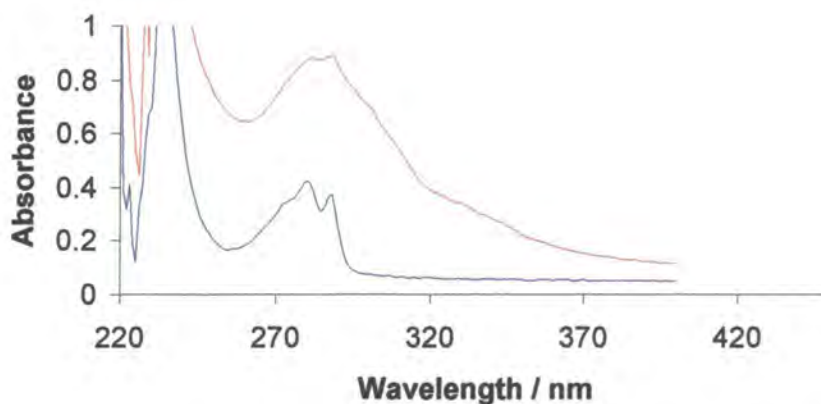

Figure 4.5 UV/Vis spectrum for 4-bromophenetole with and without N_2O_5 in PP6 at 25°C

The change in absorbance with time was measured at 298nm for solutions of 4-bromophenetole in PP6 containing various concentrations of N_2O_5 (always in excess). The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.3**) to give k_2, derived as explained previously.

[4-bromophenetole] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /$dm^3 mol^{-1}s^{-1}$
2.00	0.0058	0.0067	1.2
	0.0077	0.0086	1.1
	0.0096	0.012	1.2
	0.012	0.015	1.3
	0.013	0.018	1.4
	0.0048	0.0074	1.5
	0.0069	0.0083	1.2
	0.0103	0.014	1.3
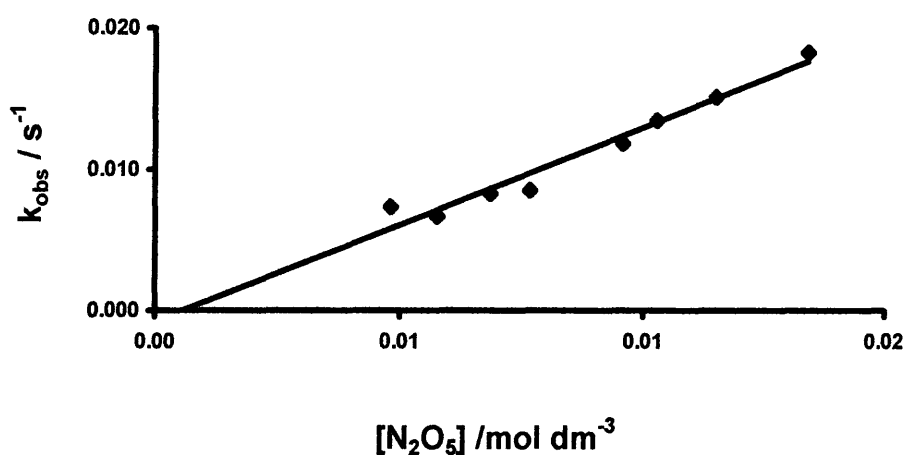
Table 4.3 k_{obs} values for the nitration of 4-bromophenetole using N$_2$O$_5$ in PP6 at 25 °C

Figure 4.6 Correlation between k_{obs} and concentration of N$_2$O$_5$ for the nitration of 4-bromophenetole with N$_2$O$_5$ in PP6

It can be seen from the plot (**Figure 4.6**) that there is a good correlation between k_{obs} and concentration of N$_2$O$_5$, therefore we can express the rate equation as first order in N$_2$O$_5$, with k_2 equal to 1.3 ± 0.3 s^{-1} mol^{-1} dm^3. Nitration will most likely occur at the *ortho* position with respect to the phenetole group giving 4-bromo-2-nitrophenetole.

4.5 2-Chlorophenol (57)
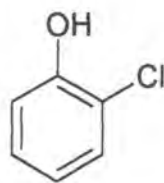
(57)

Various chlorophenols are commercially available and were found to react with N_2O_5. In order to investigate the mechanism involved in nitration using N_2O_5 in PP6, they were also studied, using the methods as described previously.

The UV/Vis spectrum of 2-chlorophenol (57), was recorded before (blue) and after (red) the addition of N_2O_5 in PP6 showing an increase in absorbance and a shift in wavelength, (**Figure 4.7**).
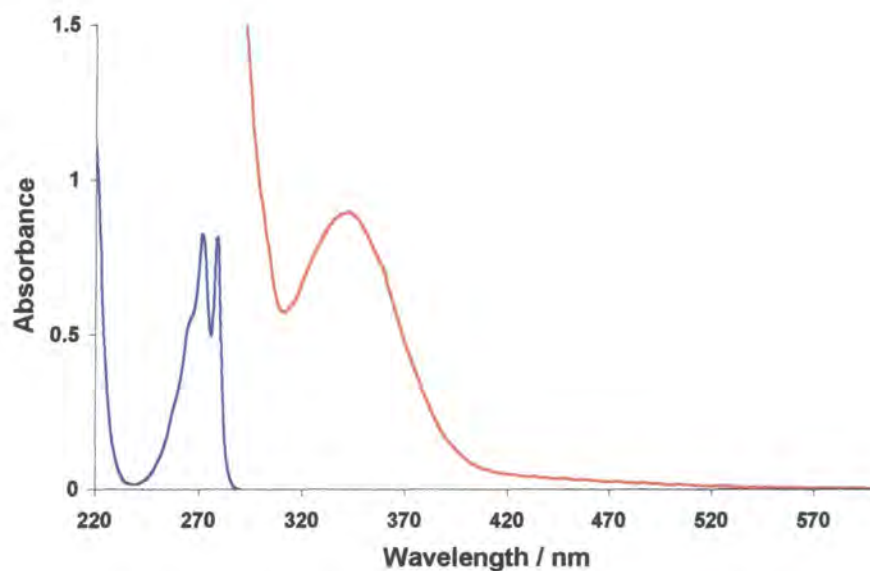

Figure 4.7 UV/Vis spectrum for 2-chlorophenol with and without N_2O_5 in PP6 at 25°C

The absorbance of 2-chlorophenol, with the addition of various concentrations of N_2O_5 in PP6, was measured with time at 342 nm, (**Figure 4.8**).
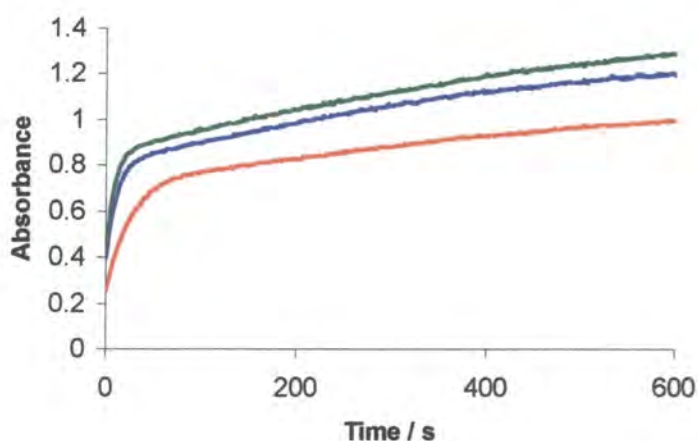
Figure 4.8 Reaction profile for the nitration of 2-chlorophenol using N_2O_5

Figure 4.8 shows the rapid absorbance increases in the first 50 seconds, followed by slower increases over the next 550 seconds. In previous reactions studied in this section the slower reaction was not observed. It is proposed that this could be due to a further reaction. Therefore rate constants were calculated assuming two reactions were involved.

First Reaction involved in the nitration of 2-chlorophenol

The observed rate constants (k_{obs}) were determined from the results in the first 50 seconds and divided by the concentrations of N_2O_5, (**Table 4.4**).

[2-chlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ / dm^{3}mol^{-1}s^{-1}
	0.0031	0.049	16
4.49	0.0062	0.084	14
	0.0092	0.104	11

Table 4.4 k_{obs} values for the nitration of 2-chlorophenol using N$_2$O$_5$ in PP6 at 25 °C for the first reaction

It can be seen that there is a reasonable correlation between k_{obs} and concentration of N$_2$O$_5$, (**Table 4.4**), therefore we can express the rate equation as first order in N$_2$O$_5$, with k_2 equal to 14 ± 2 s^{-1} mol^{-1} dm^3 for the first reaction.

Second Reaction involved in the nitration of 2-chlorophenol

The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N$_2$O$_5$, (**Table 4.5**).

[2-chlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ / dm^{3}mol^{-1}s^{-1}
	0.0031	0.0021	0.68
4.49	0.0062	0.0039	0.63
	0.0092	0.0054	0.59

Table 4.5 k_{obs} values for the nitration of 2-chlorophenol using N$_2$O$_5$ in PP6 at 25 °C for the second reaction
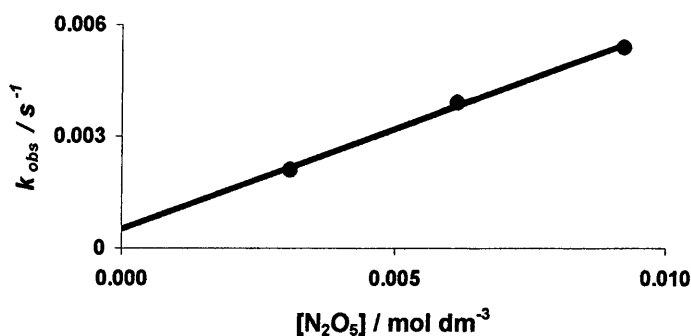
Figure 4.9 Correlation between k_{obs} and concentration of N_2O_5 for the nitration of 2-chlorophenol with N_2O_5 in PP6 for the second reaction

It can be seen that there is a good correlation between k_{obs} and concentration of N_2O_5 (**Figure 4.9**), therefore we can express the rate equation as first order in N_2O_5, with k_2 equal to 0.6 ± 0.1 s^{-1} mol^{-1} dm^3 for the second reaction.

The results indicate that the nitration of 2-chlorophenol in PP6 is first order in N_2O_5 and involves two processes. It was necessary to carry out a synthetic experiment to check the nature of the product, i.e. the position of nitration.

4.5.1 Synthetic experiment for the nitration of 2-chlorophenol

A solution of N_2O_5 in PP6 (0.04 mol dm^{-3}) was allowed the react with 2-chlorophenol (9 mmol dm^{-3}) in PP6 at ambient temperature and with stirring. An aliquot was taken after 20 seconds, distilled water was added and the solid was collected by filtration. The remainder of the reaction was stirred for 20 minutes.

The composition of the sample removed after 20 seconds, based on the integral ratio from the ^1H NMR spectrum, was 30 % 2-chloro-6-nitrophenol and 70 % 2-chloro-4,6-dinitrophenol. The product after 20 minutes contained 100 % 2-chloro-4,6-dinitrophenol.

Hence the two reactions followed kinetically are likely to be mononitration to give the 2-chloro-6-nitrophenol (**58**) followed by dinitration to give 2-chloro-4,6-dinitrophenol (**59**), **Scheme 4.2**.

(**58**)   (**59**)
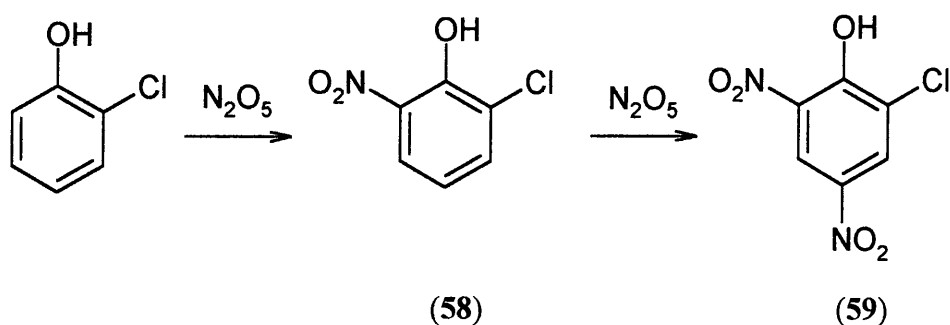
Scheme 4.2 Nitration of 2-chlorophenol using N_2O_5

4.6 4-Chlorophenol (60)

(**60**)
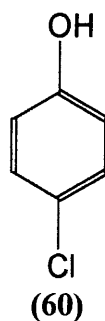
The UV/Vis spectrum of 4-chlorophenol (**60**), were recorded before (blue) and after (red) the addition of N_2O_5 in PP6 (**Figure 4.10**).
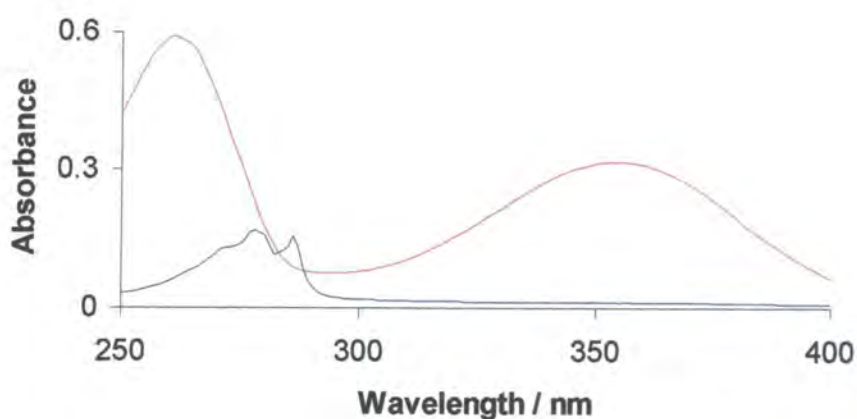
Figure 4.10 UV/VIS spectrum for 4-chlorophenol with and without N_2O_5 in PP6 at 25 °C

The change in absorbance with time was measured at 354 nm for solutions of 4-chlorophenol in PP6 containing various concentrations of N_2O_5.
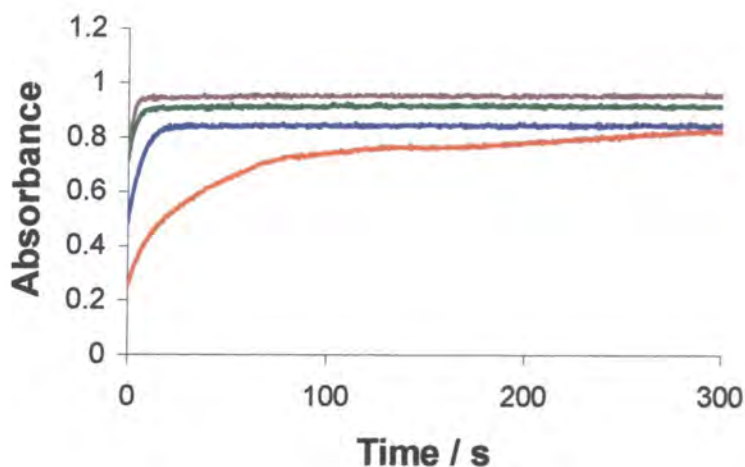

Figure 4.11 Reaction profile for the nitration of 4-chlorophenol using N_2O_5

The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.6**).

| [4-chlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /$dm^3mol^{-1}s^{-1}$
	0.00098	0.052	53
4.40	0.00196	0.105	54
	0.00392	0.219	56
	0.00588	0.340	58

Table 4.6 k_{obs} values for the nitration of 4-chlorophenol using N$_2$O$_5$ in PP6 at 25 °C

It can be seen that there was a good correlation between k_{obs} and concentration of N$_2$O$_5$ (**Table 4.6**), therefore we can express the rate equation as first order in N$_2$O$_5$, with k_2 equal to 55 ± 2 s^{-1} mol^{-1} dm^3. In view of the high value obtained for k_2 it was necessary to perform a synthetic experiment to check the nature of the product, i.e. the position of nitration.

## 4.6.1 Synthetic experiment for the nitration of 4-chlorophenol

A solution of N$_2$O$_5$ in PP6 was added to a solution of 4-chlorophenol in PP6 at ambient temperature and left to stir for 10 minutes. The concentrations were 0.03 mol dm^{-3} and 0.007 mol dm^{-3} respectively. On addition of distilled water to the solution a solid was formed which was collected by filtration.

The composition of the sample based on the ^{1}H NMR spectrum was 100 % 4-chloro-2-nitrophenol, (**Scheme 4.3**).
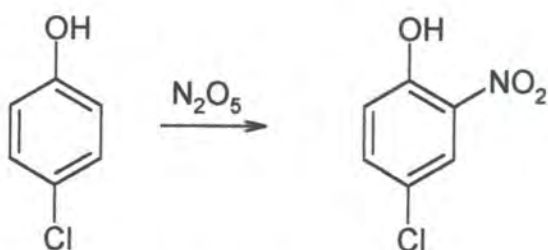
Scheme 4.3 Nitration of 4-chlorophenol using N_2O_5

4.7 2,4-Dichlorophenol (61)

(61)
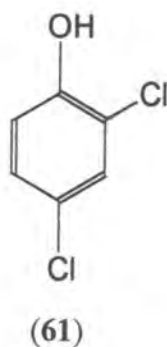
The UV/Vis spectrum of 2,4-dichlorophenol (61) in PP6 was recorded before (blue) and after (red) the addition of N_2O_5 in PP6 (**Figure 4.12**).
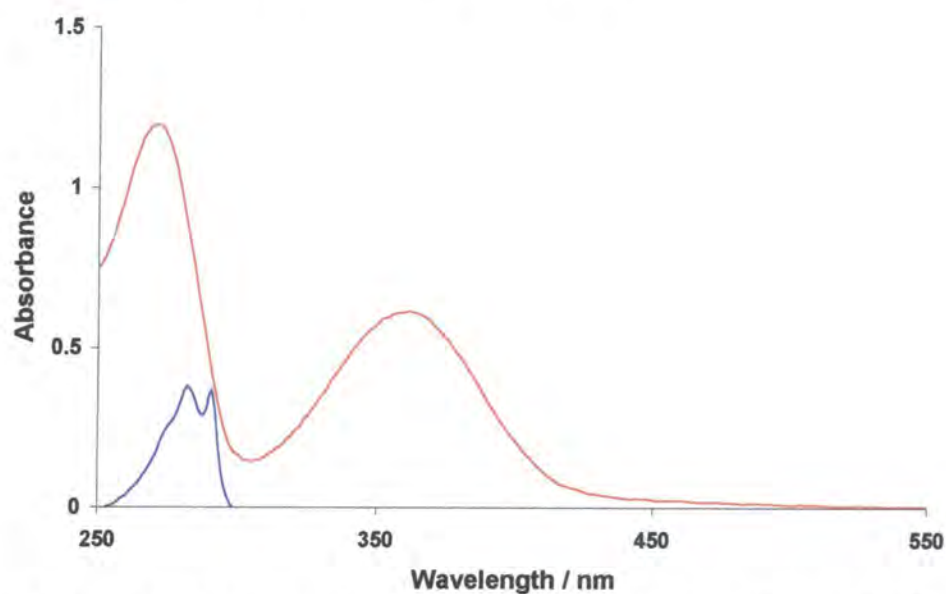

Figure 4.12 UV/Vis spectrum for 2,4-dichlorophenol with and without N_2O_5 in PP6 at 25°C

The change in absorbance over time was measured at 360 nm for solutions of 2,4-dichlorophenol in PP6 containing various concentrations of N_2O_5, (**Figure 4.13**).
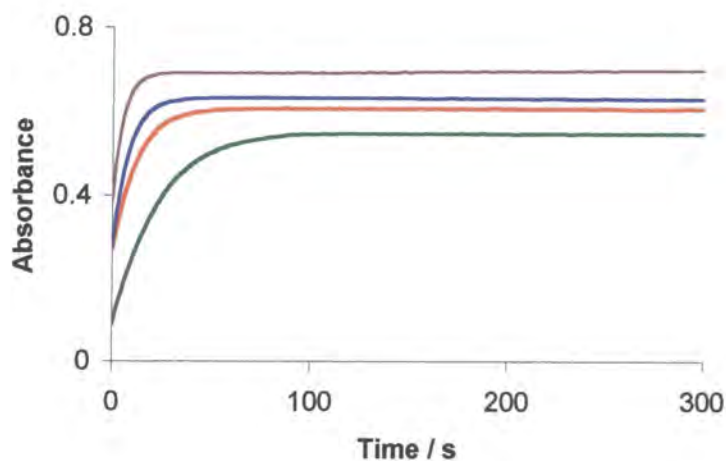

Figure 4.13 Reaction profile for the nitration of 2,4-dichlorophenol using N_2O_5

The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.7**).

[2,4-dichlorophenol] / 10^{-4} mol dm^{-3}	[N_2O_5] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /$dm^3mol^{-1}s^{-1}$
	0.0015	0.046	29
	0.0031	0.072	23
1.78	0.0062	0.115	19
	0.0092	0.165	18

Table 4.7 k_{obs} values for the nitration of 2,4-dichlorophenol using N_2O_5 in PP6 at 25 °C
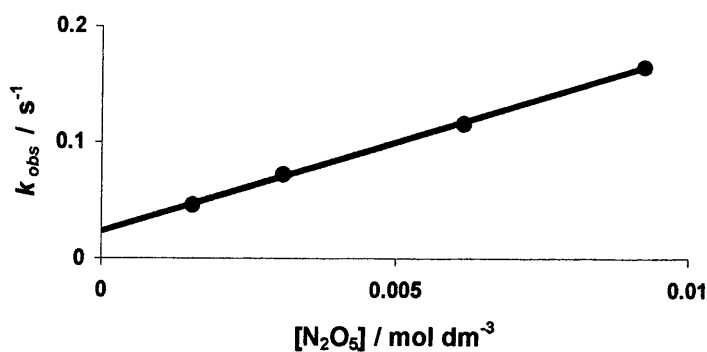
Figure 4.14 Correlation between k_{obs} and concentration of N_2O_5 for the nitration of 2,4-dichlorophenol with N_2O_5 in PP6

It can be seen that there is a reasonable correlation between k_{obs} and concentration of N_2O_5 (**Figure 4.14**). Therefore we can express the rate equation as first order in N_2O_5, with k_2 equal to 22 ± 7 s^{-1} mol^{-1} dm^3. The product from the nitration is most likely to be 2,4-dichloro-6-nitrophenol.

4.8 2,6-Dichlorophenol (62)
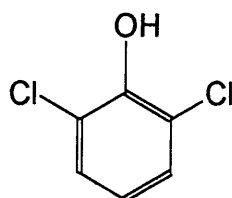
(62)

The UV/Vis spectrum of 2,6-dichlorophenol in PP6 was recorded before (blue) and after (red) the addition of N_2O_5 in PP6 (**Figure 4.15**).
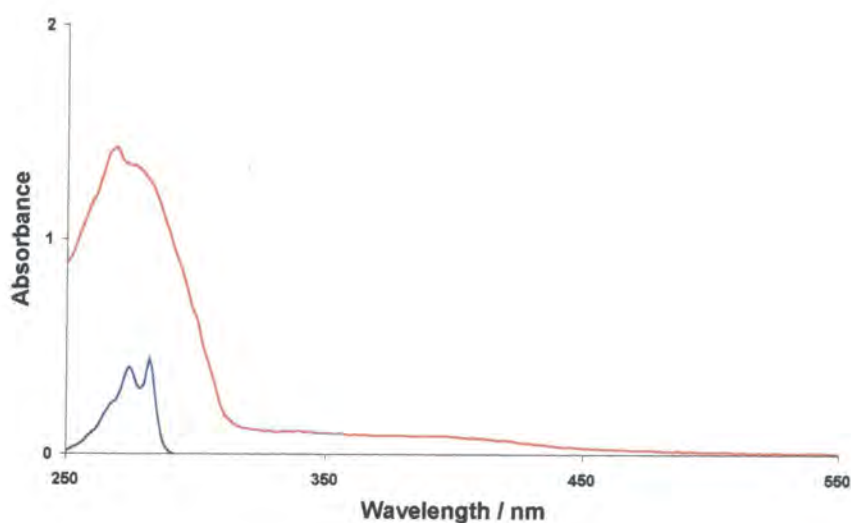
Figure 4.15 UV/Vis spectrum for 2,6-dichlorophenol with and without N_2O_5 in PP6 at 25°C

The change in absorbance with time was measured at 274 nm for solutions of 2,6-dichlorophenol in PP6 containing various concentrations of N_2O_5.
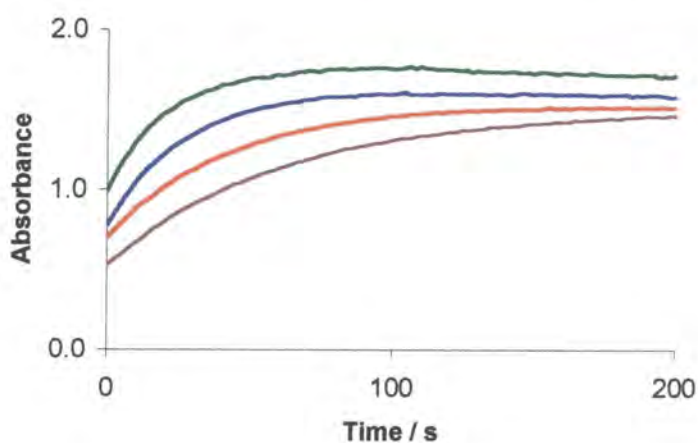

Figure 4.16 Reaction profile for the nitration of 2-6-dichlorophenol using N_2O_5
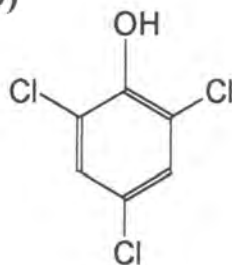
The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.8**).

[2,6-dichlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\frac{k}{[N_2O_5]}$ / $dm^3 mol^{-1} s^{-1}$
	0.0015	0.017	11
1.86	0.0031	0.032	10
	0.0062	0.050	8

Table 4.8 k_{obs} values for the nitration of 2,6-dichlorophenol using N$_2$O$_5$ in PP6 at 25 °C

It can be seen that there is a good correlation between k_{obs} and concentration of N$_2$O$_5$ (**Table 4.8**). Therefore we can express the rate equation as first order in N$_2$O$_5$, with k_2 equal to 10 ± 2 s^{-1} mol^{-1} dm^3. The product from the nitration is most likely to be 2,6-dichloro-4-nitrophenol.

4.9 2,4,6-Trichlorophenol (63)

(63)

The UV/Vis spectrum of 2,4,6-trichlorophenol (**63**) in PP6, was recorded before (blue) and after (red 1 minute, green 2 minutes, turquoise 5 minutes, pink 10 minutes) the addition of N$_2$O$_5$ in PP6 (**Figure 4.17**).
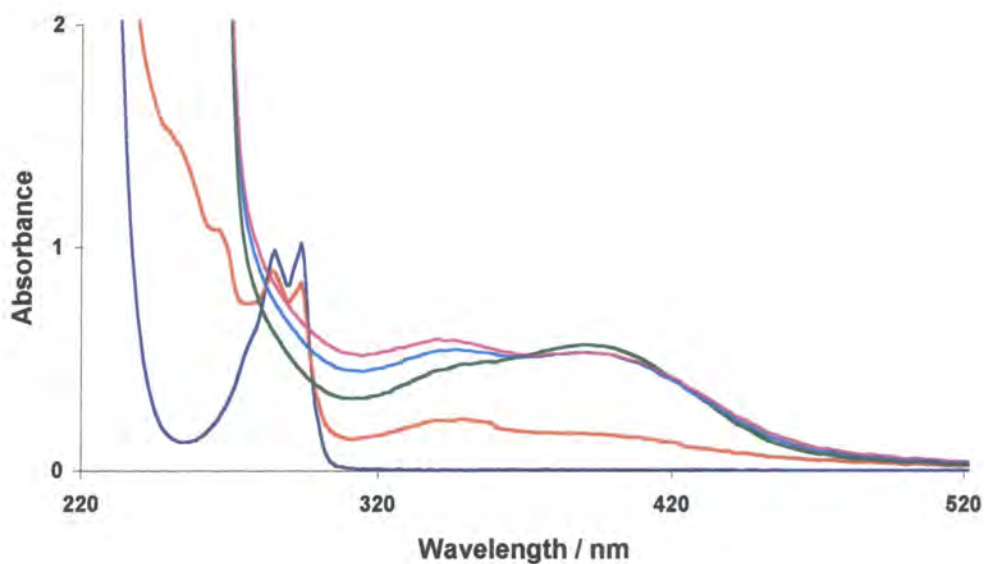
Figure 4.17 UV/Vis spectrum for 2,4,6-trichlorophenol with and without N_2O_5 in PP6 at 25°C

The change in absorbance with time was measured at 389 nm for solutions of 2,4,6-trichlorophenol in PP6 containing various concentrations of N_2O_5.
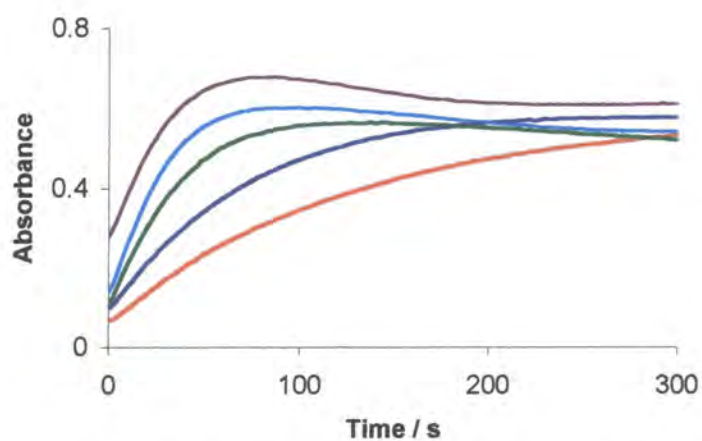

Figure 4.18 Reaction profile for the nitration of 2,4,6-trichlorophenol using N_2O_5

The observed rate constants (k_{obs}) were determined and divided by the concentrations of N_2O_5, (**Table 4.9**).

[2,4,6-trichlorophenol] / 10^{-4} mol dm^{-3}	[N_2O_5] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ / $dm^3 mol^{-1} s^{-1}$
	0.0019	0.0069	3.7
	0.0037	0.0126	3.4
3.90	0.0075	0.0254	3.4
	0.0112	0.0351	3.1
	0.0149	0.0401	2.7

Table 4.9 k_{obs} values for the nitration of 2,4,6-trichlorophenol using N_2O_5 in PP6 at 25 °C
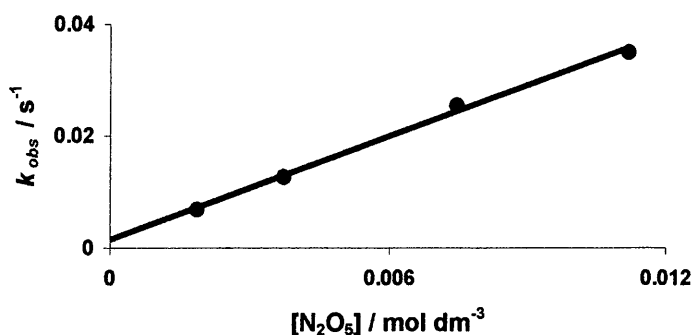
Figure 4.19 Correlation between k_{obs} and concentration of N_2O_5 for the nitration of 2,4,6-trichlorophenol with N_2O_5 in PP6

It can be seen that there is a good correlation between k_{obs} and concentration of N_2O_5 (**Figure 4.19**). Therefore we can express the rate equation as first order in N_2O_5, with k_2 equal to 3.3 ± 0.3 s^{-1} mol^{-1} dm^3

The reaction profile (**Figure 4.18**) indicates the possibility of more than one nitration step. Therefore a synthetic experiment was performed to check the nature of the product.

4.9.1 Synthetic experiment for the nitration of 2,4,6-trichlorophenol

A solution of N_2O_5 in PP6 was added to a solution of 2,4,6-trichlorophenol in PP6 at ambient temperature and left to stir for 1 hour. The concentrations in the mixture were 0.04 mol dm^{-3} and 0.08 mol dm^{-3} respectively. The solvents were allowed to evaporate, resulting in a yellow solid.

Mass spectroscopy indicated that the product was mono nitrated trichlorophenol, (**Figure 4.20**).
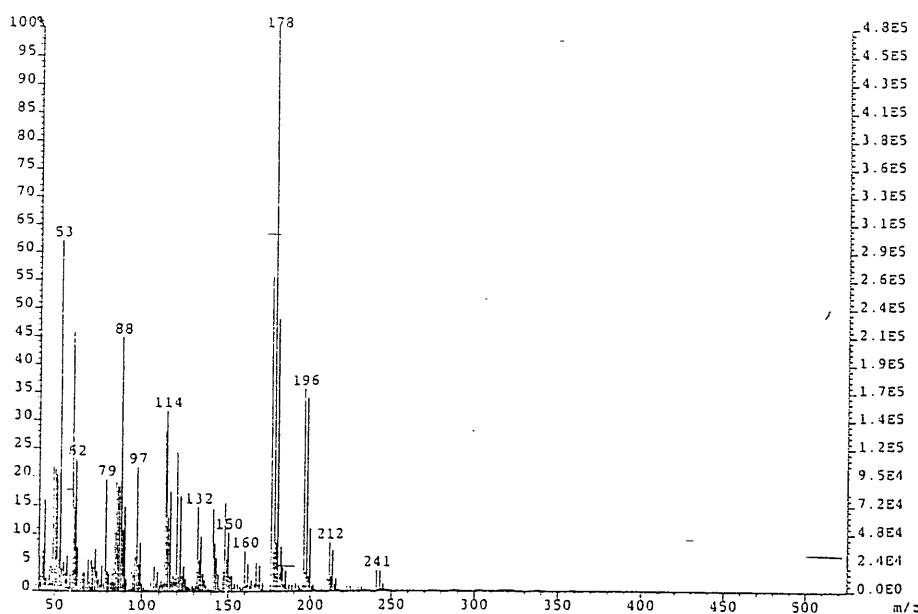
Figure 4.20 EI mass spectrum for nitrated 2,4,6-trichlorophenol using N_2O_5 in PP6 at 25 °C (m/z for mono nitrated trichlorophenol is 241)
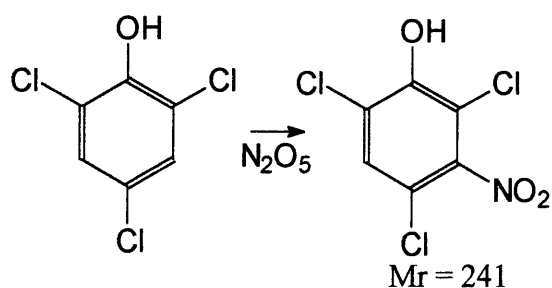
Scheme 4.4 Nitration of 2,4,6-trichlorophenol using N_2O_5

It was concluded that the kinetics were unlikely to involve dinitration because the synthetic experiment showed no evidence of dinitration. The reaction followed was most likely to be the nitration of 2,4,6-trichlorophenol giving 2,4,6-trichloro-3-nitrophenol, (**Scheme 4.4**).

4.10 4-Bromophenol (64)

(64)
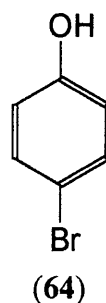
The UV/Vis spectra of 4-bromophenol (**64**) in PP6 were recorded before (blue) and after (red) the addition of N_2O_5 in PP6, (**Figure 4.21**).
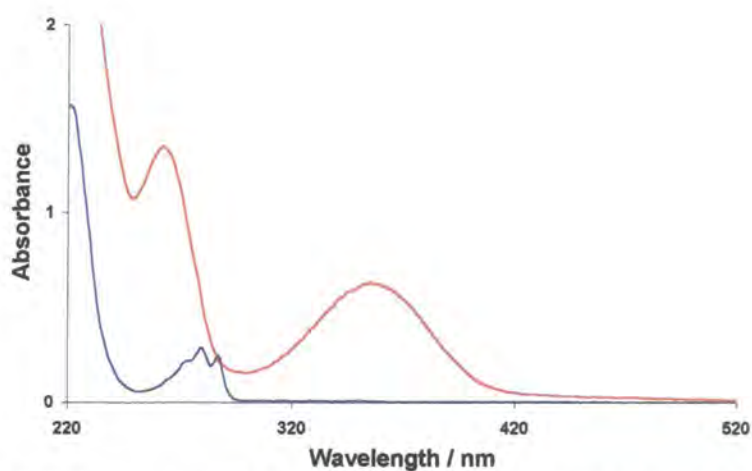
Figure 4.21 UV/Vis spectrum for 4-bromophenol with and without N_2O_5 in PP6 at 25°C

The change in absorbance with time was measured at 354 nm for solutions of 4-bromophenol in PP6 containing various concentrations of N_2O_5. The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.10**).

[4-bromophenol] /10^{-4} mol dm^{-3}	$[N_2O_5]$ / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /dm^{3}mol^{-1}s^{-1}
	0.0019	0.12	65
	0.0032	0.21	65
1.84	0.0048	0.29	62
	0.0064	0.39	61

Table 4.10 k_{obs} values for the nitration of 4-bromophenol using N_2O_5 in PP6 at 25 °C
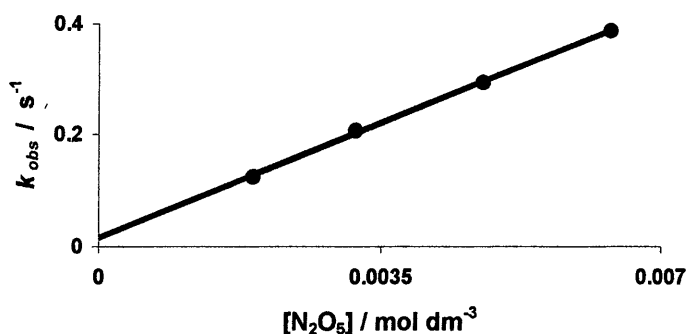
Figure 4.22 Correlation between k_{obs} and concentration of N_2O_5 for the nitration of 4-bromophenol with N_2O_5 in PP6

It can be seen that there is a good correlation between k_{obs} and concentration of N_2O_5 (**Figure 4.22**). Therefore we can express the rate equation as first order in N_2O_5, with k_2 equal to 63 ± 2 s^{-1} mol^{-1} dm^3. It is necessary to carry out a synthetic experiment to check the nature of the product, i.e. the position of nitration.

4.10.1 Synthetic experiment for the nitration of 4-bromophenol

A solution of N_2O_5 in PP6 was added to a solution of 4-bromophenol in PP6 at room temperature and was allowed to stir for 1 minute. The concentrations were 0.03 mol dm^{-3} and 0.04 mol dm^{-3} respectively. ^{1}H NMR analysis indicated that the sole product was 4-bromo-2-nitrophenol. Hence the reaction followed kinetically is likely to be mononitration to give the 4-bromo-2-nitrophenol, (**Scheme 4.5**).
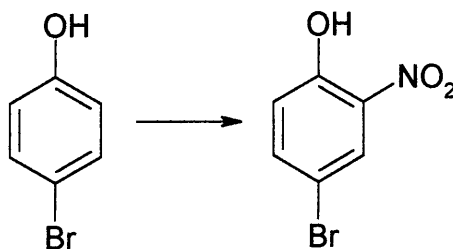
Scheme 4.5 Nitration of 4-bromophenol using N_2O_5

4.11 Attempted kinetic measurements on substrates

It was hoped to make kinetic measurements on the following substrates (2-chloroanisole (**65**), 3-chloroanisole (**66**), benzoic acid (**67**) and bromophenylether (**68**)). However reaction with N_2O_5 in PP6 resulted in little change in UV/Vis spectrum so that spectrophotometric measurements were not possible.

(65)   (66)   (67)   (68)
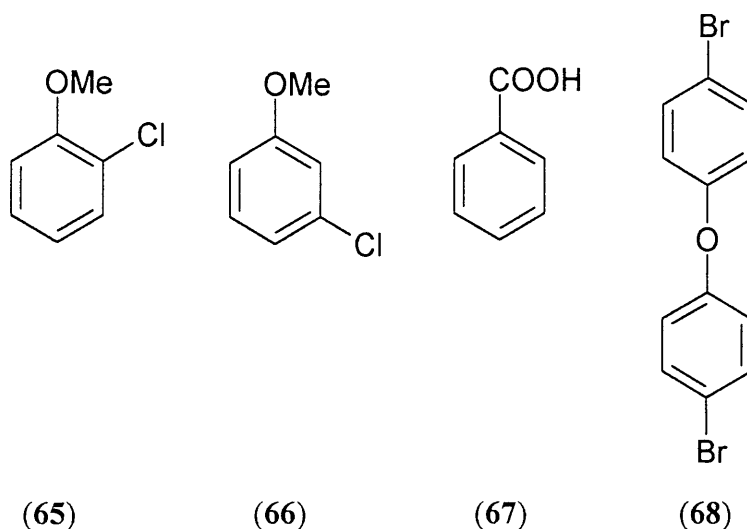
Phenol (69)

(69)
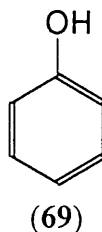
The rate of nitration of phenol was too fast to measure kinetically, λ_{max} of the product formed was 335 nm. The UV/Visible spectra for 4-nitrophenol ($\lambda_{max} = 311$ nm in methanol) and 2,4-dinitrophenol ($\lambda_{max} = 292$ nm in methanol) did not correspond to the product formed in the nitration of phenol. A synthetic experiment was carried out to check the nature of the product, i.e. the position of nitration.

The solution of N_2O_5 in PP6 was added to a solution of phenol in PP6 at ambient temperature and left to stir for 10 minutes. On the addition of distilled water to the solution a solid formed and was filtered. ^1H NMR spectroscopy was used to determine the

composition of the product. The experiment was carried out twice using various molar equivalents of N_2O_5 shown in **Table 4.11.**

PFC	Nitrating agent	ME of N_2O_5	Reaction time	Temp /°C	% Yield	Product
PP6	N_2O_5	3	10 minutes	Ambient		2,4-DNP (24 %) 4-NP (24 %) 2,6-DNP (8 %) 2,4,6-TNP (44 %)
PFE	N_2O_5	7	2 hours	Ambient	97	2,4,6-TNP (100 %)

Where 2,4-DNP is 2,4-dinitrophenol, 4-NP is 4-nitrophenol, 2,6-DNP is 2,6-dinitrophenol and 2,4,6-TNP is 2,4,6-trinitrophenol. ME is molar equivalent.

Table 4.11 Reactions of phenol with N_2O_5

Figure 4.23 ^{1}H NMR of 2,4,6-trinitrophenol
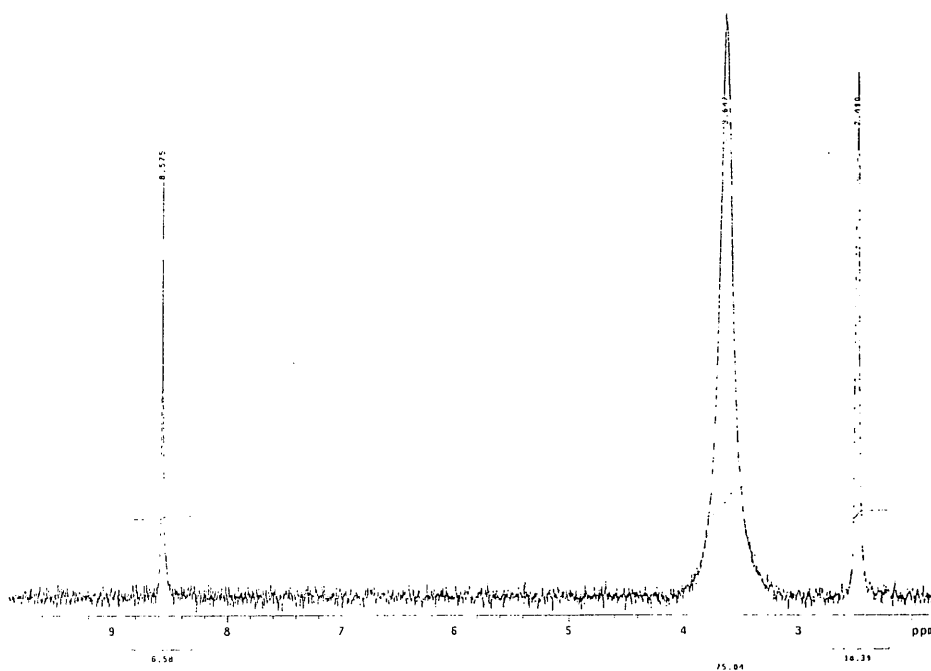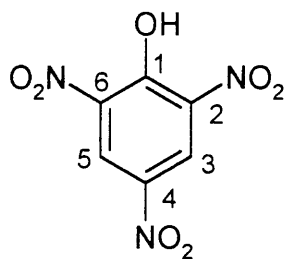

(**70**)

The ^{1}H NMR spectrum, **Figure 4.23** shows the signals due to the spectrum of the product for the reaction of phenol with seven molar equivalents of N_2O_5. The singlet at δ 8.575 ppm corresponds to protons in positions 3 and 5 in 2,4,6-trinitrophenol (**70**). Therefore it was concluded that the trinitration of phenol is easily achieved using this system.

Chlorobenzene (71)

Cl
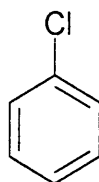
(71)

The UV/Vis spectrum was recorded of chlorobenzene (71) before and after the addition of N_2O_5. The spectrum of chlorobenzene did not change on the addition of N_2O_5 and it was thought this could be because chlorobenzene had not been nitrated with the N_2O_5. It was necessary to check this prediction by a synthetic experiment.

A solution of N_2O_5 in PP6 was added to a solution of chlorobenzene in PP6 at ambient temperature and was allowed to stir for 1 hour. Concentrations were 0.03 mol dm^{-3} and 0.08 mol dm^{-3} respectively. When distilled water was added to the reaction mixture no solid was formed; the water was removed under vacuum but nothing remained. The PP6 layer was also allowed to evaporate but nothing remained. It is unlikely that chloronitrobenzene will be sufficiently volatile to vaporise under these conditions. However chlorobenzene (B.pt. 132 °C) may have been lost by evaporation. Therefore it was concluded that chlorobenzene cannot be successfully nitrated by N_2O_5 under these conditions.

4.12 Kinetic isotope effect[2]

In order to determine more information about the mechanism involved in the nitration of chlorophenols with N_2O_5 the kinetic isotope effect was measured.

4.12.1 Synthesis of deuterated 4-chlorophenol[3,4,5]

Ring penta-deuterated phenol is commercially available. Before attempting experiments with this compound measurements were made with phenol.

Phenol was dissolved in acetic acid and the solution was cooled in an ice bath. Chlorine gas was bubbled through the solution and the weight increase was determined. Several experiments were performed and in each case chlorinated phenols were isolated by allowing the solvent to evaporate. It was found that trichlorination could be readily be achieved under these conditions, **Scheme 4.6**.
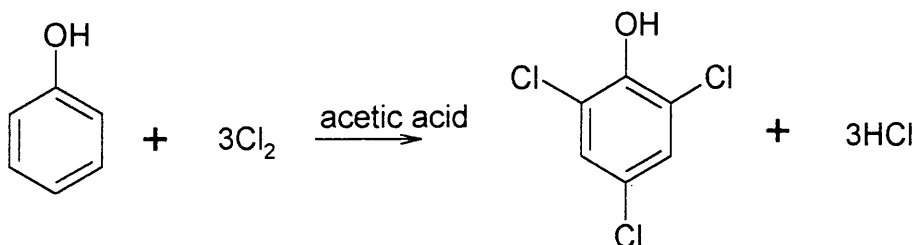
Scheme 4.6 Trichlorination of phenol

However reaction with one equivalent of chlorine gave the monochlorinated derivative.

The experiment was repeated using deuterated phenol. Once the required weight increase had occurred the acetic acid was evaporated to give the chlorinated product. The composition of the product was determined using GC mass spectroscopy. Results are shown in **Figure 4.24** and **Table 4.12.** The chromatogram shows a major peak at 630s with smaller peaks at 606, 636 and 775s. The major peak was identified by mass spectroscopy as

monochlorophenol (87 %) and the impurities were two isomeric dichlorophenols (12 %) and trichlorophenol (0.7 %).

Use of ^{13}C NMR spectroscopy identified the major product as 4-chlorophenol. The spectrum in **Figure 4.25** shows bands at δ 153.4, 116.8, 130.1, and 127.6 ppm. These positions are close to those calculated using substituent effects. [6]

For the carbons of the 1, 2 and 6, 3 and 5, and 4 positions of 4-chlorophenol. The bands of δ 116.8 and 130.1 are triplets, J ≈ 25 Hz, as expected for carbon atoms adjacent to deuterium atoms. [7]

It was therefore concluded that the major product of the reaction is 4-chlorophenol deuterated at the 2, 3, 5 and 6 positions as shown in **Scheme 4.7**.
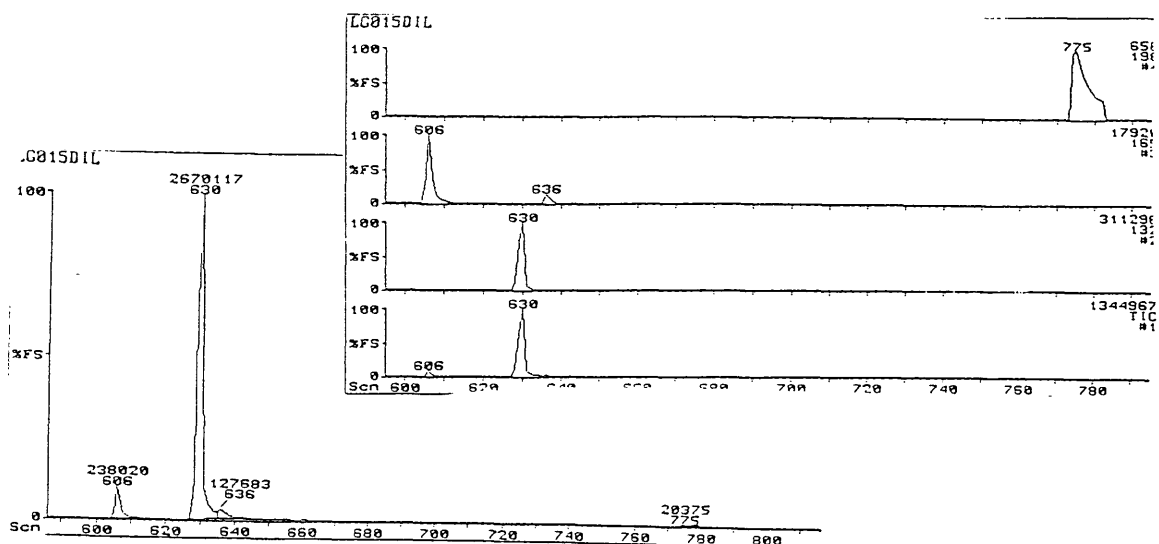
Figure 4.24 GC mass spectrum of deuterated chlorophenol

Peak	Mr/g	Compound	Amount	%
606	165	DCP	238020	7.8
630	132	MCP	2670117	87.4
636	165	DCP	127683	4.2
775	198	TCP	20375	0.67

Table 4.12 Peaks and assignments of molecular mass and % composition from **Figure 4.24**
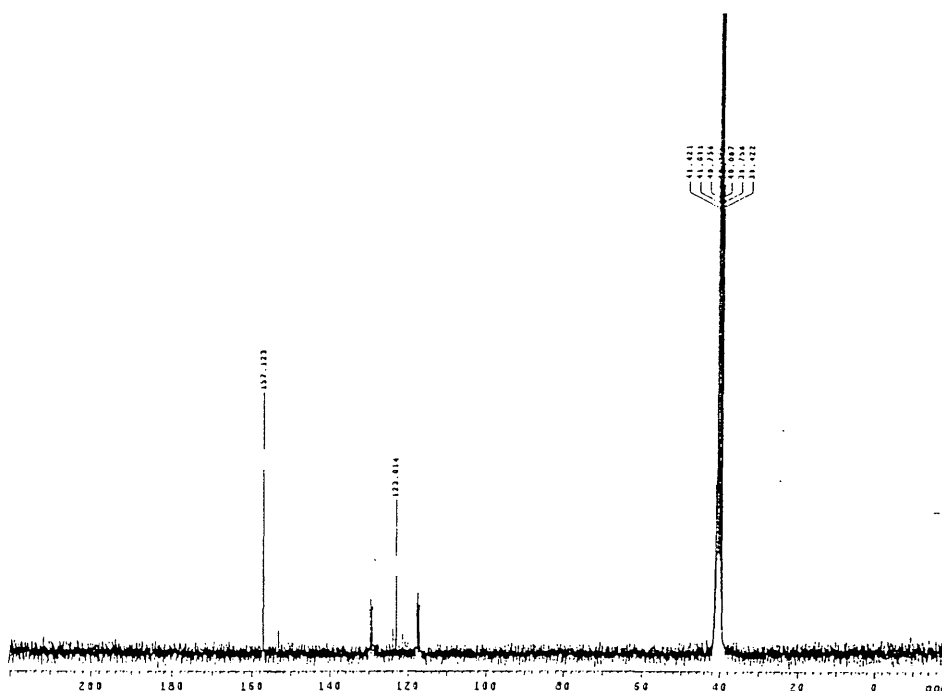
Figure 4.25 ^{13}C NMR of deuterated chlorophenol
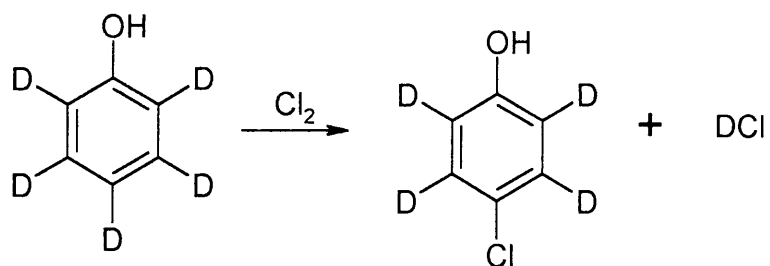
Scheme 4.7 Chlorination of deuterated phenol

The next step was to determine the kinetics on the deuterated sample and compare them to the kinetics for 4-chlorophenol (**Section 4.6**).

4.12.2 Kinetics of deuterated 4-chlorophenol (72)

(**72**)
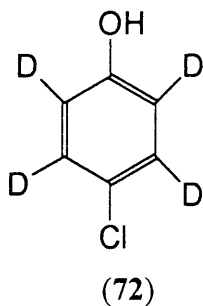
The absorbance of deuterated 4-chlorophenol (**72**), with the addition of various concentrations of N_2O_5 in PP6, was measured with time at 354nm (**Figure 4.26**).
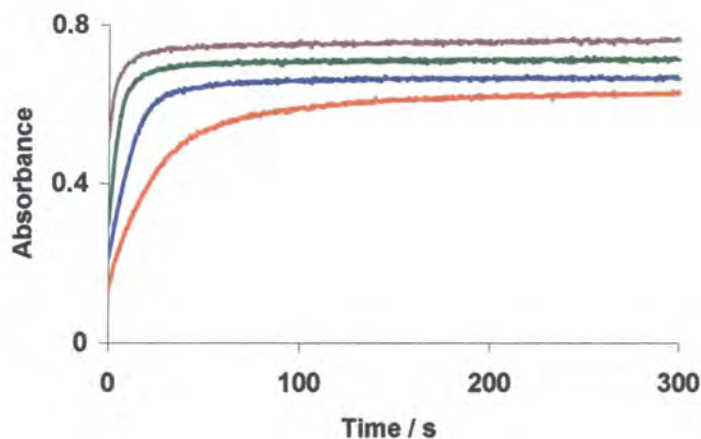
Figure 4.26 Reaction profile for the nitration of deuterated 4-chlorophenol using N_2O_5

The observed rate constants (k_{obs}) were determined and were divided by the concentrations of N_2O_5, (**Table 4.13**).

[4-chlorophenol$_{d4}$] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /dm^{3}mol^{-1}s^{-1}
	0.00098	0.04	40
4.40	0.0020	0.08	41
	0.0039	0.17	44
	0.0059	0.24	41

Table 4.13 k_{obs} values for the nitration of deuterated 4-chlorophenol using N_2O_5 in PP6 at 25°C
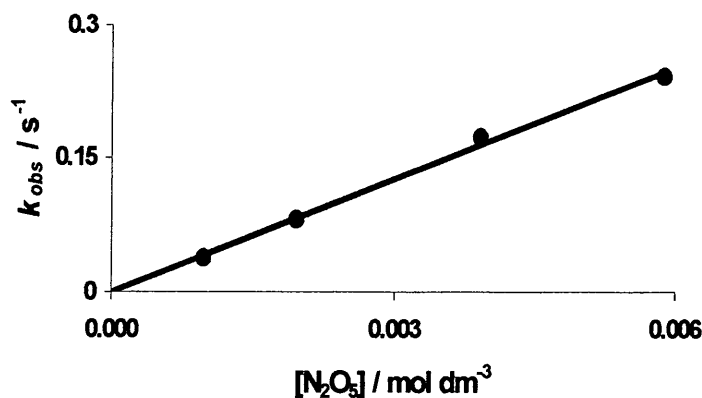
Figure 4.27 Correlation between k_{obs} and concentration of N_2O_5 for the nitration of deuterated 4-chlorophenol with N_2O_5 in PP6

It can be seen that there is a good correlation between k_{obs} and concentration of N_2O_5, (**Figure 4.27**), indicating a first order dependence on N_2O_5, with k_2 value of 42 ± 3 s^{-1} mol^{-1} dm^3. Kinetic results have already been established for 4-chlorophenol giving a k_2 value of 55 ± 2 s^{-1} mol^{-1} dm^3.

What is the kinetic isotope effect?

During nitration a nitro group is introduced on carbon at the expense of ring-hydrogen. It is unlikely that proton loss precedes reaction with the nitro-group since this would involve a carbanion intermediate.[8] Likely pathways are:

1. Synchronous C-N formation and C-H breaking,

2. Reaction via an intermediate with:
   (a) Rate determining formation of the C-N bond and rapid loss of a proton,
   (b) Rapid formation of the C-N bond followed by rate determining proton loss.

The value of the kinetic isotope effect, k_H/k_D, allows a distinction to be made between 2(a) and 2 (b). If a value of $k_H/k_D \approx 1$ is observed then proton transfer is not involved in the rate determining step, corresponding to case 2 (a). Conversely a value of $k_H/k_D \approx 7$ correponds to case 2 (b).

In case 1, the synchronous mechanism, some C-H bond breaking occurs in the rate determining step so that a value of $k_H/k_D > 1$ is to be expected.

The result obtained for k_H/k_D for 4-chlorophenol was 1.3. Therefore it can be concluded that the reaction must occur by a slow rate determining step involving the formation of the bond between the nitro group and the aromatic ring, automatically followed by the loss of a proton.

4.13 Nitration via nitrosation

Nitration via nitrosation has already been discussed previously in chapter one. It was noted that for the reaction of 4-chloroanisole (**Scheme 4.8**) and 4-nitrophenol (**Scheme 4.9**) with nitric acid in acetic acid, nitration was accelerated in the presence of nitrous acid. With 4-chloroanisole there was evidence for nitration both by nitric and nitrous acids. However, with phenols the nitrous acid pathway was dominant.[9]
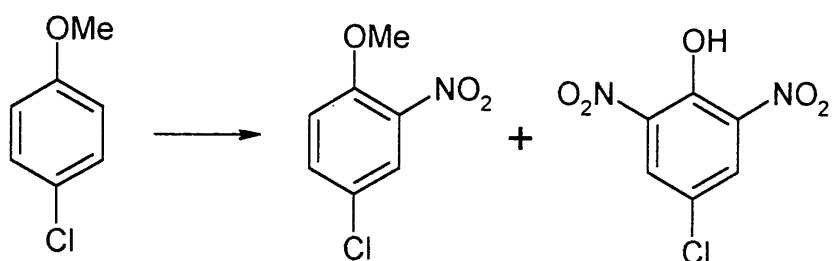
Scheme 4.8 Reaction of 4-chloroanisole with nitric acid (4-10 Molar) in acetic acid at −15 to +35 °C. Ratio of products approximately 2:1 respectively
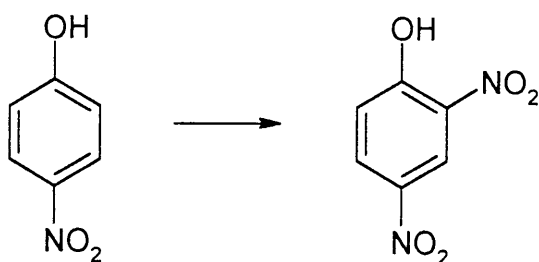
Scheme 4.9 Reaction of 4-nitrophenol with nitric acid (1.4-6 Molar) in acetic acid at 20°C

It was decided to investigate the possibility that nitration via nitrosation may be involved in the mechanism of the nitration using N_2O_5 in PP6. Urea (**73**)[10] and penicillamine (**74**) have been reported as nitrous acid traps. Therefore, if nitration via nitrosation were involved in the mechanism adding these reagents would be expected to affect the rate of reaction.

(**73**)   (**74**)
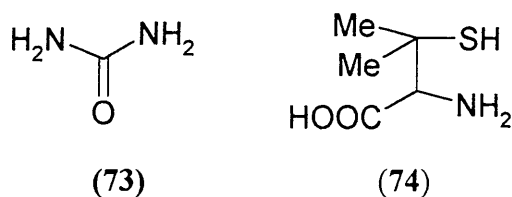
A saturated urea solution (1 cm^3, 3 mmol dm^{-3}) was added to a solution of 2-chlorophenol in PP6 (2 cm^3, 0.45 mmol dm^{-3}). On the addition of a solution of N_2O_5 in PP6 (20 µl, 1.155 mol dm^{-3}) the absorbance was measured with time at 342nm and k_{obs} was calculated for a sample with and without urea, **Table 4.14**. In this reaction two processes are involved. The results show that values of k_{obs} are little changed by the presence of urea.

	k_{obs} / s^{-1}	
	1st	2nd
without urea	0.060	0.0038
with urea	0.085	0.0029

Table 4.14 k_{obs} for the nitration of 2-chlorophenol in the presence of urea and without urea in PP6 at 25 °C

The experiment was repeated using penicillamine. A saturated penicillamine solution (1 cm^3, unknown concentration) was added to a solution of 2-chlorophenol in PP6 (2 cm^3, 0.45 mmol dm^{-3}). On the addition of a solution of N$_2$O$_5$ in PP6 (20 μl, 1.155 moldm^{-3}) the absorbance was measured with time at 342 nm and k_{obs} was calculated for a sample with and without penicillamine, (**Table 4.15**).

	k_{obs} / s^{-1}	
	1st	2nd
without penicillamine	0.08	0.0025
with penicillamine	0.10	0.0026

Table 4.15 k_{obs} for the nitration of 2-chlorophenol in the presence of penicillamine and without penicillamine in PP6 at 25 °C

The observed first order rate constants with and without a nitrous acid trap are the same within experimental error. This shows that nitrous acid does not affect the rate of reaction and therefore the mechanism does not involve nitration via nitrosation.

4.14 Radical mechanism

Another possibility is that the mechanism could involve radical intermediates. This has been discussed previously in chapter one. Free radical nitrations can occur via nitrogen oxides present in dilute nitric acid and are promoted by raising the temperature.[11] Dinitrogen pentoxide dissociates to radicals homolytically, (**Scheme 4.10**).

$$N_2O_5 \rightleftharpoons NO_2^{\cdot} + NO_3^{\cdot}$$
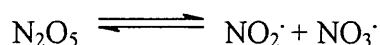
Scheme 4.10 N$_2$O$_5$ dissociates to radicals with heat in CCl$_4$

The first step in the radical mechanism was suggested as the attack of the aromatic by the nitrate radical, to form an aromatic nitrate radical, which could be susceptible to hydrolysis and could be converted to phenol (**Scheme 4.11**), which can easily convert to nitro phenols, sometimes as the main reaction products. [12]
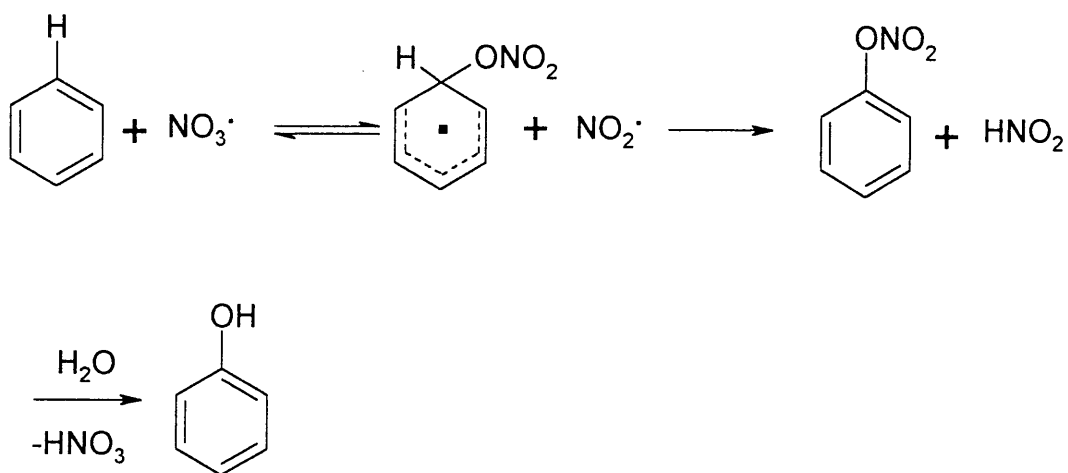
Scheme 4.11 Free radical nitration using dinitrogen pentoxide giving phenol

The mechanism of *p*-dinitrobenzene formation during nitration of benzene can be seen in **Scheme 4.12**. The product of $NO_3^{\bullet}$ addition to benzene by the action of N_2O_5 results in either directly, or through an intermediate reaction with $NO_2^{\bullet}$ addition to oxygen, to dinitrate. This with $NO_2^{\bullet}$ results in a derivative of cyclohexane and subsequent reactions of HNO_3 converts it into *p*-dinitrobenzene.
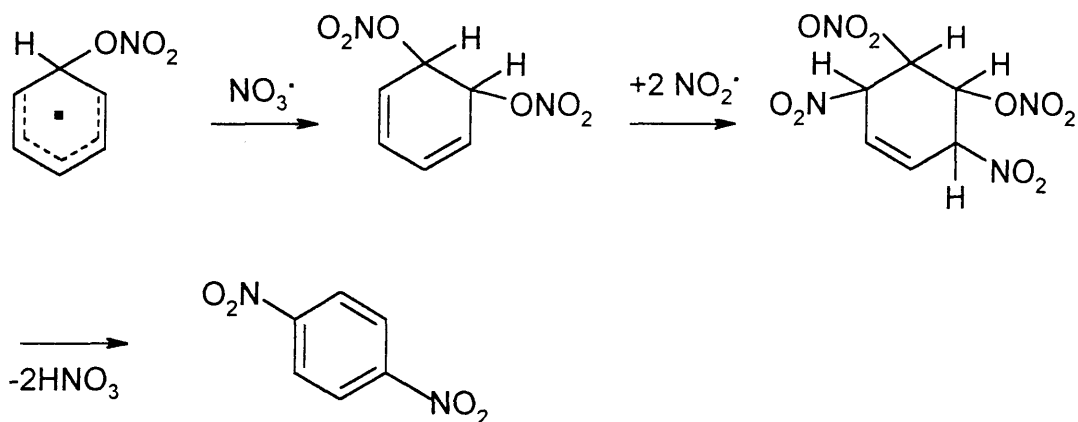
Scheme 4.12 Free radical nitration using dinitrogen pentoxide giving *p*-dinitrobenzene

Using 1,3-dinitrobenzene as a radical trap

1,3-Dinitrobenzene is a powerful electron acceptor and hence might be expected to react readily with radical species present in a nitration pathway. Hence experiments were carried out to see whether the presence of dinitrobenzene affected the kinetics.

A saturated 1,3-dinitrobenzene solution (1 cm^3, unknown concentration) in PP6 was added to a solution of 2,4-dichlorophenol in PP6 (2 cm^3, 0.31 mmol dm^{-3}). On the addition of a solution of N$_2$O$_5$ in PP6 (10 μl, 20μ l, 30 μl, of 1.02 moldm^{-3}) the absorbance was measured with time at 342 nm and k_{obs} was calculated for a sample with (**Table 4.16**) and without (**Table 4.17**) the presence of 1,3-dinitrobenzene.

[2,4-dichlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /dm^{3}mol^{-1}s^{-1}
	0.0034	0.094	28
2.1	0.0068	0.16	24
	0.0102	0.20	19

Table 4.16 k_{obs} values for the nitration of 2,4-dichlorophenol with 1,3-dinitrobenzene using N$_2$O$_5$ in PP6 at 25 °C

[2,4-dichlorophenol] / 10^{-4} mol dm^{-3}	[N$_2$O$_5$] / mol dm^{-3}	k_{obs} / s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /dm^{3}mol^{-1}s^{-1}
	0.0034	0.09	27
2.1	0.0068	0.15	21
	0.0102	0.19	18

Table 4.17 k_{obs} values for the nitration of 2,4-dichlorophenol using N$_2$O$_5$ in PP6 at 25 °C

The results show that nitration of 2,4-dichlorophenol k_2 is 22 ± 5 s^{-1} mol^{-1} dm^3 and in the presence of 1,3-dinitrobenzene k_2 is 23 ± 5 s^{-1} mol^{-1} dm^3. Therefore we can conclude that 1,3-dinitrobenzene does not effect the nitration of chlorophenols using N$_2$O$_5$ in PP6 and the mechanism is unlikely to go via a radical intermediate.

4.15 Checking for decomposition of N$_2$O$_5$

N$_2$O$_5$ is known to decompose at high temperatures and in the presence of moisture.[13] Our kinetic results for the nitration of various chlorophenols had been recorded on different days using different solutions of N$_2$O$_5$ in PP6. Although the concentration of the N$_2$O$_5$ solution was measured and the solution was cooled it was necessary to check that decomposition of N$_2$O$_5$ was not affecting the results. The kinetics of the following

chlorophenols were measured in the same day using the same N_2O_5 solution. Only one kinetic run was taken for each compound.

Compound	[substrate] / 10^{-4} moldm^{-3}	[N_2O_5] / moldm^{-3}	k_{obs} /s^{-1}	$\dfrac{k_{obs}}{[N_2O_5]}$ /dm^{3}mol^{-1} (k_2)	Previous k_2 / dm^3 mol^{-1}
2,6-DCP	2.16	0.0061	0.05	9	10
2-CP	2.24	0.0061	0.08	13	14
2,4-DCP	1.90	0.0061	0.13	22	22
4-CP	1.50	0.0061	0.29	48	55

Where 2-CP is 2-chlorophenol, 4-CP is 4-chlorophenol, 2,4-DCP is 2,4-dichlorophenol and 2,6-DCP is 2,6-dichlorophenol

Table 4.18 k_{obs} values for the nitration of various chlorophenols using the same solution of N_2O_5 in PP6 at 25 °C

The results in **Table 4.18** show that the k_2 values from the same day kinetics show good correlation with previous results. Therefore it was concluded that decomposition of N_2O_5 did not greatly affect the results.

4.16 Nitration of chlorophenols with N_2O_5 in perfluoroether (HT 135)

$$CF_3 \!\!-\!\! \left[(O\!\!-\!\!\underset{\underset{CF_3}{|}}{CF}\!\!-\!\!CF_2)n\!\!-\!\!(O\!\!-\!\!CF_2)m \right]\!\!-\!\!O\!\!-\!\!CF_3$$

(32)
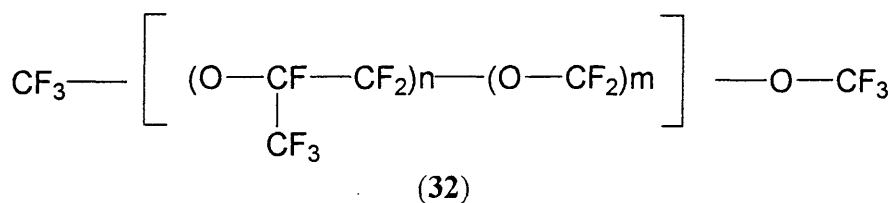
N_2O_5 dissolves in Perfluoroether (HT135) (32) resulting in a concentration of *ca* 1 mol dm^{-3}.

The kinetics of various chlorophenols was measured in perfluoroether (HT135), in order to compare the results to the previous results in the PP6 perfluorocarbon.

Compound	k_2 in PP6 / $dm^3\ mol^{-1}\ s^{-1}$	k_2 in perfluoroether / $dm^3\ mol^{-1}\ s^{-1}$
2CP	14 ± 2	17 ± 2
4CP	55 ± 2	45 ± 2
2,4DCP	22 ± 7	20 ± 4
2,6DCP	10 ± 2	8 ± 1

Where 2-CP is 2-chlorophenol, 4-CP is 4-chlorophenol, 2,4-DCP is 2,4-dichlorophenol and 2,6-DCP is 2,6-dichlorophenol

Table 4.19 Comparison of solvents when nitrating using N_2O_5

The k_2 values for chlorophenols in PP6 and perfluoroether only differ within experimental error. Therefore we can conclude that the change in solvent did not have an effect on the kinetics of the reactions studied.

4.17 Comparison of k_2 values
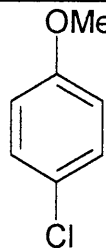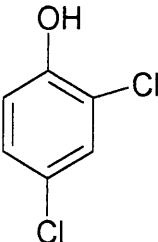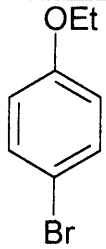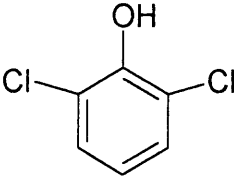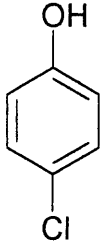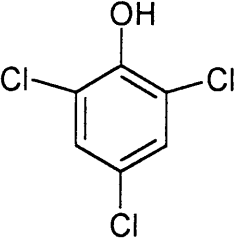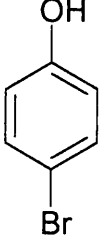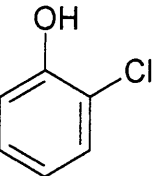
Structure	k_2 / dm^3 mol^{-1} s^{-1}	Structure	k_2 / dm^3 mol^{-1} s^{-1}
OMe / Cl (structure)	0.5 ± 0.2	OH / 2,4-dichloro (structure)	22 ± 7
OEt / Br (structure)	1.3 ± 0.3	OH / 2,6-dichloro (structure)	10 ± 2
OH / Cl (structure)	55 ± 2	OH / 2,4,6-trichloro (structure)	3.3 ± 0.3
OH / Br (structure)	63 ± 2	OH / 2-chloro (structure)	Fast reaction 14 ± 2 Slow reaction 0.6 ± 0.1

Table 4.20 Summary of the substrates that were nitrated using N_2O_5 in PP6 and the corresponding k_2 value

Results of synthetic experiments show that nitration occurs preferentially *ortho* to the hydroxy or alkoxy function. When this is blocked as in 2,6-dichlorophenol reaction occurs *para* to the hydroxy-group. Only in 2,4,6-trichlorophenol does the reaction occur *meta* to

the hydroxy function. This is in accord with the electronic effect expected for the hydroxy function. The data in **Table 4.21** show that the strong activation to electrophilic attack is expected from the para (and *ortho* position) while there is slight de-activation from the *meta* position. The values also show that halogen atoms are deactivating, particularly from the *meta* position.

	σ values		
	σ *meta*	σ *para*	σ^+ *para*
OH	0.12	-0.37	-0.92
OMe	0.12	-0.27	-0.78
Cl	0.37	0.23	-
Br	0.39	0.23	-

Table 4.21 Electronic effect of substituents [14]

Chlorine versus bromine

The k_2 values for 4-chloroanisole and 4-bromophenetole are similar. This can also be seen with 4-chlorophenol and 4-bromophenol; therefore it can be concluded that substituting chlorine for bromine does not significantly affect the rate (the k_2 value) of the nitration of these substrates.

Number of chlorine atoms

Comparison of the k_2 values for the chlorophenols indicates that the more chlorine atoms substituted on the ring the slower the reaction is (lower the k_2 value). This could be due to chlorine deactivating the ring towards electrophilic attack. Trichlorophenol has three chlorines and has the lowest k_2 value, although this is definitely not the only factor influencing the rate of reaction.

Hughes, Ingold and Reed obtained the following first order rate constants for nitrations in 99.8% acetic acid with nitric acid.[15]

	$10^5 k_1 / s^{-1}$
o-dichlorobenzene (75)	25.7
m-dichlorobenzene (76)	49.8
p-dichlorobenzene (77)	20.0

Table 4.21 First order rate constants for nitration with nitric acid[15]

(75) (76) (77)

Meta deactivation from Chlorine
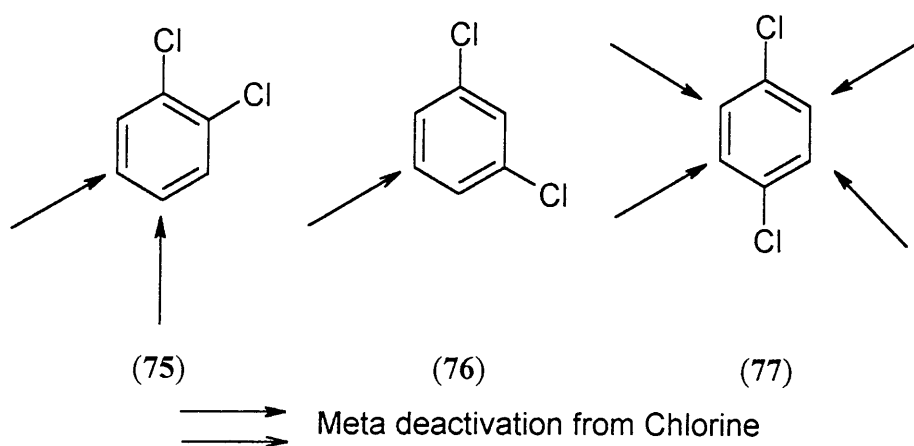
The differences between the rates for the isomeric dichlorobenzenes can be explained due to the deactivation of the *meta* position by chlorine to nitration (shown in **75, 76, 77**). In *m*-dichlorobenzene the two chlorines are deactivating the same *meta* position therefore leaving the other positions reactive. In *o* and *p*-dichlorobenzene different positions are being deactivated by the two chlorine atoms. Therefore *m*-dichlorobenzene is more reactive than the other two isomeric dichlorobenzenes.

The de-activation towards nitration of a meta-chlorine atom is also apparent from partial rate factors. This effect can also be seen in the results presented here.

Why is 2,4-dichlorophenol slightly faster than 2,6-dichlorophenol?

The OH group activates the ring towards electrophiles and is an *ortho/para* director but preferably *ortho*. In 2-6-dichlorophenol the *para* activation at position 4 from the OH group is rivalled by *meta* double deactivation from the two chlorine atoms. In 2,4-dichlorophenol double deactivation from the two chlorine atoms is rivalled by a stronger *ortho* activation from the OH group yielding a slightly faster reaction than 2,6-dichlorophenol.

Why do 4-chlorophenol and 4-bromphenol react so rapidly?

In 4-chlorophenol the ortho activation in position 2 and 6 is rivalled by only a single deactivation from the chlorine atom resulting in a faster nitration reaction compared to the other chlorophenols studied.

4-chlorophenol has a k_2 value 100 times greater than the k_2 value for 4-chloroanisole. A similar factor is observed for 4-bromophenol in comparison to 4-bromophenetole. These large factors are difficult to account for in terms of electronic effects, since the hydroxy and alkoxy groups have similar values for the Hammett σ parameter.

Moodie and co-workers[16] have shown that in reactions with nitric acid in sulfuric acid, 4-chlorophenol is more reactive than 4-chloroanisole by a factor of *ca* 2.

If ionisation of the phenol to give phenolate anion occurred as shown in **Scheme 4.13** then greater activation to electrophilic attack would be expected. However such ionisation is not likely in the non-polar media used in the present work.
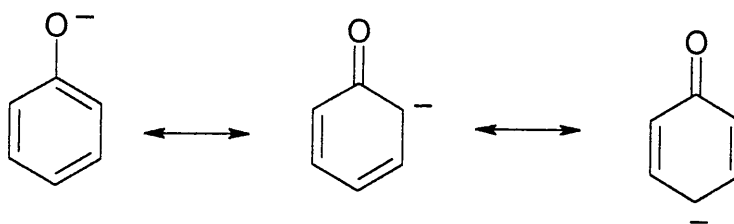
Scheme 4.13 Ionisation of phenol

Nitrating agent

The reagent used in the present work is N_2O_5 and the evidence suggests that this is the nitrating agent in the solvents used. N_2O_5 will readily hydrolyse to produce nitric acid. However the solubilities of the water in PP6 is very low, *ca* 10^{-4} mol dm^{-3}, and nitric acid itself is extremely insoluble. Hence it is unlikely that the reactions observed are due to nitric acid. During the aromatic nitration process, nitric acid will be produced, **Scheme 4.14.**

$$N_2O_5 + ArH \longrightarrow ArNO_2 + HNO_3$$
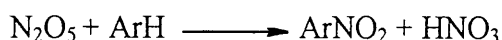
Scheme 4.14 Nitration using N_2O_5

However in the systems studied here $[N_2O_5] \gg [ArH]$, so that the concentration of nitric acid produced will be much lower than the overall concentration of N_2O_5.

Ingold and co-workers[1] used carbon tetrachloride as solvent in which nitric acid has some solubility. They worked under the condition $[ArH] \gg [N_2O_5]$, and found evidence for two pathways. The first involved direct reaction of the aromatic compound with N_2O_5 and the second involved catalysis of the reaction by nitric acid. In the latter process nitric acid was thought to enhance the polarity of the medium so that N_2O_5 would ionise to yield a nitronium ion. Due to the insolubilities of nitric acid in PP6 or perfluoroether (HT135) it was not possible to investigate the possibilities of a related catalysed pathway in the present work

The possibility that the reactions studied here involve a radical pathway is unlikely by

  i)   The absence of any kinetic effect of 1,3-dinitrobenzene which might be expected to interact with radicals and
  ii)   the regiospecifities of the reactions.

Radicals generally show dimerisation in the position of ring attack. Hence reactions via radical intermediates would be expected to yield a variety of substitution products. The results obtained indicate that the reaction occurs specifically at carbon atom *ortho* or *para* to the hydroxy group.

Ingold et al suggested a mechanism for the uncatalysed reaction with N_2O_5 involving a cyclic transition state shown in **Figure 4.28**. This is an attractive possibility since the ring proton is transferred to an incipient nitrate ion. However this does not explain the higher reactivity observed for phenol, than for alkyl ethers, nor does it explain the high reactivity at positions *ortho* to the hydroxy group. Another possible reaction pathway is shown in **Scheme 4.15.**
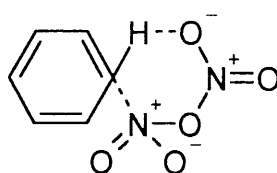
Figure 4.28 The Ingold transtition state in aromatic nitration with N_2O_5
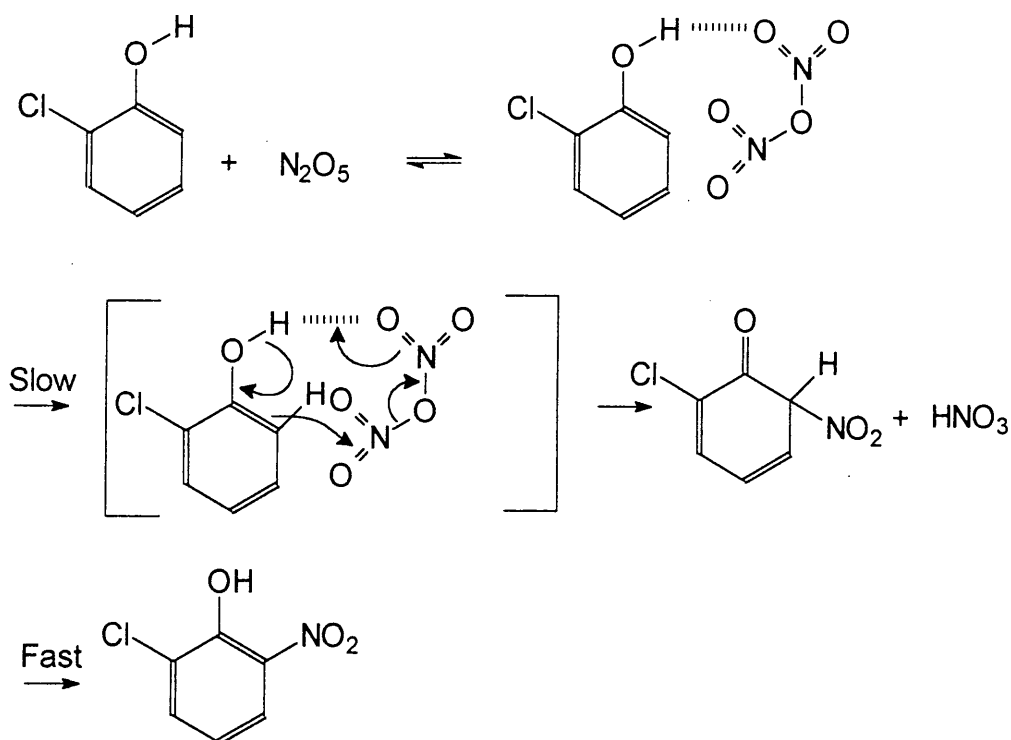
Scheme 4.15 Proposed mechanism for the nitration of chlorophenols with N_2O_5 in PP6 at 25 °C

This shows initial interaction of hydrogen bonding between the N_2O_5 molecule and 2-chlorophenol which could be the factor which causes the preferential nitration in chlorophenols compared to 4-chloroanisole. The next step shows the slow addition of the NO_2 group via a cyclic transition state, the final stage being the quick loss of a proton resulting in the product, 2-chloro-6-nitrophenol. The rate determining step was determined using the kinetic isotope effect as the slow addition of the NO_2 group.

A related scheme may also be possible involving reaction of the position *para* to the hydroxy group

4.18 Conclusions

The results show that nitration of 4-chloroanisole, 4-bromophenetole, 4-bromophenol, 2- and 4-chlorophenol, 2,4- and 2,6-dichlorophenol and 2,4,6-trichlorophenol are all first order in N_2O_5. Changing the solvent from PP6 to perfluoroether (HT135) did not affect the rate of nitration.

The mechanism has been investigated and does not involve nitrosation or radicals. The kinetic isotope effect determined that the reaction must occur by a slow RDS involving the formation of the bond between the nitro group and the aromatic ring, automatically followed by the loss of a proton. There is preferential reaction *ortho* to the OH group which could be due to an initial hydrogen bonding interaction.

4.19 References

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Chapter Five

5 Synthesis of nitramines

This chapter will discuss the nitration/nitrolysis of various amines with dinitrogen pentoxide and nitric acid in perfluorocarbon solvents. Synthetic results for nitramines relating to morpholine, pyrrolidine, piperidine, oxazolidinone and hexahydropyrimidine have been obtained. N-Acyl, N-trimethylsilyl and N-tert-butoxycarbonyl derivatives have been investigated.

5.1 Introduction

Synthesis of nitramines using dinitrogen pentoxide has previously been discussed in **chapter one**. Nitramines are industrially important because they are used in propellant and explosive technology.[1] Cyclo-1,3,5-trimethylenetrinitramine (RDX), (**6**) and cyclo-1,3,5,7-tetramethylenetetranitramine (HMX), (**7**) are used as explosives and can be prepared with 99.8% HNO_3 from hexamine (**Scheme 5.1**).[2]

(**6**) (**7**)
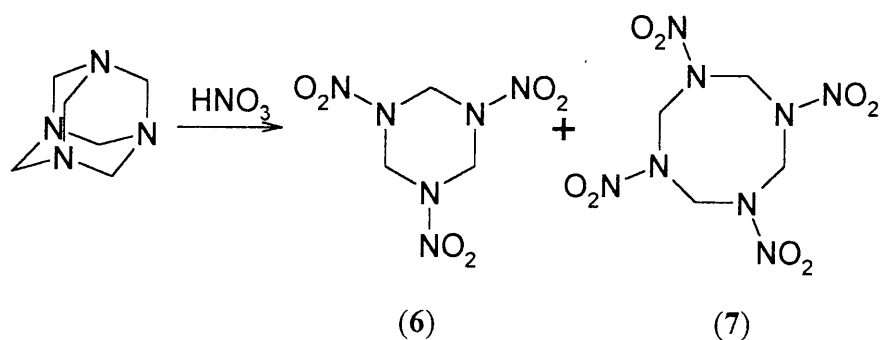
Scheme 5.1 Synthesis of RDX and HMX

The nitrolysis of dialkylamides, carbamates and sulphonamides also gives nitramines, generally in good yield, as can be seen in the preparation of RDX by nitrolysis of a variety of 1,3,5-triacylhexahydro-s-triazines (**Scheme 5.2**).[3]

R = CH₃C(O)-, C₂H₅C(O)-, C₂H₅OC(O)-, *p*-CH₃C₆H₄S(O)₂-
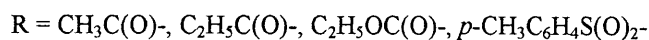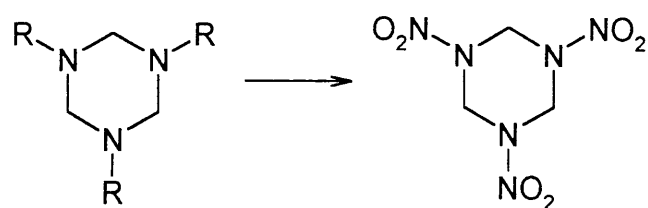
Scheme 5.2 Nitrolysis using $HNO_3/(P_2O_5)$ or $HNO_3/(CF_3CO_2)_2O$

The most common method of preparing nitramines involves the reaction of secondary amides with nitric acid in the preparation of a dehydrating agent, such as acetic anhydride.[4] One disadvantage in this reaction is the formation of an acyl nitrate co-product which in itself in an efficient nitrating agent, (**Scheme 5.3**). The disposal of these acyl nitrates poses potentially serious safety problems.

| amine | amide (R" = alkyl) carbamate (R" = alkoxy) | nitramine | acyl nitrate (R" = alkyl) |

Reagents: a) acylating agent (R"COCl)

b) nitrating agent (pure HNO_3, $NO_2^+BF_4^-$ or N_2O_5)
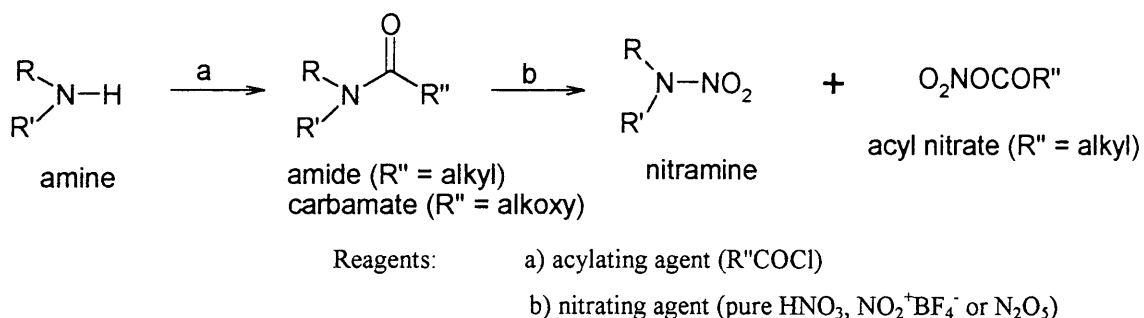
Scheme 5.3 Acylation followed by nitrolysis in the synthesis of nitramines

A further drawback of the nitrolysis of acylamines is that cleavage of N-C bonds other than the acyl linkage can occur resulting in lower yields and product contamination.[5] Additionally some acyl derivatives are completely inert to nitrolysis.[6] These problems could be due to the inertness of the nitrogen atom towards electrophilic attack as a result of the electron-withdrawing acyl group, and therefore employment of substituents with a positive inductive effect, (electron donating substituent), are likely to be

beneficial. Recently silylamines and disilylamines have been studied and were found to be very successful in the synthesis of nitramines,[7] **see chapter one**.

N-tert-Butoxycarbonyl (BOC) derivatives have also recently been investigated for their use in the synthesis of nitramines.[8] The BOC group is extensively used in peptide synthesis as an acid labile amine protecting group.[9,10,11] The conversion of *N*-BOC derivatives to corresponding nitramines requires mild nitration conditions. The avoidance of excess acid and high temperatures favours nitrolysis over other competing cleavage reactions. Thus treatment of *N*-BOC-piperidine with 100% nitric acid gave only traces (<5%) of 1-nitropiperidine. However nitric acid with acetic or trifluoroacetic acid anhydrides converted *N*-BOC-piperidine to 1-nitropiperidine in 87-94% yields. Nitronium tetrafluoroborate in acetonitrile also effected the same conversion in 79% yield, (**Scheme 5.4**).[12] N_2O_5 in dichloromethane gave a 1:1 mixture of unreacted *N*-BOC-piperidine and 1-nitropiperidine proving evidence that this is an exceptionally mild nitration reagent.[8]
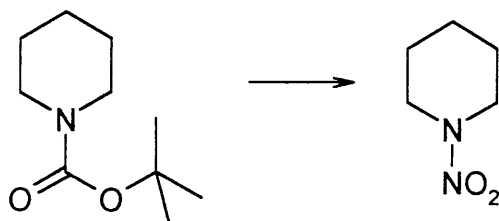
Scheme 5.4 Nitrolysis of *N*-BOC-piperidine using $HNO_3/(CH_3CO)_2O$, $HNO_3/(CF_3CO)_2O$ or NO_2BF_4/CH_3CN at –23 °C to ambient temperature, 79-94%

5.2 Morpholine (85)
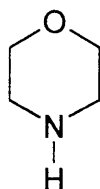
(**85**)

We decided to investigate the synthesis of nitramines using nitric acid and N_2O_5 in perfluorocarbon solvents. Experimental results are given in **chapter 6, section 6.7**.

A solution of morpholine in PP6 and nitric acid were mixed together and stirred at ambient temperature overnight. A solid was formed and separated. A possibility was to see the *N*-nitration of morpholine (**Scheme 5.5**) but ^{1}H NMR spectroscopy established that the product was protonated morpholine (**Scheme 5.6**)
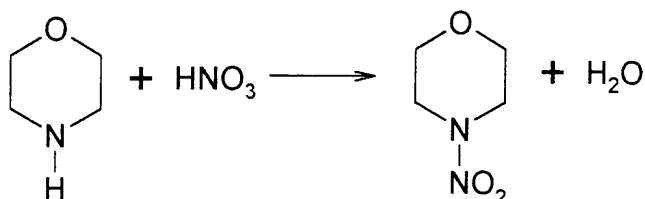
Scheme 5.5 Nitration of morpholine
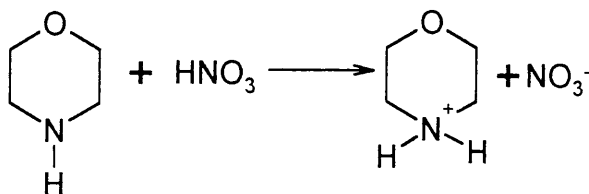
Scheme 5.6 Protonation of morpholine

We attempted to nitrate morpholine using N_2O_5. A solution of morpholine in PP6 and N_2O_5 in PP6 were mixed together and were left for 1 hour. The resulting product was characterised using ^{1}H NMR spectroscopy as protonated morpholine.

PFC	Nitrating reagent	Molar ratio (substrate : nitrating agent)	Reaction time /hrs	Temp. / °C	Yield	Product
PP6	HNO₃	1:1	24	ambient	<5%	protonated morpholine
PP6	N₂O₅	1:1	1	-5	<1%	protonated morpholine

Table 5.1 Summary of conditions used in the attempted nitration of morpholine

5.3 *N*-Acetylmorpholine (86)
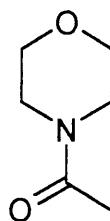
(86)

It was decided to use *N*-acetylmorpholine to overcome the problem of protonation. A solution of *N*-acetylmorpholine in PP6 and the nitrating agent were mixed and allowed to stir for a period of time at various temperatures (**Table 5.2**). Distilled water was added, the aqueous layer separated and extracted with dichloromethane. The dichloromethane was left to evaporate and the resulting product was characterised by ^{1}H NMR spectroscopy.

PFC	Nitrating reagent	Molar ratio (substrate : nitrating agent)	Reaction time /hrs	Temp. /°C	Yield	Product
PP6	HNO$_3$	1:6	48	70	<5%	*N*-nitromorpholine
PP2	HNO$_3$	1:6	2	70	<5%	morpholine
			1	ambient		
PP2	HNO$_3$	1:6	24	ambient	<5%	morpholine
PP6	HNO$_3$	1:6	336	ambient	<5%	*N*-nitromorpholine
PP6	N$_2$O$_5$	1:2	24	ambient	<5%	morpholine
PP6	HNO$_3$/H$_2$SO$_4$ – ZnCl$_2$	1:6:6	3	ambient	<5%	morpholine
				50	<5%	morpholine

Table 5.2 Attempted synthesis of *N*-nitro morpholine from *N*-acetyl morpholine using various reagents and conditions

Synthesis of *N*-nitromorpholine was attempted several times, using nitric acid, nitric and sulfuric acid with ZnCl$_2$ as a catalyst[13] and using N$_2$O$_5$. In all cases the reactions were unsuccessful, yielding less than 5 % of the desired product. The extraction procedure was changed.

N-acetylmorpholine was dissolved in PP2 and a solution of N$_2$O$_5$ in PP2 (4 molar equivalents) was added and stirred for three hours at ambient temperature. The product was extracted using dichloromethane and was then neutralised with KHCO$_3$. The dichloromethane was decanted off and then evaporated. The resulting clear liquid was characterised using ^{1}H NMR spectroscopy (**Figure 5.1**) and GCMS (**Figure 5.2**) methods.
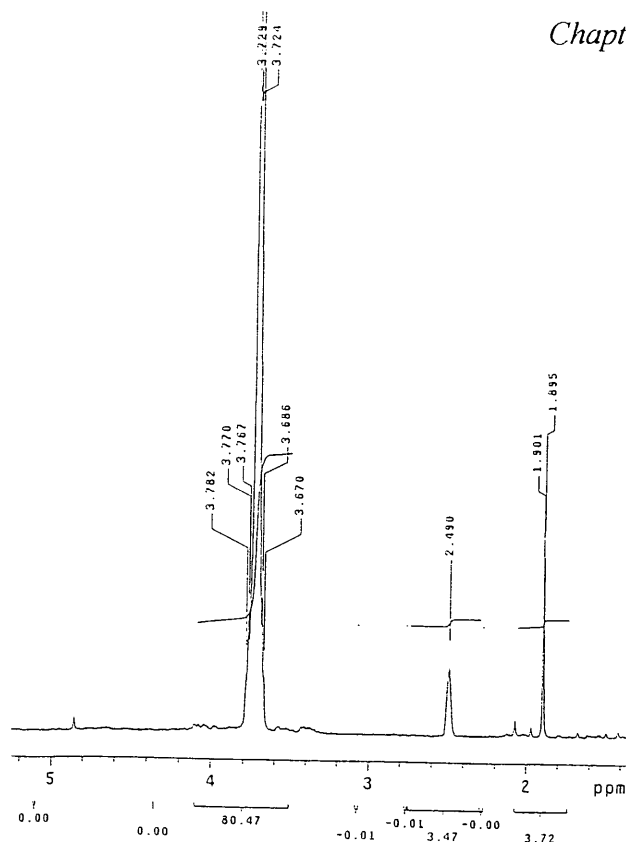
Figure 5.1 ¹H NMR spectrum of *N*-nitromorpholine
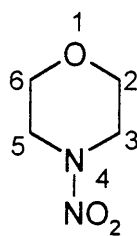
(**87**)

Shift / ppm	Multiplicity	Inference
1.90	s	impurity
2.49	m	DMSO (solvent)
3.72	m	protons in positions 2, 3, 5 and 6 in (**87**)

Table 5.3 Shifts, multiplicity and inference for the ¹H NMR spectrum of *N*-nitromorpholine (**Figure 5.2**)
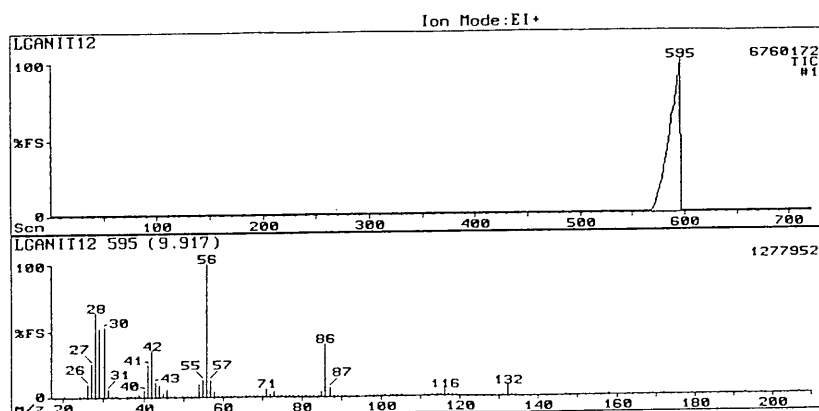
Figure 5.2 GCMS of *N*-nitromorpholine

The ^{1}H NMR spectrum (**Figure 5.1**) of the product formed in the reaction (using no water in the extraction procedure) was consistent with the spectrum of *N*-nitromorpholine (**87**) (lit.[7] δ 3.80 (s) ppm in $CDCl_3$). An authentic sample of *N*-nitromorpholine was supplied by the DERA and the ^{1}H NMR spectrum was recorded for comparison (δ 3.72 (m) ppm in d_6-DMSO). The GCMS (**Figure 5.2**) contains a signal at 595s that corresponds to the correct molecular mass of 132.

The crude yield was 105%, with an unidentified signal in the ^{1}H NMR spectrum (**Figure 5.1**) at δ 1.9 ppm, which could be due to a small amount of impurity in the product. The product should be a solid (lit.[12] M.pt. 50-52 °C) at room temperature. However the GCMS did not show any impurities.

Using this methodology we can successfully nitrate *N*-acetylmorpholine in near quantitative yield, (**Scheme 5.7**)
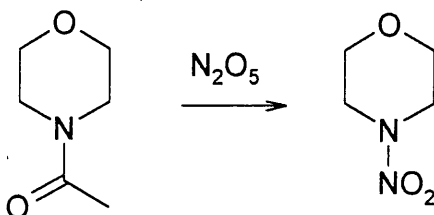
Scheme 5.7 Nitrolysis of *N*-acetylmorpholine in PP2 using N_2O_5

5.4 Silylamines

5.4.1 *N*-Trimethylsilylmorpholine (88)
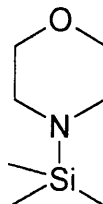
(88)

N-Trimethylsilylmorpholine was dissolved in PP6, and a solution of N_2O_5 in PP6 was added. The solutions were mixed together and left for a period of time at various temperatures, (shown in **Table 5.4**).

PFC	Nitrating reagent	Molar ratio (substrate : nitrating agent)	Reaction time / hrs	Temp. / °C	Separation of product	Yield / %	Product
PP6	N_2O_5	1:3	1	ambient	1	<5	*N*-nitromorpholine
PP6	N_2O_5	1:3	1	ambient	2.	54	*N*-nitromorpholine and *N*-TMS-morpholine
PP2	N_2O_5	1:3	3	ambient	3.	87	*N*-nitromorpholine and morpholinium nitrate

1. Distilled water was added and the aqueous layer was separated. The aqueous layer was extracted with dichloromethane. The dichloromethane was allowed to evaporate leaving a liquid.

2. The PP6 was distilled leaving a liquid.

3. The product was extracted using dichloromethane and neutralised with $KHCO_3$. The dichloromethane was decanted off then evaporated, leaving a liquid.

Table 5.4 Attempted synthesis of *N*-nitro morpholine from *N*-trimethylsilylmorpholine using various conditions and extraction procedures.

The products formed in the experiment were characterised using ^1H NMR spectroscopy. The ^1H NMR spectrum of the product formed using the third separation method is shown in **Figure 5.3.**
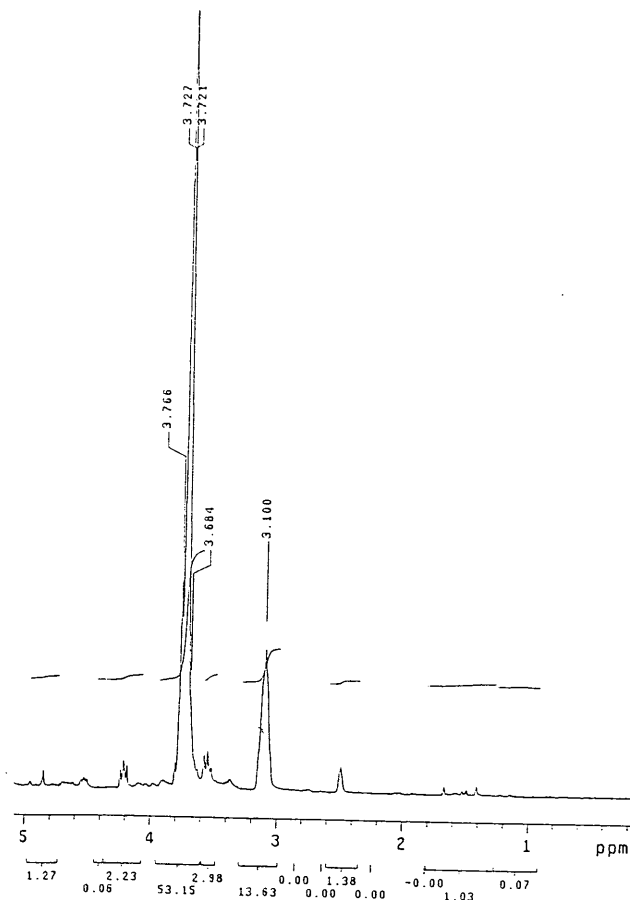
Figure 5.3 ^{1}H NMR spectrum of nitrated *N*-trimethylsilylmorpholine using the third separation method.

Shift	Multiplicity	Inference
2.49	p	DMSO (solvent)
3.10	m	morpholine salt
3.73	m	protons in positions 2, 3, 5 and 6 in (87)

**Table 5.5** Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitromorpholine (**Figure 5.3**)

The ^{1}H NMR spectrum (**Figure 5.3**) is consistent with the spectrum for *N*-nitromorpholine but also showed a signal at δ 3.10 ppm. Ethanol was added to the product and a small

amount of white solid was formed. The spectrum of the white solid showed signals at δ 3.10 and δ 3.75 which are consistent with the formation of a morpholine salt, possibly morpholinium nitrate. This was confirmed by ESMS, (shown in **Figure 5.4** and **5.5**).

Figure 5.4 ESMS$^+$ of protonated morpholine
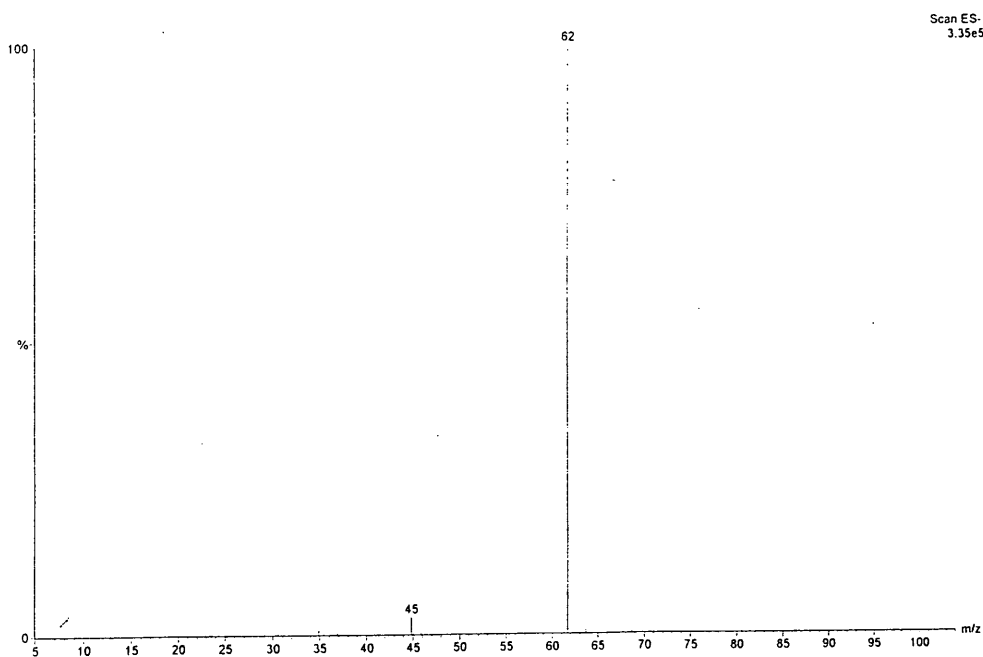
Figure 5.5 ESMS$^-$ of NO$_3^-$
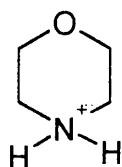
(89)   (90)

ES mass spectra (**Figure 5.4 and 5.5**) indicated the presence of ions with 88(+) m/z (**89**) and 62(-) m/z (**90**). The ^{1}H NMR spectrum of the product (**Figure 5.3**) indicates a mixture of *N*-nitromorpholine, δ 3.72 ppm, together with the salt (25%), δ 3.10 ppm and δ 3.72 ppm. Presumably in the extraction with dichloromethane with both *N*-nitromorpholine and morpholine are present, and the latter is protonated by HNO_3. From the ^{1}H NMR spectrum (**Figure 5.3**) the yield of *N*-nitromorpholine could be estimated at 65 %.

It can be concluded that the nitrodesilylation of *N*-trimethylsilylmorpholine was possible using this system, (**Scheme 5.8**) although not as efficient as in the previous case with *N*-acetylmorpholine.
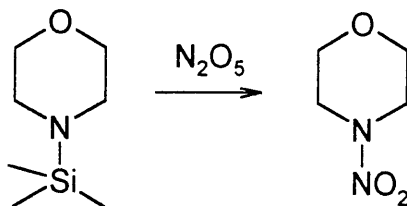
Scheme 5.8 Nitrolysis of *N*-trimethylsilylmorpholine using N_2O_5 in PP6

5.4.2 3-Trimethylsilyl-2-oxazolidinone (91)

(91)
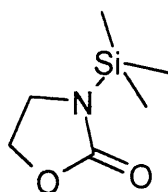
3-Trimethylsilyl-2-oxazolidinone was dissolved in PP6, and N_2O_5 in PP6 was added. The solutions were mixed together and left for 1 hour at temperature, (shown in **Table 5.6**).

PFC	Nitrating reagent	Molar ratio (substrate : nitrating agent)	Reaction time / hrs	Temp./ °C	Separation of product	Yield (%)	Product
PP6	N_2O_5	1:3	1	ambient	1.	16	*N*-nitro-1,3-oxazolidin-2-one
PP6	N_2O_5	1:3	1	ambient	2.	73	*N*-nitro-1,3-oxazolidin-2-one

1.   The reaction mixture was quenched with water, the aqueous layer was separated and neutralised, a white solid formed which was filtered.

2.   The reaction mixture was left to evaporate resulting in a white solid.

Table 5.6 Conditions for the synthesis of *N*-nitro-1,3-oxazolidin-2-one using various extraction procedures

The ^{1}H NMR spectrum from both reactions showed a multiplet at δ 4.30 ppm in d_6-DMSO, which is consistent of the spectrum for *N*-nitro-1,3-oxazolidin-2-one (lit.[7] is δ 4.42 (s) ppm in CDCl₃). The ^{1}H NMR spectrum and CIMS from reaction using the second separation method are shown in **Figure 5.4** and **Figure 5.5** respectively.
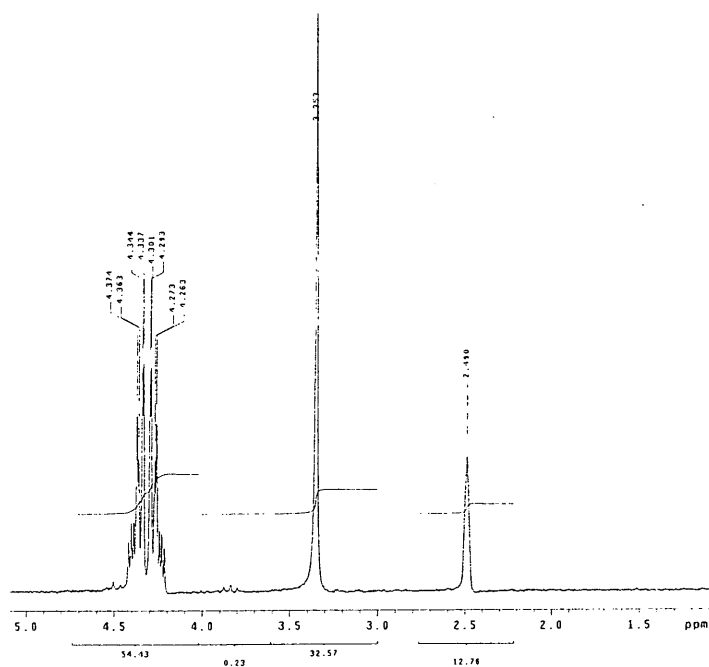
Figure 5.6 ¹H NMR spectrum of *N*-nitro-1,3-oxazolidin-2-one
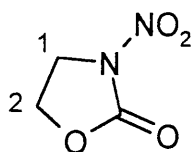
(**92**)

Shift	Multiplicity	Inference
2.49	m	DMSO (solvent)
3.31	s	H₂O
4.37	m	Protons in positions 1 and 2 in (**92**)

Table 5.7 Shifts, multiplicity and inference for the ¹H NMR spectrum of *N*-nitro-1,3-oxazolidin-2-one (**Figure 5.6**)
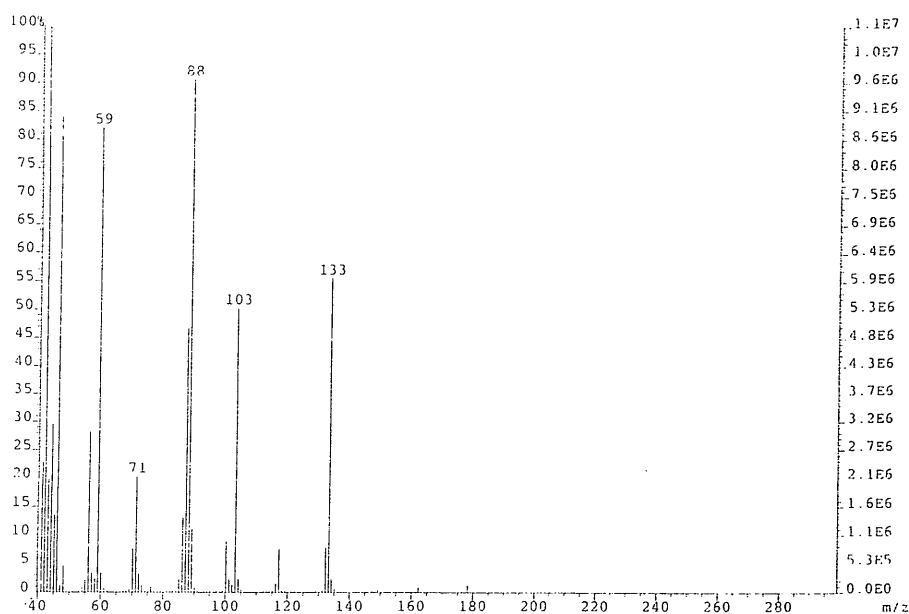
Figure 5.7 CIMS of *N*-nitro-1,3-oxazolidin-2-one

The CI mass spectrum (**Figure 5.7**) shows a molecular mass of 132 (Mr = 133-1 =132 for CIMS) which corresponds to *N*-nitro-1,3-oxazolidin-2-one (Mr 132). The melting point of the product was 106 –107.8 °C (lit.[14] 108-109.5 °C). Therefore we can conclude that nitrodesilylation of 3-trimethylsilyl-2-oxazolidinone can be successfully achieved using this method (**Scheme 5.9**).
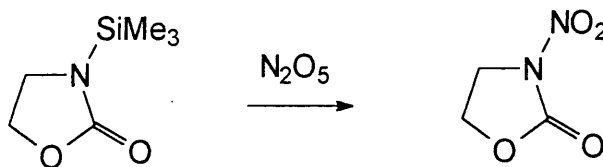
Scheme 5.9 Nitrodesilylation of 3-trimethylsilyl-2-oxazolidinone

5.4.3 *N*-Trimethylsilylpyrrolidine (93)
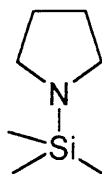
(93)

N-Trimethylsilylpyrrolidine was dissolved in PP6, and N_2O_5 in PP6 was added. The solutions were mixed together and left for a period of time at ambient temperature, (shown in **Table 5.8**).

PFC	Nitrating reagent	ME	Reaction time /hrs	Temp. / °C	Separation of product	Yield (%)	Product
PP6	N_2O_5	1:2.5	1	ambient	1.	<5	*N*-nitropyrrolidine
PP6	N_2O_5	1:3	3	ambient	2	42	*N*-nitropyrrolidine

1. Added water, the aqueous layer was separated and extracted with dichloromethane yielding an oil.

2. The product was extracted using dichloromethane. Neutralised with $KHCO_3$. The dichloromethane was filtered then evaporated yielding an oil.

ME - molar equivalent of substrate to nitrating agent

Table 5.8 Conditions for the synthesis of *N*-nitropyrrolidine using various extraction procedures

The ^{1}H NMR spectrum of *N*-nitropyrrolidine using the second extraction procedure is shown in **Figure 5.8**.
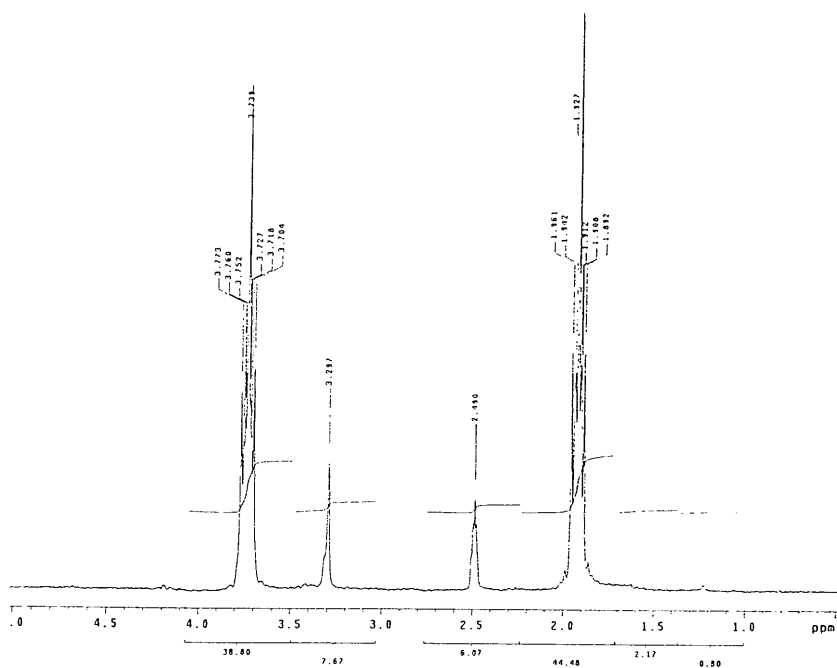
Figure 5.8 ^{1}H NMR spectrum of *N*-nitropyrrolidine
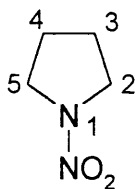
(**94**)

Shift	Multiplicity	Inference
2.49	m	DMSO (solvent)
3.29	s	H$_2$O
1.93	m	Protons in positions 3 and 4 in (**94**)
3.74	m	Protons in positions 2 and 5 in (**94**)

Table 5.9 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitropyrrolidine (**Figure 5.8**)

The ^{1}H NMR spectrum from both reactions showed multiplets at δ1.92 ppm and δ 3.73 ppm (lit. [7] δ 2.00 ppm (m) and δ 3.70 ppm (m) in CDCl$_3$). An authentic sample of *N*-nitropyrrolidine was supplied by the DERA and the ^{1}H NMR spectrum was recorded for comparison (δ 1.93 (m) ppm, δ 3.74 (m) ppm in d$_6$-DMSO). Therefore we can conclude that the nitrodesilylation of *N*-trimethylsilylpyrrolidine was successful in this system although the yield could be improved, (**Scheme 5.10**).

The product should be a solid at room temperature (lit. [15] M.pt. 58 °C), which suggests that there may be slight impurity in the product.
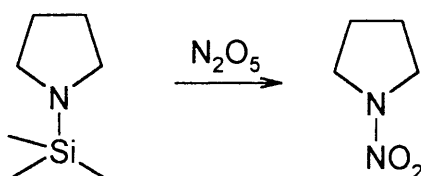
Scheme 5.10 Nitrodesilylation of *N*-trimethylsilylpyrrolidine using N$_2$O$_5$ in PP6

5.5 *N*-BOC-amines[8]

5.4.1 *N*-BOC-morpholine (95)

(95)

Synthesis of N-BOC-morpholine

(96)
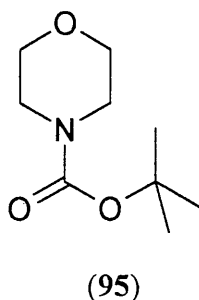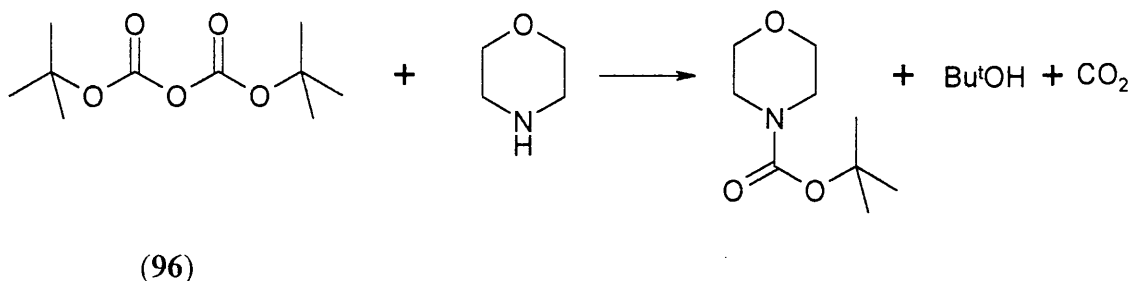
Scheme 5.11 Synthesis of *N*-BOC-morpholine

Morpholine was dissolved in dichloromethane and triethylamine was added, followed by a solution of BOC-anhydride (96) in dichloromethane. The solution was allowed to stir at ambient temperature for three hours after which the dichloromethane, triethylamine and butanol were removed under reduced pressure.

Nitrolysis of N-BOC-morpholine

N-BOC-morpholine was dissolved in perfluorocarbon and a solution of N_2O_5 in perfluorocarbon was added. This solution was stirred for 3 hours at ambient temperature. The product was extracted using dichloromethane and neutralised. The dichloromethane was decanted off then evaporated, yielding an oil.

Expt.	PFC	Nitrating reagent	ME	Reaction time /hrs	Temp. / °C	Yield (%)	Product
1	PP2	N_2O_5	1:1	3	ambient	76	*N*-nitromorpholine
2	PP6	N_2O_5	1:3	3	ambient	89	*N*-nitromorpholine

ME - molar equivalent of substrate to nitrating agent

Table 5.10 Conditions for the synthesis of *N*-nitromorpholine using various molar ratios

The products from both experiments gave a ^{1}H NMR spectrum consistent with the presence of *N*-nitromorpholine. The ^{1}H NMR spectrum (**Figure 5.9**) and EIMS (**Figure 5.10**) and HPLC (**Figure 5.11**) of the product from the second experiment are shown below.

Figure 5.9 ^{1}H NMR spectrum of nitrated *N*-BOC-morpholine.

(**87**)

Shift	Multiplicity	Inference
1.55	s	1,1-dimethylethylnitrate (**Scheme 5.13**)
2.49	p	DMSO (solvent)
3.29	m	H$_2$O
3.73	m	Protons in positions 2, 3, 5 and 6 in (**87**)

Table 5.11 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitromorpholine (**Figure 5.9**)
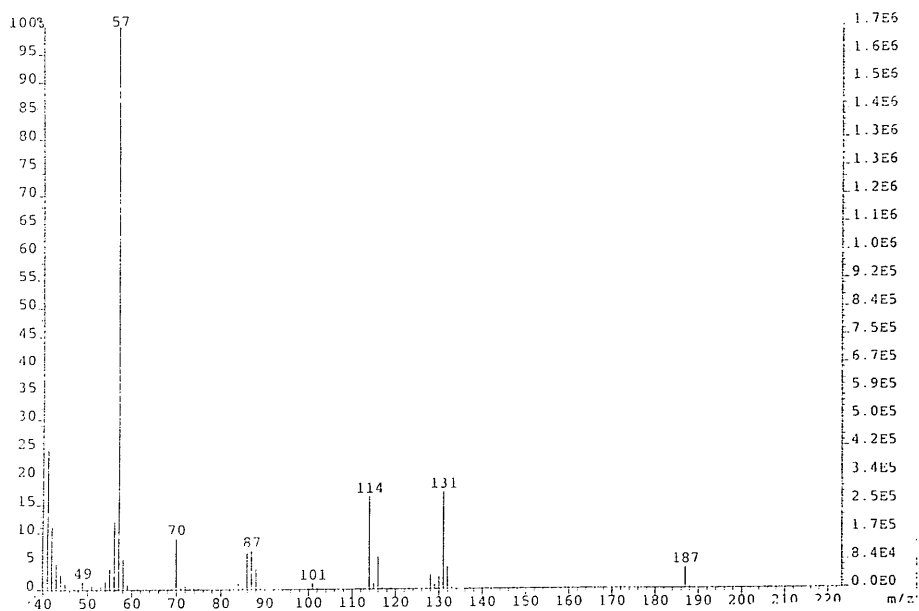
Figure 5.10 EIMS of *N*-nitromorpholine
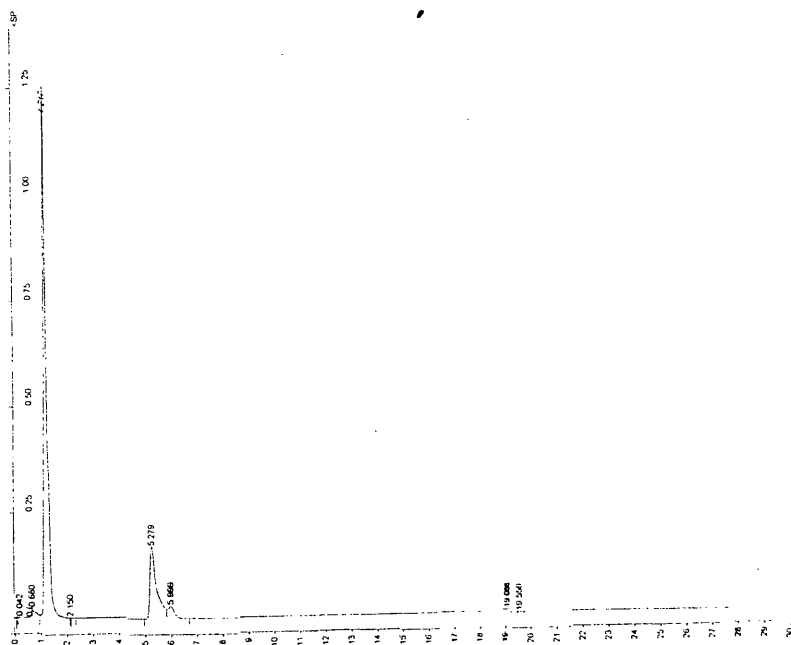
Figure 5.11 HPLC of *N*-nitromorpholine

-174-

The EIMS shows a mass ion at 132 m/z (Mr of *N*-nitromorpholine is 132).
The yield assuming that the isolated sample contains only *N*-nitromorpholine is 83 %.
However the ¹H NMR spectrum indicates an impurity may be present which as shown later
in **Scheme 5.14** could be 1,1-dimethylethylnitrate.

In order to test the purity of the isolated samples a comparison, using HPLC, was made
with an authentic sample of pure *N*-nitromorpholine supplied by DERA.

The HPLC trace in **Figure 5.11** shows peaks at 1.3 minutes due to *N*-nitromorpholine and
at 5.3 minutes due to dibutylphthalate, added as an internal reference. Comparison of the
intensities of these peaks with traces for the product obtained in the present work, and from
authentic *N*-nitromorpholine shows a purity of 100 %.

N-BOC-morpholine can be successfully nitrated with N_2O_5 to give *N*-nitromorpholine in
PP2 and PP6 (**Scheme 5.12**). The product should be a solid at room temperature. Therefore
there may be a slight impurity in the product although this was not detected by HPLC. The
impurity could be 1,1-dimethylethylnitrate (**Scheme 5.14**).
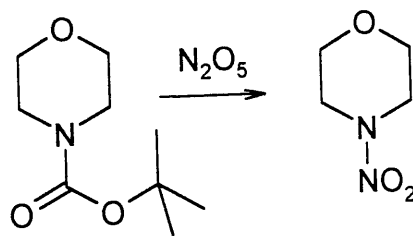
Scheme 5.12 Nitrolysis of *N*-BOC-morpholine

5.5.2 *N*-BOC-pyrrolidine (97)

(97)
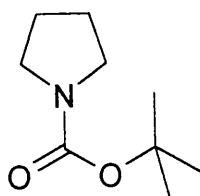
Synthesis of N-BOC-pyrrolidine

A sample was available from previous work. It had been prepared in the following way. A solution of BOC-anhydride in tetrahydrofuran was added to a mixture of pyrrolidine in tetrahydrofuran and sodium hydroxide added. The reaction mixture was extracted with ether yielding *N*-BOC-pyrrolidine.

Nitrolysis of N-BOC-pyrrolidine

A solution of *N*-BOC-pyrrolidine in PP6 was treated with N_2O_5 in PP6. The solution was stirred for various times at ambient temperature (**Table 5.12**). The solutions were all extracted with dichloromethane and neutralised.

Expt	PFC	Nitrating reagent	ME	Reaction time / hrs	Temp. / °C	Yield / %	Product
1	PP6	N_2O_5	1:3	2	ambient	45	*N*-nitropyrrolidine
2	PP6	N_2O_5	1:2	1	ambient	88	*N*-nitropyrrolidine
3	PP6	N_2O_5	1:1	3	ambient	65	*N*-nitropyrrolidine

ME - molar equivalent of substrate to nitrating agent

Table 5.12 Conditions for the synthesis of *N*-nitropyrrolidine using various molar ratios and reaction times

The ^{1}H NMR spectrum (**Figure 5.12**) and the GCMS (**Figure 5.13**) and HPLC (**Figure 5.14**) of the product from the third experiment are shown below.
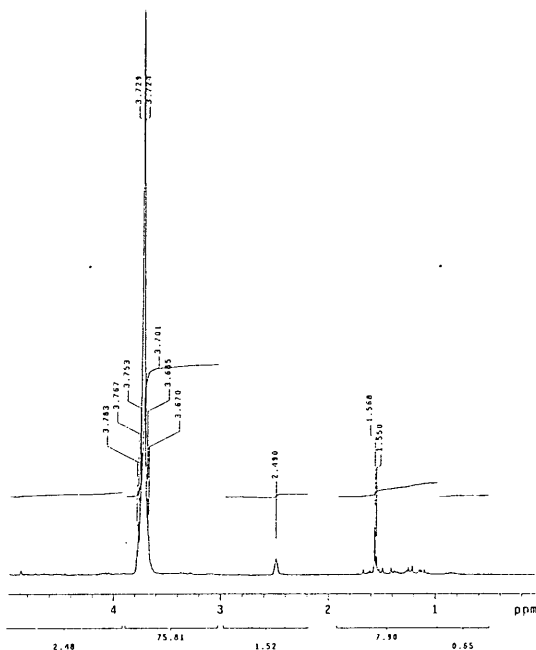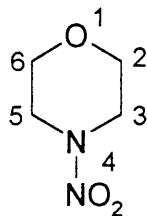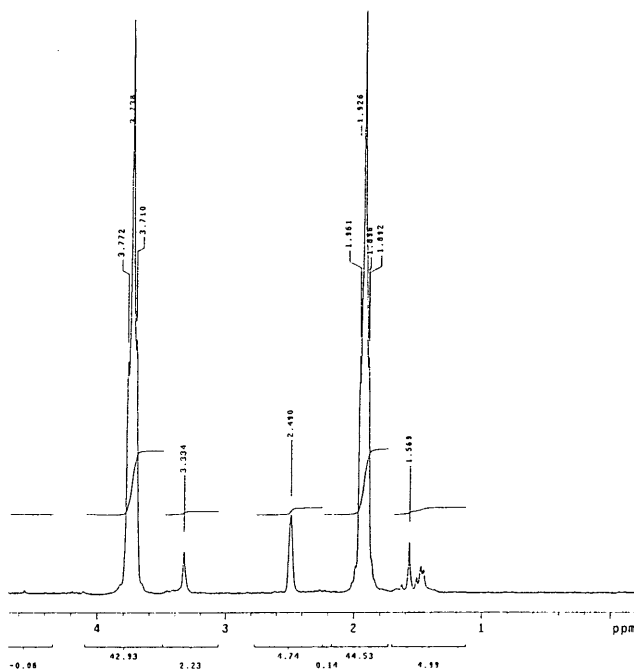

Figure 5.12 ^{1}H NMR spectrum of *N*-nitropyrrolidine

Shift	Multiplicity	Inference
1.57	m	1,1-dimethylethylnitrate (**Scheme 5.14**)
1.93	m	Protons in positions 3 and 4 in (**94**)
2.49	p	DMSO (solvent)
3.30	s	H_2O
3.73	m	Protons in positions 2 and 5in (**94**)

**Table 5.13** Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitropyrrolidine (**Figure 5.12**)
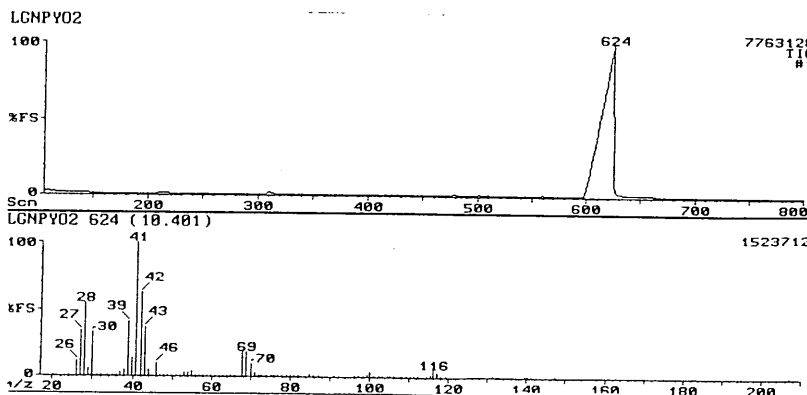
Figure 5.13 GCMS of *N*-nitropyrrolidine
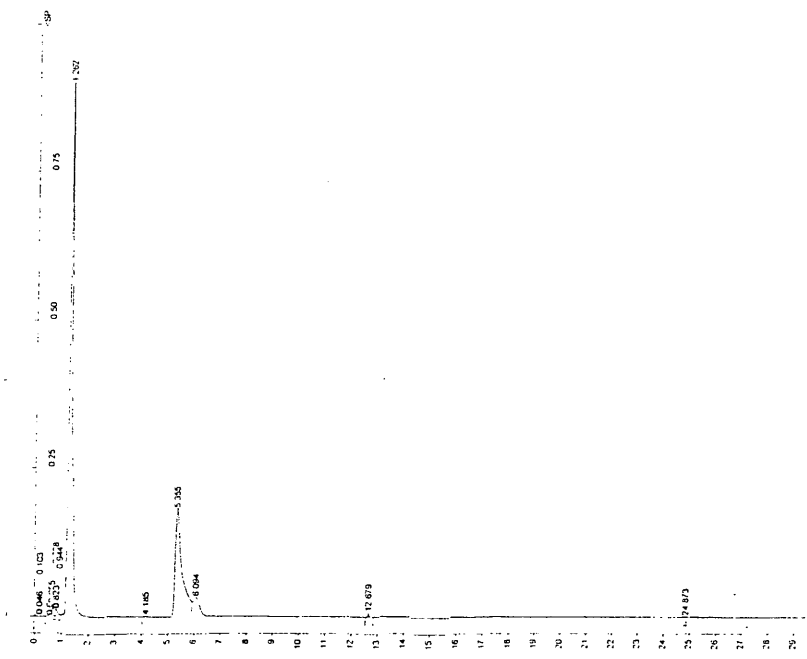
Figure 5.14 HPLC of *N*-nitropyrrolidine

The ^{1}H NMR spectra of the products from each experiment were consistent with an authentic sample of *N*-nitropyrrolidine. The crude yield was 110 % and from the ^{1}H NMR spectrum of the product in the second experiment we could estimate yield to be around 88 %. The ^{1}H spectrum of the product in the third experiment is shown above, (**Figure 5.12**) and contains a small impurity signal at δ 1.56 ppm which is likely to be 1,1-dimethylethylnitrate.

The GCMS (**Figure 5.13**) gave a chromatograph signal at 624 s corresponding to a molecular mass of 116, (Mr of *N*-nitropyrrolidine is 116).

The yields given in **Table 5.12** assume that all the product separated from the experiment is *N*-nitropyrrolidine. The ^{1}H NMR spectra indicate small amounts of an impurity, probably 1,1-dimethylethylnitrate. Hence the actual yields of *N*-nitropyrrolidine will be slightly lower.

The purity of the sample was tested using HPLC by comparison with an authentic sample of pure *N*-nitropyrrolidine supplied by DERA. Solutions were made up in acetonitrile containing *N*-nitropyrrolidine and butylphthalate, a reference compound. The relative masses of *N*-nitropyrrolidine and reference were the same in each experiment.

The HPLC trace containing N-nitropyrrolidine produced from the third experiment in **Table 5.12** is shown in **Figure 5.14**. Signals are observed due to the product (at 1.3 minutes) and the reference (at 5.4 minutes). The results in **Table 5.14** show that the purity of the products obtained from the experiments described here is equal to or better than the purity of the authentic sample.

Compound	Intensities		
	1.3 minutes	5.5 minutes	Ratio
Authentic *N*-nitropyrrolidine	59.5	33.8	1.76
Product from experiment 2	64.3	28.8	2.23
Product from experiment 3	63.3	30.6	2.07

Table 5.14 HPLC results of nitrated pyrrolidine

N-BOC-pyrrolidine can be successfully nitrated with N_2O_5 giving *N*-nitropyrrolidine, (**Scheme 5.13**).
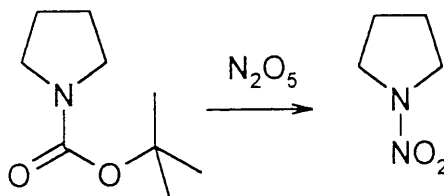
Scheme 5.13 Nitrolysis of *N*-BOC-pyrrolidine using N_2O_5 in PP6

In some of the products small impurities were found. Therefore in order to determine what these impurities could be we looked at the reaction in detail, **Scheme 5.14.**
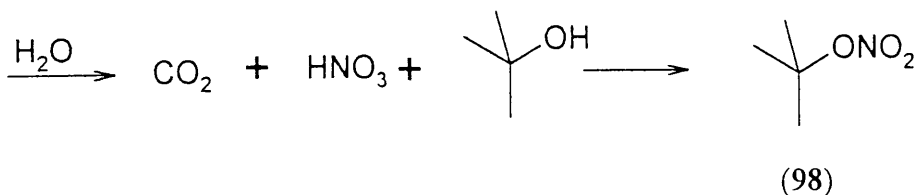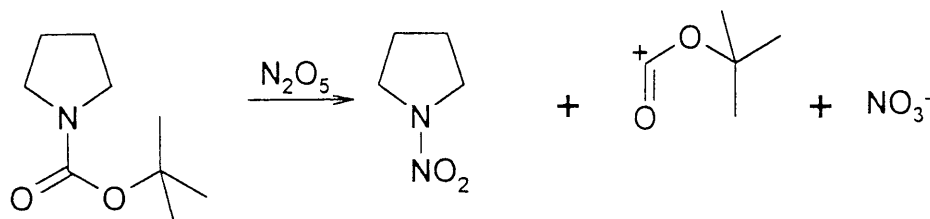
Scheme 5.14 Likely side products from the reaction

The side products from the reaction are HNO_3 which is neutralised in the extraction process, CO_2 which is a gas and ^{t}butylalcohol which has a B.pt. of 82.3 °C and should be removed under reduced pressure. A ^{1}H NMR spectrum was recorded on an authentic sample of ^{t}butylalcohol δ 1.24 ppm (CH_3) and δ 4.29 ppm (OH). This spectrum does not correspond to the observed impurity. However the literature[17] spectrum for 1,1-dimethylethylnitrate is $δ_H$ ($CDCl_3$) 1.55 (9H, s). Therefore the impurity in the compounds may be 1,1-dimethylethylnitrate (98).

5.5.3 *N*-BOC-piperidine (99)

(99)
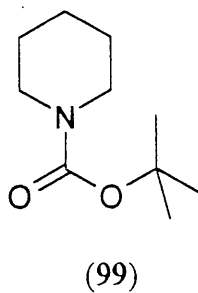
Synthesis of N-BOC-piperidine

Piperidine was dissolved in dichloromethane and triethylamine was added followed by BOC-anhydride in dichloromethane. The solution was allowed to stir for three hours at ambient temperature. The dichloromethane and triethylamine were evaporated giving a white solid, which was characterised using ^{1}H NMR spectroscopy.

Nitrolysis of N-BOC-piperidine

N-BOC-piperidine dissolved in PP6 was treated with three molar equivalents of N_2O_5 in PP6. The solution was stirred for two hours at ambient temperature, the product extracted using dichloromethane. The organic layer was neutralised and removed under reduced pressure giving a brown oil.

The ^{1}H NMR spectrum (**Figure 5.15**) and GCMS (**Figure 5.16**) recorded on the product are shown below.
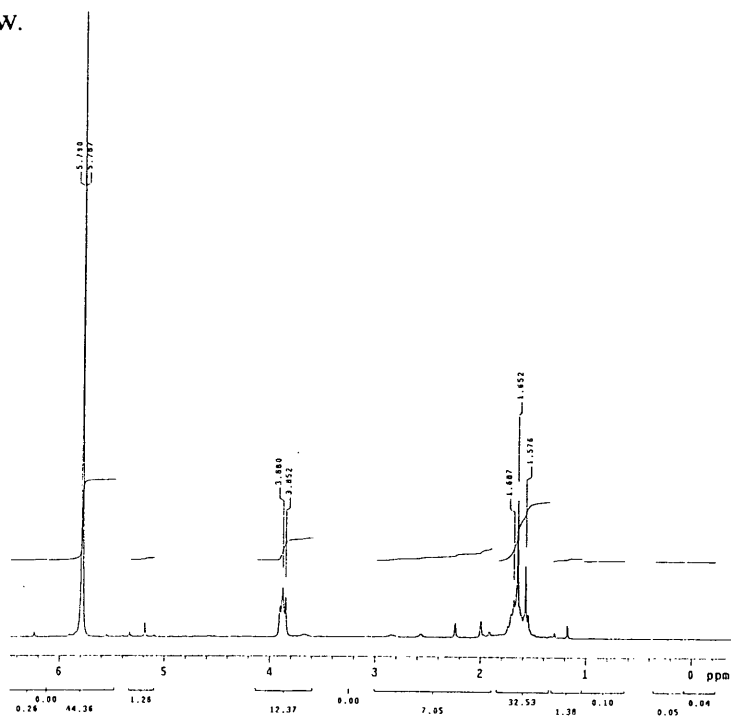
Figure 5.15 ^{1}H NMR spectrum of *N*-nitropiperidine
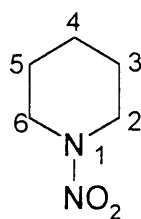
(**100**)

Shift	Multiplicity	Inference
1.58	s	1,1-dimethylethylnitrate
1.65	m	protons in positions 3, 4, 5 in (**100**)
2.49	p	DMSO (solvent)
3.88	m	protons in positions 2, 6 in (**100**)
5.79	s	dichloromethane (added as reference)

Table 5.15 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitropiperidine (**Figure 5.15**)
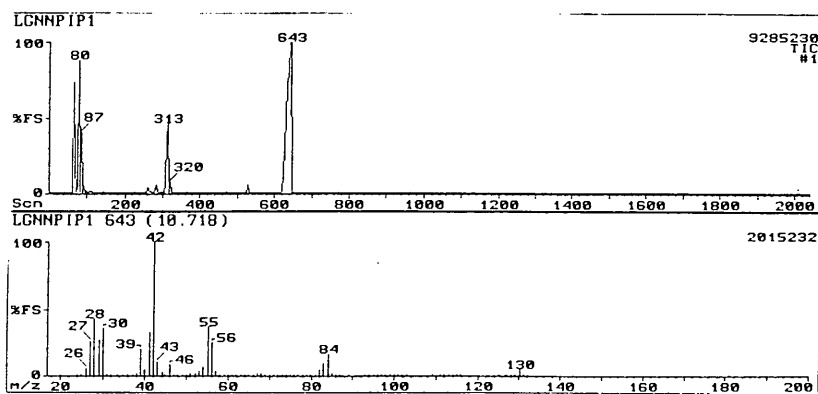

Figure 5.16 GCMS of *N*-nitropiperidine

The ^{1}H NMR spectrum (**Figure 5.13**) from the reaction contained multiplets at $\delta1.65$ ppm and δ 3.88 ppm (lit.^{7} δ 1.65 ppm (m) and δ 3.85 ppm (m) in CDCl$_3$). The GCMS (**Figure 5.14**) contains a chromatograph signal at 643s that corresponds to a molecular mass of 130, (Mr of *N*-nitropiperidine is 130).

N-BOC-piperidine can be successfully nitrated with N$_2$O$_5$ using this system, (**Scheme 5.15**). The crude yield for the total product was 133 %. Assuming that the impurity is 1,1-dimethylethylnitrate the ^{1}H NMR spectrum shows the product was about 70% pure. Therefore we can estimate the yield of *N*-nitropiperidine to be 95 %.
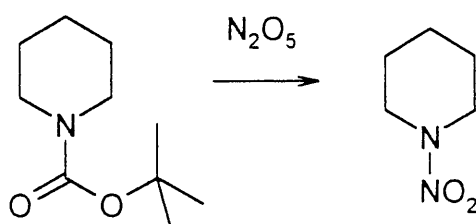
Scheme 5.15 Nitrolysis of *N*-BOC-piperidine in PP6 using N$_2$O$_5$

5.5.4 *N*-di-BOC-Hexahydropyrimidine (101)

(101)
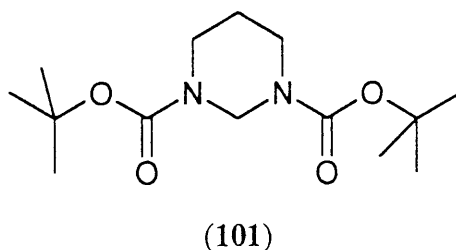
It was of interest to see whether reaction with N$_2$O$_5$ in PP6 could be used to prepare a derivative containing two *N*-nitro groups. It is known[17] that the reaction of 1,3-diaminopropane with formaldehyde may yield hexahydropyrimidine. It was planned to prepare this parent di-amine, react it in situ with BOC-anhydride to yield the di-*N*-BOC derivative, and finally to carry out a nitrolysis reaction.

Synthesis of Hexahydropyrimidine

1,3-Diaminopropane was dissolved in water and hydrochloric acid solution was added until neutralised. A further portion of 1,3-diaminopropane was added followed by formaldehyde. The solution was cooled and sodium hydroxide was added. The product was extracted with dichloromethane. The product was left in the dichloromethane for the following reaction and was not characterised because it was known to be very unstable.

The reaction pathway is outlined in **Scheme 5.16**. The initial step is designed to produce the mono-hydrochloride. Reaction with formaldehyde will result in formation of a carbinolamine which may dehydrate to yield an imine.
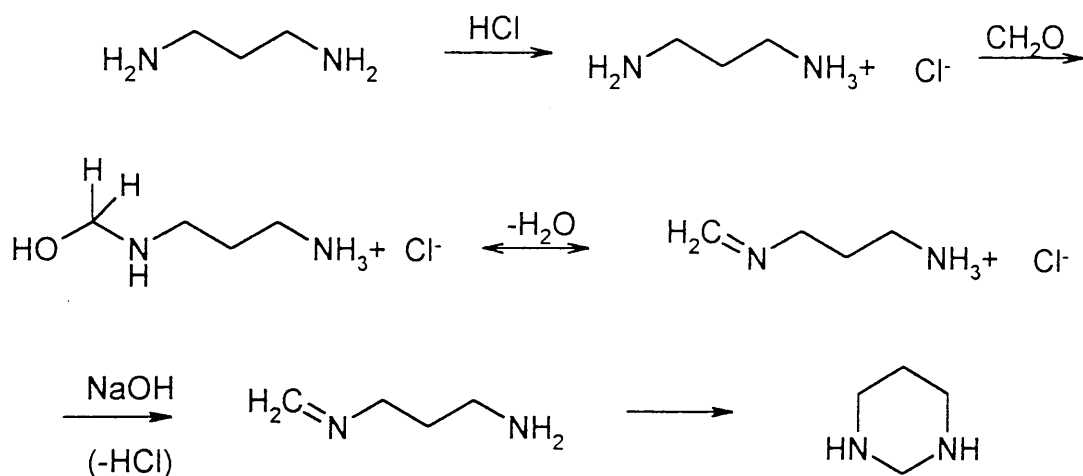
Scheme 5.16 Synthesis of hexahydropyrimidine

The function of the sodium hydroxide is to liberate the second amino group, so that cyclisation to hexahydropyrimidine may occur.

Synthesis of di-N-BOC-hexahydropyrimidine

BOC-anhydride was added to the solution of hexahydropyrimidine in dichloromethane followed by triethylamine. The reaction mixture was stirred for three hours at ambient temperature and the dichloromethane was evaporated yielding the product as an oil.

Nitrolysis of N-BOC-hexahydropyrimidine

Di-*N*-BOC-hexahydropyrimidine dissolved in PP6 was treated with N_2O_5 in PP6 and the solution stirred for three hours at ambient temperature. The product was extracted with dichloromethane, neutralised and the dichloromethane evaporated. The product (oil) was examined by ${}^1H$ NMR spectroscopy (**Figure 5.17**) and GCMS.

The product has not been completely characterised. However there is evidence that some dinitrohexahydropyrimidine is present.
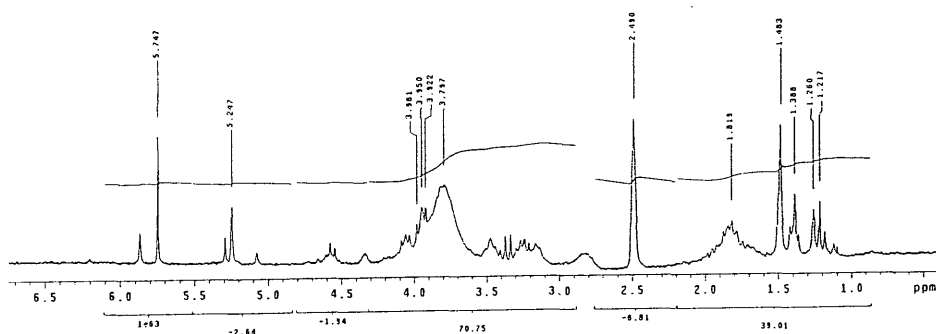
Figure 5.17 ${}^1H$ NMR spectrum of nitrated hexahydropyrimidine (**102**)
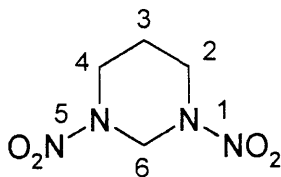
(**102**)

Shift / ppm	Multiplicity	Inference
		impurity
1.82	m	protons in positions 3 in (102)
2.49	p	DMSO (solvent)
3.95	m	protons in positions 2, and 4 in (102)
5.75	s	protons in position 6 in (102)

Table 5.16 Shifts, multiplicity and inference for the ^{1}H NMR spectrum of *N*-nitropiperidine (**Figure 5.17**)

The ^{1}H NMR spectrum (**Figure 5.17**) of the product contained signals at δ 5.75 ppm (s), δ 3.9 ppm (m) and δ 1.8 ppm (m), which could be assigned to the dinitroderivative (**102**). There was also a signal at δ 5.25 (s) which could be assigned to the mononitroderivative. Impurities could also be seen.

The GC mass spectrum contains a signal at 130 m/z, which could correspond to the loss of one NO_2 from the dinitroderivative. The crude yield was 86 % but impurities were present.

5.6 Nitration of ^{t}butylpyrrolidine (106) by chloride catalysis[18]
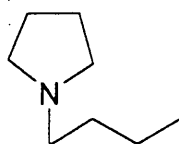
(106)

Cliff[18] has reported the chloride-assisted nitrolysis of cyclic tertiary amines. The process is effective for heterocyclic systems containing a single tertiary amine moiety and gives good

yields for primary, secondary and tertiary alkyl leaving groups. Heterocyclic systems were nitrated via a ^{t}butyl leaving group.

Attempted nitration of ^{t}butyl-pyrrolidine

N-Butylpyrrolidine was dissolved in PP6 and tetra-methylammoniumchloride was added followed by nitric acid to give a two phase system. The solution was extracted using dichloromethane and characterised using ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum showed signals that could be assigned to the product *N*-nitropyrrolidine, but also contained several impurities. Therefore this approach was not continued.

5.7 Solubility of hexamine, DAPT, and DNPT in perfluorocarobons

Saturated solutions of hexamine (**103**), 3,7-diacetyl-1,3,5,7-tetra-aza-bicyclononane DAPT (**104**), and 3,7-dinitro-1,3,5,7-tetra-aza-bicyclononane DNPT (**105**) were prepared in PP6 and perfluoroether (HT135). UV/Vis spectra and IR spectra were recorded on the saturated solutions. Both sets of spectra showed no absorbance. It was concluded that the hexamine, DAPT and DNPT were insoluble in PP6 and PFE. Therefore these compounds were not tested further.

(103)   (104)   (105)
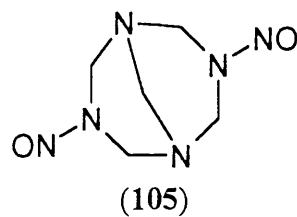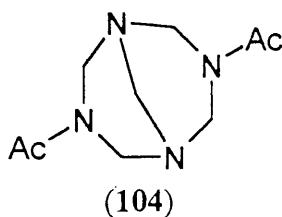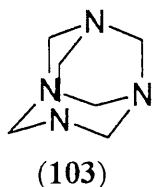
5.8 Summary of the reactions of amines with N_2O_5
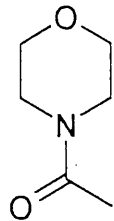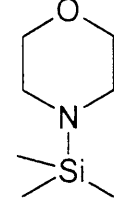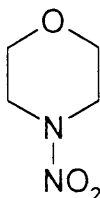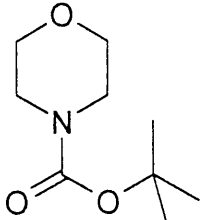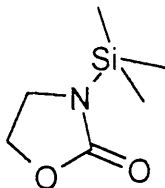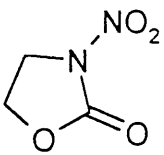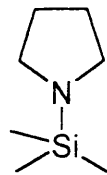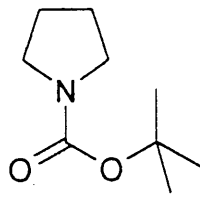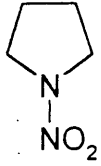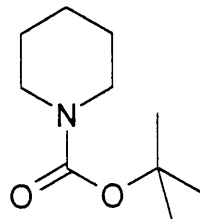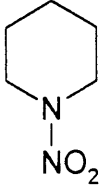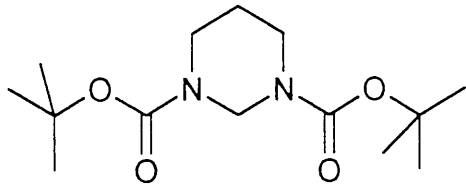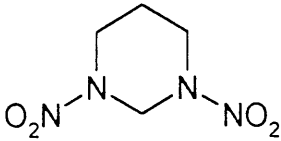
Amine	Nitramine	Yield / %	ME of N_2O_5
		100	4
		53	3
		89	3
		73	3
		42	3
		88	2
		95	3

Table 4.17 Reactions of amines with N_2O_5

Dinitramine

Amine	Dinitramine	Yield %	ME of N_2O_5
		86	6

ME represents molar equivalents

Table 4.18 Reactions of di-nitramines with N_2O_5

A summary of all the reactions described in this chapter is given in **Table 4.17** and **Table 4.18.**

5.9 Conclusions

Previously silyl-amines have been successfully nitrated using N_2O_5 in dichloromethane[7] and we report similar results and similar yields (**Table 4.19**).

Amine (*N*-trimethly silyll-)	Lit.[7] results in dichloromethane				Our results in PFC			
	Time / hr	Temp / °C	Molar equivalent of N_2O_5	Yield / %	Time / hr	Temp / °C	Molar equivalent of N_2O_5	Yield / %
Morpholine	2	0	1	80	3	ambient	3	53
Pyrrolidine	0.5	0	1	86	3	ambient	3	42
Oxazolidinone	0.7	0	1	80	1	ambient	3	73

Table 4.19 Comparison with literature results for the nitrolysis of various *N*-silylamines

The results obtained with the silylamine indicate that reaction with N_2O_5 in perfluorocarbon solvent successfully yields nitramine derivatives. In general three molar equivalents of N_2O_5 were used, but it may be possible to achieve comparable yields using smaller excesses of the nitrating agent.

The results in **Table 4.17** show that excellent yields are obtainable starting from *N*-BOC amines. Generally three equivalents of N_2O_5 were used. However the results suggest that

yields may be only slightly reduced using one equivalent of N_2O_5. There have been no previous reports of the successful nitration of *N*-BOC amines with N_2O_5 but the results presented here indicate that this is a useful method.

Therefore it can be concluded that the synthesis of nitramines in the systems used is successful and has many advantages over previous methods using nitric acid in acetic anhydride.

The extraction process which proved most successful involved washing the products from the perfluorocompounds with dichloromethane. Hence there is the possibility of recycling the perfluorocarbon solvent without purification. In this work the nitramines were obtained by allowing dichloromethane to evaporate. However in a commercial operation distillation would allow recovery of dichloromethane. The use of this method could have an impact on the environment in future manufacture of energetic materials.

5.10 References

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Chapter Six

6 Experimental methods

6.1 Materials

Most materials were purchased commercially from Aldrich and used without further purification unless otherwise stated.

The perfluorocarbon solvents were obtained from F2 Chemicals LTD. Perfluoroether (HT135) was supplied from Ausimont.

100% nitric acid was prepared from 98% sulfuric acid and potassium nitrate (**see section 6.3**).

Dinitrogen pentoxide was supplied by DERA and was stored in a freezer at –60 °C.

6.2 Equipment

Absorption Spectra

The absorption spectra were recorded on a Perkin-Elmer Lambda 2 or a Shimadzu 2101-PC U.V./Visible spectrometer at 25 °C using 1 cm stoppered quartz cuvettes. All kinetic measurements were made under pseudo first order conditions and observed rate coefficients were determined by following the change in absorbance at an appropriate wavelength. Exponential fits for kinetic runs were obtained using a graphical method, which calculates the observed rate coefficient k_{obs}, which was based on the following derivation;

For a first order kinetic process (**Equation 6.1**), the rate of formation of B or the removal of A can be expressed by **Equation 6.2.**

$$A \xrightarrow{k_{obs}} B$$
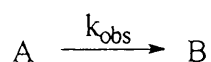
Equation 6.1

$$-\frac{d[A]}{dt} = \frac{d[B]}{dt} = k_{obs}[A]$$

Equation 6.2

Integration of **Equation 6.2** gives an expression for the observed first order rate constant, k_{obs} (**Equation 6.3**).

$$\ln[A]_0 - \ln[A]_t = k_{obs}t$$

Equation 6.3

(where $[A]_0$ and $[A]_t$ are the concentrations of species A at times $t = 0$ and $t = t$ respectively).

Using the Beer-Lambert law ($A = \varepsilon cl$, where A is the absorbance, ε is the molar extinction coefficient, c is the concentration and l the path length), and assuming the latter to be 1cm, the expression of the absorbance at $t = 0$ and $t = t$ can be derived (**Equations 6.4 and 6.5**).

$$A_0 = \varepsilon_A[A]_0$$

$$A_t = \varepsilon_A[A]_t + \varepsilon_B[B]_t$$

Equations 6.4 and 6.5 respectively

As $[B]_t = [A]_0 - [A]_t$, substituting for $[B]_t$ into **Equation 6.5** gives-

$$A_t = \varepsilon_A[A]_t + \varepsilon_B[A]_0 - \varepsilon_B[A]_t$$

Equation 6.6

At the end of reaction, $t = \infty$ and $[B]_\infty = [A]_0$, so-

$$A_\infty = \varepsilon_B[A]_0$$

Equation 6.7

Substituting into equation 6.6-

$$A_t = \varepsilon_A[A]_t + A_\infty - \varepsilon_B[A]_t, \text{ thus}$$

$$[A]_t = \frac{(A_t - A_\infty)}{(\varepsilon_A - \varepsilon_B)}$$

Equation 6.8

Similarly, at time $t = 0$-

$$A_0 = \varepsilon_A[A]_0$$

Equation 6.9

Hence, subtracting **Equation 6.7** from **Equation 6.9**-

$$(A_0 - A_\infty) = \varepsilon_A[A]_0 - \varepsilon_B[A]_0, \text{ and}$$

$$[A]_0 = \frac{(A_0 - A_\infty)}{(\varepsilon_A - \varepsilon_B)}$$

Equation 6.10

Substituting **Equations 6.8** and **6.10** into **Equation 6.3** yields-

$$k_{obs} = \frac{1}{t} \ln \frac{(A_0 - A_\infty)}{(A_t - A_\infty)}$$

Equation 6.11

Rearranging gives-

$$\ln(A_t - A_\infty) = -k_{obs}t + \ln(A_0 - A_\infty)$$

Equation 6.12

Therefore, a plot of $\ln(A_t - A_\infty)$ against t should be linear with a slope of $-k_{obs}$. The infinity values A_∞, were determined after a period of ten half lives and the disappearance of absorbance followed for at least two half lives.

In the reactions followed kinetically, there is an increase in absorbance with time. Hence the concentration of reactant is measured by the value of $(abs)_\infty$ - abs.

NMR spectra

^1H, and ^{13}C NMR spectra were recorded on a Varian VXR-200 VXR-300 or VRX-400 (400 MHz) instruments.

DMSO-d_6 was used as the solvent unless otherwise stated. Chemical shifts are quoted as δ values relative to tetramethylsilane (TMS). NMR data in experimental methods are set out in following way: shift (number of protons, multiplicity, coupling constant, assignment)

Mass spectra

Mass spectra were recorded by electron ionisation method on a VG 707E instrument supplied by V.G.Analytical Limited. Electron ionisation (EIMS), chemical ionisation(CIMS) or gas chromatography (GCMS) were employed.

HPLC measurements

HPLC measurements were carried out by L. Lauchlan using a Varian star system.

Melting Points

Melting points were obtained using an Electrothermal 9100 apparatus and were not corrected.

IR spectroscopy

IR spectra were obtained using a Perkin-Elmer 1600 series FTIR spectrometer using golden gate attachment.

6.3 General methods

Preparation of 100% nitric acid

A quick fit distillation apparatus was set-up. This consisted of a three necked 500 ml round bottom flask, fitted with a gas introduction tube, a stopper, and a thermometer used to measure the head temperature, attached to a descending Liebig condenser. The descending condenser was attached to a receiver bend with a vacuum take off and a 100 ml collection conical flask. The apparatus was dried overnight.

The apparatus was assembled under a stream of dry nitrogen. 98 % sulfuric acid (200 g, 2.02 mol) was placed in the distillation flask and potassium nitrate (103.1 g, 1.03 mol) was added with magnetic stirring. The distillation flask was placed on an oil bath under a slow stream of nitrogen. A weak vacuum was applied by water aspirator, (15 mmHg).

Nitric acid started to distil at a pot temperature of 120-140 °C and head temperature of 55 °C. Nitric acid was collected when the solution started to clear, the first 10ml fraction was yellow then the solution cleared, increasing the flow of nitrogen helped clear the solution and drive off the remaining nitric acid.

The apparatus was allowed to cool and the spent acid was disposed of by carefully addition, with stirring, to a large volume of iced water followed by neutralistion by sodium hydrogen carbonate.

The 100 % nitric acid was stored in a fridge and could be used until discoloration occurred.

Preparation of N$_2$O$_5$ in solution

Dinitrogen pentoxide was supplied by DERA and was stored in a freezer at –60 °C. The best method for transferring N$_2$O$_5$ into solution was found to be simply pouring the N$_2$O$_5$ into the solvent carefully. The solution can then be stored in a freezer at –30 °C, in a round-bottom flask fitted with a septum. Other methods were tried but resulted in discoloration of solution. The solution was then transferred by glass syringe into reaction vessels.

Determination of the concentration of N₂O₅ in solution

To determine the concentration of the N_2O_5 in solution a sample was taken from the stock solution (1 cm^3) and added to a known amount of distilled water (50 cm^3) carefully, (**Equation 6.13**).

$$N_2O_5 + H_2O \leftrightarrow 2HNO_3$$
Equation 6.13

This solution was then titrated (5 cm^3 portions) with NaOH (0.01 mol dm^{-3}), using phenol red as indicator (yellow-red), (**Equation 6.14**).
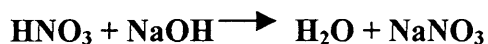
$$HNO_3 + NaOH \rightarrow H_2O + NaNO_3$$
Equation 6.14

The molarity of the N_2O_5 in solution can then be calculated.

Solubility of N₂O₅ in PP6

In order to determine the solubility of N_2O_5 in PP6, the molarity of a saturated solution was measured. The molarity of the saturated solution was about 1 mol dm^{-3}.

6.4 Chapter two experimental

Toluene (33)

(**33**)
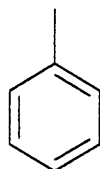
Using nitric acid

Experiment 1 in PP11

PP11 (30 cm^3) was placed in round-bottom flask fitted with an upright condenser. This was heated using an oil bath to 75 °C and toluene (0.724 g, 7.87 mmol) was added until the solution was saturated. Three times the volume of 100 % concentrated nitric acid was added (2.5 cm^3, 59.5 mmol) carefully. The solution was refluxed for 2 hours at 75 °C and constantly stirred using a magnetic stirrer. The solution was left to cool overnight and distilled water was added. The top layer was separated and sodium hydrogen carbonate was added to neutralise the acid and a solid was formed. The yellow solid (0.8561 g, 60 %) was filtered under a vacuum and washed with distilled water. It was were left to dry and a ^{1}H NMR spectrum was recorded on the product.

The bottom layer was washed with distilled water which was then extracted with diethyl ether in order to remove any product in the perfluorocarbon. The diethylether was evaporated off and nothing was left. Therefore the product was situated in the top acid layer.
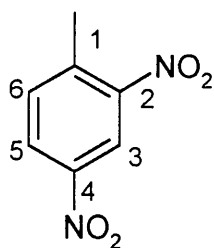
(34)   (35)
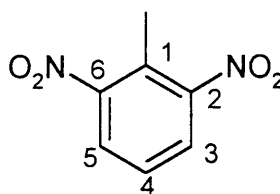
^{1}H NMR spectrum of product;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.80 (1H, d, J$_{65}$=8.3 Hz, H6), 8.45 (1H, dd, J$_{56}$=8.3 Hz,

J$_{53}$ = 2.4 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (80 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, J$_{43\ 45}$ = 8.1 Hz H4), 8.22 (2H, d, J$_{34}$=8.1 Hz,

H3, H5); 2,6-dinitrotoluene (**35**) (20 %)

Comparison of literature and authentic samples for nitrotoluene derivatives

^{1}H NMR spectra were recorded on a sample of 4-nitrotoluene, 2,4-dinitrotoluene, 2,6-
dinitrotoluene.
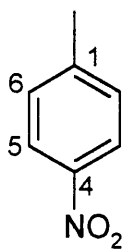
(43)   (34)   (35)
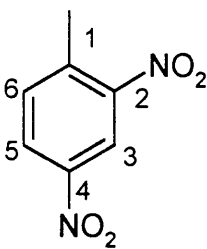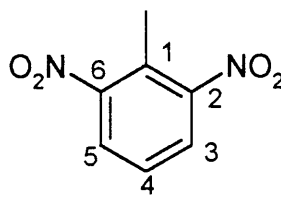
δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.46 (2H, dd, J$_{65\ 23}$ = 7.4 Hz, H2, H6), 8.12 (2H, dd, J $_{56\ 32}$
= 7.4 Hz, H3, H5); 4-nitrotoluene (**43**)

δ_H (d$_6$-DMSO) 2.62 (3H, s, C$\underline{H}_3$), 7.80 (1H, d, J$_{65}$=8.5 Hz, H6), 8.45 (1H, dd, J$_{56}$=8.5 Hz,

J$_{53}$ = 2.4 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**)

δ_H (d_6-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, $J_{43\,45}$ = 8.1 Hz, H4), 8.23 (2H, d, J_{34}=8.1 Hz, H3, H5); 2,6-dinitrotoluene (**36**)

Experiment 2 in perfluoroether (HT135)

A solution of toluene (0.400 g, 4.3 mmol) in perfluoroether (HT135) and 100% concentrated nitric acid (1.0 cm^3, 21.5 mmol) were mixed together and heated to 70 °C for a total of 6 hours. An aliquot was taken from the top layer at 2 hour intervals, distilled water was added and the solution was neutralised with potassium hydrogen carbonate and filtered yielding a yellow solid, (0.3361 g, 43 %).

A ^{1}H NMR spectrum was recorded on each sample.

^{1}H NMR spectrum of product 2 hours;
δ_H (d_6-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.42 (2H, dd, H2, H6), 8.09 (2H, dd, H3, H5); 4-nitrotoluene (**43**) (trace)
δ_H (d_6-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.80 (1H, d, J_{65}=8.4 Hz, H6), 8.44 (1H, dd, J_{56}=8.6 Hz, J_{53} = 2.6 Hz, H5), 8.72 (1H, d, J_{35} = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (95 %)
δ_H (d_6-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (5 %)

^{1}H NMR spectrum of product 4 hours;
δ_H (d_6-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.42 (2H, dd, H2, H6), 8.09 (2H, dd, H3, H5); 4-nitrotoluene (**43**) (trace)
δ_H (d_6-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.80 (1H, d, J_{65}=8.6 Hz, H6), 8.44 (1H, dd, J_{56}=8.6 Hz, J_{53} = 2.6 Hz, H5), 8.72 (1H, d, J_{35} = 2.2 Hz, H3); 2,4-dinitrotoluene (**34**) (95 %)
δ_H (d_6-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, J_{34}=8.1 Hz, H3, H5); 2,6-dinitrotoluene (**35**) (5 %)

^{1}H NMR spectrum of product 6 hours;

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.48 (2H, dd, H2, H6), 8.09 (2H, dd, H3, H5); 4-nitrotoluene (**43**) (trace)

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.80 (1H, d, J_{65} =8.8 Hz, H6), 8.44 (1H, dd, J_{56}=8.6 Hz, J_{53} = 2.6 Hz, H5), 8.72 (1H, d, J_{35} = 2.2 Hz, H3); 2,4-dinitrotoluene (**34**) (95 %)

δ_H (d$_6$-DMSO) 2.43 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, J_{34}=8.1 Hz, H3, H5); 2,6-dinitrotoluene (**35**) (5 %)

Using nitric acid and sulfuric acid

Experiment 1 in PP11

A solution of toluene (0.500 g, 5.44 mmol) in PP11 (20 cm^3) and 100 % concentrated nitric acid (2 cm^3, 47.6 mmol) and 98 % concentrated sulfuric acid (2 cm^3, 37.5 mmol) were mixed and heated to 75 °C for two hours. Distilled water was added and the two layers were separated, the acid layer was neutralised with sodium hydrogen carbonate and the solid were filtered (0.890 g, 83 %). The solvent layer was reused in the following experiment.

(**36**)
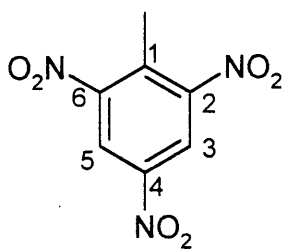
δ_H (d$_6$-DMSO) 2.62 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J_{65} =8.4 Hz, H6), 8.45 (1H, dd, J_{56}=8.5 Hz, J_{53} = 2.5 Hz, H5), 8.72 (1H, d, J_{35} = 2.5 Hz, H3); 2,4-dinitrotoluene (**43**) (57 %)

δ_H (d$_6$-DMSO) 2.43 (3H, s, C$\underline{H}_3$), 7.71 (1H, t, H4), 8.22 (2H, d, $J_{34\,54}$=8.1 Hz, H3, H5); 2,6-dinitrotoluene (**35**) (8 %)

δ_H (d$_6$-DMSO) 2.54 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (35 %)

Experiment 2 further nitration and recycling of solvent

The solvent was reused from the previous experiment. A solution of toluene (0.500 g, 5.44 mmol) and 100 % concentrated nitric acid (3 cm^3, 71.4 mmol) and 98 % concentrated sulfuric acid (3 cm^3, 56.3 mmol) in PP11 (20 cm^3) were mixed together and heated to 75 °C for a total of six hours The yellow solid (0.770 g, 63 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

A ^{1}H NMR spectrum was recorded on each sample taken at 2 hour intervals;

^{1}H NMR spectrum of product 2 hours;
δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.6 Hz, H6), 8.45 (1H, dd, J$_{56}$=8.5 Hz, J$_{53}$ = 2.5 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (40 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (60 %)

^{1}H NMR spectrum of product 4 hours;
δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.6 Hz, H6), 8.45 (1H, dd, J$_{56}$=8.5 Hz, J$_{53}$ = 2.5 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (15 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (85 %)

^{1}H NMR spectrum of product 6 hours;
δ_H (d$_6$-DMSO) 2.66 (3H, s, C$\underline{H}_3$) in 2,4-dinitrotoluene (**34**) only a small aliphatic band could be seen (5%)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6), in 2,4,6-trinitrotoluene (**36**) (95%)

Experiment 3 in PP6

A solution of toluene (1.300 g, 14.1 mmol) and 100% concentrated nitric acid (3 cm^3, 71.4 mmol) and 98 % concentrated sulfuric acid (4 cm^3, 75.1 mmol) in PP6 (30 cm^3) were mixed together and warmed to 80 °C for a total of 6 hours. An aliquot was taken at 2 hour intervals. The yellow solid (0.690 g 22 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate

A ^{1}H NMR spectrum was recorded on each sample taken at 2 hour intervals;

^{1}H NMR spectrum of product 2 hours;
δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.5 Hz, H6), 8.45 (1H, dd, J$_{56}$ = 9.1 Hz, J$_{53}$ = 2.5 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.7 Hz, H3); 2,4-dinitrotoluene (**34**) (30 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (70 %)

^{1}H NMR spectrum of product 4 hours;
δ_H (d$_6$-DMSO) 2.64 (3H, s, C$\underline{H}_3$) in 2,4-dinitrotoluene (**34**) only a small aliphatic band could be seen (10 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (90 %)

^{1}H NMR spectrum of product 6hours;
δ_H (d$_6$-DMSO) 2.66 (3H, s, C$\underline{H}_3$) in 2,4-dinitrotoluene (**34**) only a small aliphatic band could be seen (3 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6), in 2,4,6-trinitrotoluene (**36**) (97%)

Experiment 4 in PP2

A solution of toluene (1.600 g, 17.4 mmol) in PP2 (30 cm^3) and 100 % concentrated nitric acid (3.6 cm^3, 85 mmol) and 98 % concentrated sulfuric acid (4.5 cm^3, 85 mmol) were mixed together and heated to 70°C for a total of six hours. An aliquot was taken at 2 hour

intervals. The yellow solid (3.300 g, 85 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

A ^{1}H NMR spectrum was recorded on each sample taken at 2 hour intervals;

^{1}H NMR spectrum of product 2 hours;
δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.5 Hz, H6), 8.45 (1H, dd, J$_{56}$= 8.4 Hz, J$_{53}$ = 2.4 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (69 %)
δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5);2,6-dinitrotoluene (**35**) (6 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (25 %)

^{1}H NMR spectrum of product 4 hours;
δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.5 Hz, H6), 8.45 (1H, dd, J$_{56}$= 8.4 Hz, J$_{53}$ = 2.4 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (49 %)
δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (8 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (43 %)

^{1}H NMR spectrum of product 6hours;
δ_H (d$_6$-DMSO) 2.66 (3H, s, C$\underline{H}_3$); 2,4-dinitrotoluene (**34**) only a small aliphatic band could be seen (3 %)
δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.01 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (97%)

Experiment 5 in perfluoroether (HT135)

A solution of toluene (0.4285 g, 4.66 mmol) in perfluoroether (HT135) (30 cm^3) and 100 % concentrated nitric acid (1.0 cm^3, 21.5 mmol) and 98 % concentrated sulfuric acid (1.2 cm^3, 22.5 mmol) were mixed together and heated to 70 °C for a total of six hours. An aliquot

was taken at 2 hour intervals. The yellow solid (0.4931 g, 60 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

A ^{1}H NMR spectrum was recorded on each sample taken at 2 hour intervals;

^{1}H NMR spectrum of product 2 hours;

δ_H (d$_6$-DMSO) 2.65 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J_{65} = 9.0 Hz, H6), 8.45 (1H, dd, J_{56} = 8.4 Hz, J_{53} = 2.4 Hz, H5), 8.73 (1H, d, J_{35} = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (71 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (12 %)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.03 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (17 %)

^{1}H NMR spectrum of product 4 hours;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J_{65} =8.4 Hz, H6), 8.45 (1H, dd, J_{56} = 8.6 Hz, J_{53} = 2.2 Hz, H5), 8.72 (1H, d, J_{35} = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (68 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (trace)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.02 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (32 %)

^{1}H NMR spectrum of product 6 hours;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J_{65} =8.6 Hz, H6), 8.45 (1H, dd, J_{56} = 8.6 Hz, J_{53} = 2.6 Hz, H5), 8.72 (1H, d, J_{35} = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (68 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (trace)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.02 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (32 %)

Experiment 6 in perfluoroether (HT135) using a larger excess of mixed acid

A solution of toluene (0.4000 g, 4.34 mmol) in perfluoroether (HT135) (30 cm^3) and 100 % concentrated nitric acid (2.0 cm^3, 47.6 mmol) and 98 % concentrated sulfuric acid (2.2 cm^3, 41.3 mmol) were mixed together and heated to 70 °C for a total of two hours. The product (0.4227 g, 43 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product 2 hours;

δ_H (d$_6$-DMSO) 2.64 (3H, s, C$\underline{H}_3$) in 2,4-dinitrotoluene (**34**) only a small aliphatic band could be seen (3 %)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.03 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (97 %)

Using nitric acid and nafion-H membrane

100 % concentrated nitric acid (2 cm^3, 47.6 mmol) (10 molar equivalents) was added to toluene (0.4038 g, 4.39 mmol) in PP2 (30 cm^3). Nafion-H membrane was added (2 cm square) to the reaction mixture. The reaction was stirred for 6 hours at 70°C. Distilled water was added and the membrane was removed. The yellow solid (0.4206 g, 65 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product 6 hours;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$=8.6 Hz, H6), 8.45 (1H, dd, J$_{56}$= 8.6 Hz, J$_{53}$ = 2.6 Hz, H5), 8.72 (1H, d, J$_{35}$ = 2.4 Hz, H3); 2,4-dinitrotoluene (**34**) (75 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.22 (2H, d, J$_{34\,54}$= 8.2 Hz, H3, H5); 2,6-dinitrotoluene (**35**) (25 %)

Using N_2O_5

Experiment 1 in PP6 at 0 °C

Toluene (0.500 g, 5.4 mmol) was dissolved in PP6 (10 cm^3) and a solution of N_2O_5 (15 cm^3, 1.025 mol dm^{-3}) in PP6 was added using a glass syringe at 0°C and was allowed to stir overnight gradually reaching ambient temperature. The yellow solid (0.370 g, 37 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product 12 hours;

δ_H (d$_6$-DMSO) 2.65 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$ = 8.4 Hz, H6), 8.45 (1H, dd, J$_{56}$ = 8.6 Hz, J$_{53}$ = 2.2 Hz, H5), 8.73 (1H, d, J$_{35}$ = 2.0 Hz, H3); 2,4-dinitrotoluene (**34**) (78 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (15.5 %)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.03 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (6.5 %)

Experiment 2 in PP6 (larger excess of N_2O_5) at 0 °C

Toluene (0.300 g, 3.26 mmol) was dissolved in PP6 (10 cm^3) and a solution of N_2O_5 (15 cm^3, 1.025 mol dm^{-3}) in PP6 was added using a glass syringe at 0 °C and was allowed to stir overnight gradually reaching ambient temperature. The yellow solid (0.330 g, 56 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product 12 hours;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J$_{65}$ = 8.4 Hz, H6), 8.45 (1H, dd, J$_{56}$ = 8.6 Hz, J$_{53}$ = 2.2 Hz, H5), 8.73 (1H, d, J$_{35}$ = 2.0 Hz, H3); 2,4-dinitrotoluene (**34**) (73 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (16 %)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.03 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (11 %)

Experiment 3 in PP6 at ambient temperature

Toluene (0.300 g, 3.26 mmol) was dissolved in PP6 (10 cm^3) and a solution of N_2O_5 (15 cm^3, 1.025 mol dm^{-3}) in PP6 was added using a glass syringe at ambient temperature and was allowed to stir overnight. The yellow solid (0.320 g, 54 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product 12 hours;

δ_H (d$_6$-DMSO) 2.63 (3H, s, C$\underline{H}_3$), 7.81 (1H, d, J_{65} = 8.4 Hz, H6), 8.45 (1H, dd, J_{56} = 8.6 Hz, J_{53} = 2.2 Hz, H5), 8.73 (1H, d, J_{35} = 2.0 Hz, H3); 2,4-dinitrotoluene (**34**) (90 %)

δ_H (d$_6$-DMSO) 2.44 (3H, s, C$\underline{H}_3$), 7.70 (1H, t, H4), 8.23 (2H, d, H3, H5); 2,6-dinitrotoluene (**35**) (10 %)

δ_H (d$_6$-DMSO) 2.55 (3H, s, C$\underline{H}_3$), 9.03 (3H, s, H6); 2,4,6-trinitrotoluene (**36**) (trace)

Benzene (38)

(38)
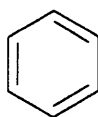
Using nitric and sulfuric acid

Experiment 1 in PP6

Into a round bottomed flask fitted with a condenser was placed PP6 (30 cm^3), and benzene (0.4 cm^3, 4.51 mmol) was added, the solution was stirred during the addition. 100% nitric acid (2 cm^3, 47.6 mmol) followed by 98% concentrated sulfuric acid (1.5 cm^3, 28.1 mmol) were added. The solution was heated to 70 °C for a total of 20 hours, (after 6 hours and 12 hours an aliquot was taken from the top acidic layer). Distilled water was added to the samples and the remaining reaction mixture, the solutions were neutralised with sodium hydrogen carbonate. The yellow solid (0.463 g, 62 %) was filtered under vacuum and ^{1}H NMR spectrum was used to characterise the product.
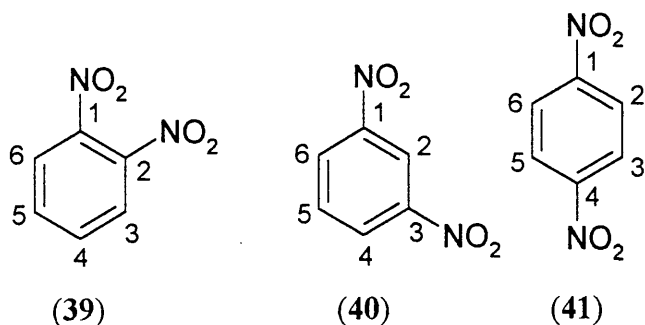
(39)   (40)   (41)

A ^{1}H NMR spectrum was recorded on each sample taken after 6, 12 and 20 hours;

^{1}H NMR spectrum of product after 6 hours;
δ_H (d$_6$-DMSO) 7.96 (1H, t, H5), 8.65 (2H, dd, $J_{45\,65}$ = 10.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, s, H2); 1,3-dinitrobenzene (**40**) (100 %)

^{1}H NMR spectrum of product after 12 hours;

δ_H (d$_6$-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (10 %)

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 11.7 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.16 Hz, H4, H6), 8.82 (1H, s, H2); 1,3-dinitrobenzene (**40**) (87 %)

δ_H (d$_6$-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (3%)

^{1}H NMR spectrum of product after 20 hours;

δ_H (d$_6$-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (10 %)

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.08 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.16 Hz, J$_{46}$ = 3Hz, H4, H6), 8.82 (1H, s, H2); 1,3-dinitrobenzene (**40**) (87 %)

δ_H (d$_6$-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (3%)

Comparison with authentic samples for nitrobenzene derivatives

A^{1}H NMR spectrum was recorded on a sample of nitrobenzene, 1,2-dinitrobenzene, 1,3-dinitrobenzene, 1,4-dinitrobenzene, and 3-nitrophenol.

(44)　(39)　(40)　(41)　(45)
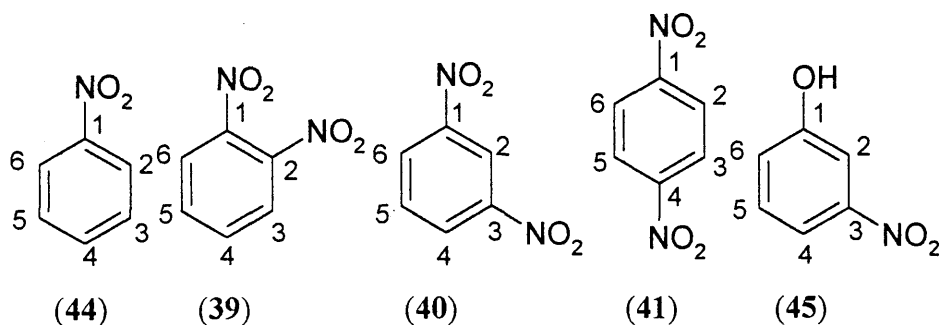
δ_H (d$_6$-DMSO) 7.63 (2H, t, J$_{32\ 56}$ = 7.2 Hz, J$_{34\ 32}$ = 7.6 Hz, H3, H5), 7.81 (1H, t, J$_{43\ 45}$ = 7.2 Hz, H4) 8.18 (2H, d, J$_{23\ 65}$ = 7.6 Hz, H2, H6); nitrobenzene (**44**)

δ_H (d$_6$-DMSO) 7.95 (2H, m, H4, H5) 8.22 (2H, m, H3, H6); 1,2-dinitrobenzene (**39**)

δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.1 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.1 Hz, J_{46} = 3Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**)

δ_H (d_6-DMSO) 8.44 (4H, s, H2, H3, H5, H6); 1,4-dinitrobenzene (**41**)

δ_H (d_6-DMSO) 7.21 (1H, m, H6), 7.45 (1H, t, H2) 7.54 (1H, t, H5) 7.65 (1H, m, H4) 10.42 (1H, s, O$\underline{H}$); 3-nitrophenol (**45**)

Experiment 2 in perfluoroether (HT135)

Benzene (0.5 cm^3, 5.6 mmol) was dissolved in perfluoroether (HT135) (30 cm^3) and 100% nitric acid (2.4 cm^3, 56 mmol) and sulfuric acid (3 cm^3, 56 mmol) were added. The solution was stirred for 6hours at 70°C. The yellow solid (0.500 g, 55 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

(**42**)

δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.1 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.1 Hz, J_{46} = 3 Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (99 %)

δ_H (d_6-DMSO) 9.46 (3H, s, H2, H4, H6); 1,3,5-trinitrobenzene (**42**)(1 %)

Using nitric acid and oleum

Experiment 1 in PP6

Benzene (0.4 cm^3, 4.5 mmol) was dissolved in PP6 (30 cm^3) and 100 % nitric acid (2 cm^3, 45 mmol) followed by oleum 12-17% free SO$_3$ (3 cm^3, 45 mmol) were added. The solution was heated for a total of 20 hours at 70 °C, (after 6 hours and 12 hours an aliquot was taken from the top acid layer). The yellow solid (0.444 g, 60 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

A ^{1}H NMR spectrum was recorded on each sample taken after 6, 12 and 20 hours;

^{1}H NMR spectrum of product after 6 hours;

δ_H (d$_6$-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (7 %)

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.4 Hz, J$_{46}$ = 2.2 Hz, H4, H6), 8.83 (1H, t, J$_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (91 %)

δ_H (d$_6$-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (2 %)

^{1}H NMR spectrum of product after 12 hours;

δ_H (d$_6$-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (8 %)

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.2 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.2 Hz, H4, H6), 8.82 (1H, t, J$_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (90 %)

δ_H (d$_6$-DMSO) 8.44 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (1.5 %)

δ_H (d$_6$-DMSO) 9.15 (3H, s, H2, H4, H6); 1,3,5-trinitrobenzene (**42**) (0.5 %)

^{1}H NMR spectrum of product after 20 hours;

δ_H (d$_6$-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (8 %)

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.2 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.2 Hz, H4, H6), 8.82 (1H, t, J$_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (89.5 %)

δ_H (d$_6$-DMSO) 8.44 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (1.5 %)

δ_H (d_6-DMSO) 9.15 (3H, s, H2, H4, H6); 1,3,5-trinitrobenzene (**42**) (1 %)

Using nitric acid oleum and nafion-H

Experiment 2 using nafion-H beads

Into a round bottomed flask fitted with a condenser was placed PP6 (30 cm^3), and benzene (0.4 cm^3, 4.5 mmol) was added. 100 % nitric acid (3.6 cm^3, 85 mmol) followed by oleum 12-17% free SO_3 (4.5 cm^3, 85 mmol) were added. Nafion-H beads were added (2.340 g). The solution was heated for a total of 12 hours, (after 6 hours a small sample was taken from the top acid layer). The yellow solid (0.284 g, 40 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

A ^{1}H NMR spectrum was recorded on each sample taken after 6, 12 and 20 hours;

^{1}H NMR spectrum of product after 6 hours;
δ_H (d_6-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (trace)
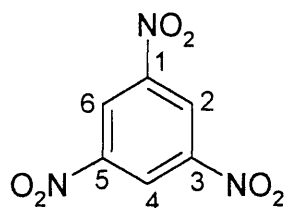δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (100 %)
δ_H (d_6-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (trace)

^{1}H NMR spectrum of product after 12 hours;
δ_H (d_6-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (4 %)
δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.2 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.2 Hz, H4, H6), 8.82 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (92 %)
δ_H (d_6-DMSO) 8.44 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (4 %)

Using N₂O₅

Experiment 1 using N₂O₅

Benzene (0.4 cm³, 4.5 mmol) was dissolved in PP6 (30 cm³), and N_2O_5 in PP6 was added (20 cm³, 1.17 mol dm⁻³). The reaction was stirred for 6 hours at ambient temperature. Distilled water was added and the top layer was separated and neutralised with potassium hydrogen carbonate. The yellow solid (0.302 g, 40 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

^{1}H NMR spectrum of product after 6 hours;

δ_H (d₆-DMSO) 7.5 (6H, s, benzene)

δ_H (d₆-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (trace)

δ_H (d₆-DMSO) 7.96 (1H, t, $J_{54\,56}$ = 8.6 Hz, H5), 8.65 (2H, dd, $J_{45\,65}$ = 8.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, t, $J_{24\,26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (100 %)

δ_H (d₆-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (trace)

Experiment 2 using N₂O₅ and extraction using dichloromethane

Benzene (0.4 cm³, 4.5 mmol) was dissolved in PP6 (30 cm³), and N_2O_5 in PP6 was added (22 cm³, 1.02 mol dm⁻³). The reaction was stirred for 6 hours at ambient temperature. Dichloromethane was added and the top layer was separated, (extraction was repeated 3 times) and neutralised with potassium hydrogen carbonate. The potassium hydrogen carbonate was decanted and the dichloromethane was evaporated yielding a yellow solid (0.643 g, 85 %).

^{1}H NMR spectrum of product after 6 hours;

δ_H (d₆-DMSO) 7.96 (2H, m, H4, H5), 8.22 (2H, m, H2, H6); 1,2-dinitrobenzene (**39**) (12 %)

δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (85 %)

δ_H (d_6-DMSO) 8.45 (4H, s, H2, H3, H5, H6); 1,4-dinitrotoluene (**41**) (3 %)

Experiment 3 using N$_2$O$_5$, nitric acid, and nafion-H beads

Benzene (0.4 cm^3, 4.5 mmol) was dissolved in PP6 (30 cm^3), and N$_2$O$_5$ in PP6 was added (14 cm^3, 0.955 mol dm^{-3}), followed by 100% nitric acid added (2 cm^3, 45 mmol). Nafion-H was added (2.510 g). The reaction was stirred for 3 hours at ambient temperature then for a further 6 hours at 70 °C. An aliquot was taken after 3 hours, distilled water was added. The remaining of the mixture was left for six hours before distilled water was added. The solutions were neutralised with potassium hydrogen carbonate and filtered under vacuum. The yellow solid (0.421 g, 56 %) was characterised using ^{1}H NMR spectroscopy.

A ^{1}H NMR spectrum was recorded on each sample taken after 3 and 9 hours;

^{1}H NMR spectrum of product after 3 hours at ambient temperature;

δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (100 %)

^{1}H NMR spectrum of product after 3 hours at ambient temperature and 6 hours at 70 °C;

δ_H (d_6-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, $J_{45\ 65}$ = 8.4 Hz, J_{46} = 2.2 Hz, H4, H6), 8.83 (1H, t, $J_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (100 %)

Experiment 4 using nitric acid, N$_2$O$_5$ and nafion-H membrane

Benzene (0.4 cm^3, 4.5 mmol) was dissolved in PP6 (30 cm^3), and N$_2$O$_5$ in PP6 was added (13 cm^{3,} 1.02 mol dm^{-3}), followed by 100% nitric acid added (1.4 cm^3, 33 mmol). Nafion-H membrane was added (2 cm square). The solution was heated for 6 hours at 70 °C. The

yellow solid (0.354 g, 46 %) was separated as in previous experiments using distilled water and sodium hydrogen carbonate.

δ_H (d$_6$-DMSO) 7.96 (1H, t, J $_{54\ 56}$ = 8.6 Hz, H5), 8.65 (2H, dd, J$_{45\ 65}$ = 8.4 Hz, J$_{46}$ = 2.2 Hz, H4, H6), 8.84 (1H, t, J$_{24\ 26}$ = 3 Hz, H2); 1,3-dinitrobenzene (**40**) (100 %)

6.5 Chapter three experimental

Styrene (48)
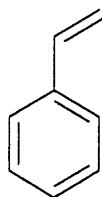
(48)

Nitration of styrene using nitric acid and sulfuric acid

Experiment 1 using ten equivalents of acid

Styrene (0.1132 g, 1.09 mmol) was dissolved in PP6 (30 cm^3) and 100 % nitric acid was added (0.5 cm^3, 11.9 mmol) followed by 98 % sulfuric acid (0.5 cm^3, 9.39 mmol). The solution was heated for 6 hours at 70 °C. Dichloromethane (3 x 10 cm^3) was used to extract the product. The dichloromethane layer was neutralised using potassium hydrogen carbonate. The dichloromethane was decanted and left to evaporate yielding a yellow liquid (0.3126 g). A ^{1}H NMR spectrum and EI mass spectrum were recorded on the product.

The ^{1}H NMR spectrum could not be assigned accurately.

EIMS: found m/z at 212

Comparison to literature and authentic samples for styrene and nitro derivatives

A ^{1}H NMR spectrum was recorded on a sample of styrene;

(48)
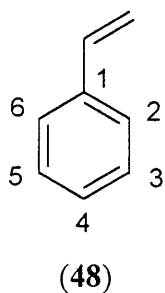
δ_H (d$_6$-DMSO) 5.24 (1H, dd, J = 11 Hz, 1 Hz, C$\underline{H}_2$), 5.81 (1H, d, J = 17 Hz, 1 Hz, C$\underline{H}_2$),

6.71 (1H, dd, J = 17 Hz, 11 Hz, C$\underline{H}$), 7.45 (2H, d, J$_{23\ 65}$ = 7 Hz, H2, H6), 7.32 (2H, t, J$_{32\ 34}$

$_{54\ 56}$ = 7 Hz, H3, H5), 7.27 (1H, t, J$_{43\ 45}$ = 7 Hz, H4); styrene (48)

Literature spectrum for nitro styrene were found to be as follows:

(55)   (24)   (25)   (26)

(27)   (46)
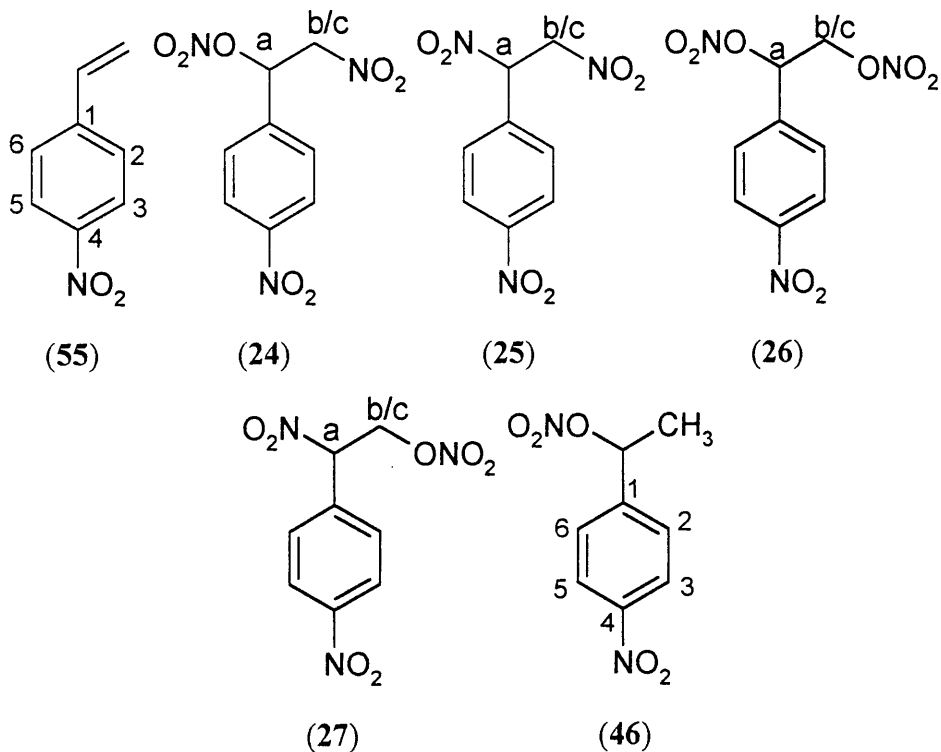
Lewis and Moodie reported the ^{1}H NMR spectrum of 4-nitrostyrene to be as follows: [1]

δ_H (CDCl$_3$) 5.75 (1H, d, C$\underline{H}_2$), 5.87 (1H, d, C$\underline{H}_2$), 6.75 (1H, dd, C$\underline{H}$), 7.50 (2H, d, H2, H6), 8.15 (2H, d, H3, H5); 4-nitrostyrene (**55**)

Lewis and Moodie only reported signals for the aliphatic species in the following examples and referred to them as follows: [1]

δ_H (CDCl$_3$) 4.80 (1H, dd, J_{ac} = 2.19 Hz, Hc) 4.94 (1H, dd, J_{bc} = 9.31 Hz, Hb), 7.63 (1H, dd, J_{ab} = 5.95 Hz, Ha); β-nitro nitrate(**24**)

δ_H (CDCl$_3$) 4.93 (1H, dd, J_{ac} = 2.00 Hz, Hc) 5.67 (1H, dd, J_{bc} = 10.15 Hz, Hb), 6.42 (1H, dd, J_{ab} = 6.72 Hz, Ha); dinitro (**25**)

δ_H (CDCl$_3$) 4.85 (2H, m, Hb, Hc) 6.28 (1H, q, $J_{ab\,ac}$ = 7.20 Hz, Ha); dinitrate(**26**)

δ_H (CDCl$_3$) 5.00 (1H, dd, J_{ac} = 2.25 Hz, Hc) 5.45 (1H, dd, J_{bc} = 8.00 Hz, Hb), 5.97 (1H, dd, J = 6.00 Hz, Ha); α-nitro nitrate(**27**)

The following was reported by Lewis and Moodie: [2]

δ_H (CDCl$_3$) 1.6 (3H, d, C$\underline{H}_3$), 5.9 (1H, q, C$\underline{H}$) 7.3 (5H, m, H2, H3, H4, H5, H6); 1-phenylethyl nitrate (**46**)

*Experiment 2 using one and a half equivalents of acid*

Styrene (0.1080 g, 1.04 mmol) was dissolved in PP6 (30 cm^3) and 100 % nitric acid was added (0.065 cm^3, 1.55 mmol) followed by 98 % sulfuric acid (0.08 cm^3, 1.50 mmol). The solution was heated for 6 hours at 70 °C. Dichloromethane (3 x 10 cm^3) was used to extract the product. The dichloromethane layer was neutralised using potassium hydrogen

carbonate. The dichloromethane was decanted and left to evaporate yielding a yellow/orange liquid (0.0681 g). A ^{1}H NMR spectrum and was recorded on the product.

The ^{1}H NMR spectrum could not be assigned accurately.

Nitration of styrene using N_2O_5

Experiment 1 using three molar equivalents of N_2O_5

Styrene (0.1289 g, 1.24 mmol) was dissolved in PP6 (30 cm^3) and N_2O_5 in PP6 (3 cm^3, 1.128 mol dm^{-3}) were added. The solution was stirred for 3 hours at ambient temperature. Dichloromethane (3 x 10 cm^3) was used to extract the product. The dichloromethane layer was neutralised using potassium hydrogen carbonate. The dichloromethane was decanted and left to evaporate yielding a red liquid (0.2019 g). A ^{1}H NMR spectrum and was recorded on the product.

The ^{1}H NMR spectrum could not be assigned accurately.

Experiment 2 using one and a half molar equivalents of N_2O_5

Styrene (0.1119 g, 1.07 mmol) was dissolved in PP6 (30 cm^3) and N_2O_5 in PP6 (1.6 cm^3, 1.62 mol dm^{-3}) were added. The solution was stirred for 3 hours at ambient temperature. Dichloromethane (3 x 10 cm^3) was used to extract the product. The dichloromethane layer was neutralised using potassium hydrogen carbonate. The dichloromethane was decanted and left to evaporate yielding a red liquid (0.1199 g). A ^{1}H NMR spectrum and was recorded on the product. The product was the separated by column chromatography (silica, eluant 20 % hexane/80 % dichloromethane going to 100 % dichloromethane then methanol).

^{1}H NMR spectrum of first fraction;
δ_H (d$_6$-DMSO) 8.14 (t) 8.27(s) 8.32 (d) 8.40 (dd) unknown compound

δ_H (d$_6$-DMSO) 7.80 (m) 8.32 (d); could be 4-nitrostyrene but no signals could be seen in the aliphatic region

GCMS: found signal at 1055s m/z 148, 1090s m/z 194 and 1096s m/z 194

^{1}H NMR spectrum of second fraction;

δ_H (d$_6$-DMSO) 7.45 (m); in compounds (**24**) (**25**) (**26**) (**27**)

***trans*-Stilbene**
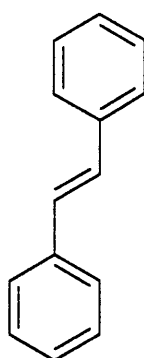
(**49**)

Nitration of trans- stilbene using nitric acid and sulfuric acid

Experiment 1 using ten equivalents of nitric and sulfuric acid

trans -Stilbene (0.1207 g, 0.67 mmol) was dissolved in PP6 (40 cm^3) and 100 % nitric acid (0.28 cm^3, 11.9 mmol) followed by 98 % sulfuric acid (0.5 cm^3, 9.39 mmol) were added. The solution was heated for 6 hours at 75 °C. The PP6 was left to evaporate and the resulting product was washed with distilled water and filtered yielding a yellow solid (0.3126 g). A ^{1}H NMR spectrum, HPLC spectrum, and EI mass spectrum were recorded on the product. The melting point of the solid was 127 °C.

The ^{1}H NMR spectrum could of the nitrated product indicated that a mixture of nitrated derivatives had been produced.

HPLC; found 1.56 mins which was separated and a ^{1}H NMR spectrum was recorded is assigned in **chapter three.**

EIMS; found signal m/z 315. (Mr of trinitrostilbene is 315 g)

Comparison with literature and authentic samples for trans-stilbene
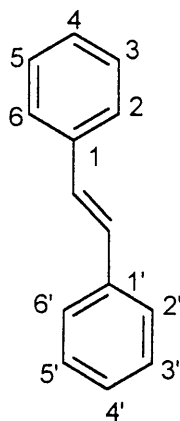
(49)

A ^{1}H NMR spectrum, HPLC spectrum and mass spectrum were recorded on a sample of *trans*-stilbene;

δ_H (d$_6$-DMSO) 3.32 (2H, s, C$\underline{H}$), 7.25 (2H, t, $J_{12\,16}$ = 7.8 Hz, H1, H1'), 7.37 (4H, t, $J_{23\,21\,65\,61}$ = 7.6 Hz, H2, H6, H2', H6'), 7.60 (4H, d, $J_{32\,56}$ = 8.0 Hz, H3, H5, H3', H5'); *trans*-stilbene (49)

HPLC; found 11.57 mins (100% *trans*-stilbene (49))

GCMS; found signal at 1062s m/z 180. (Mr of *trans*-stilbene is 180 g)

Nitration of trans-stilbene using N₂O₅

Experiment 1 using one molar equivalents of N₂O₅

trans-Stilbene (0.0992 g, 0.55 mmol) was dissolved in PP6 and N_2O_5 (0.5 cm³, 1.17 mol dm⁻³) was added. The solution was stirred for 3 hours at ambient temperature. Water was added to quench the reaction followed by potassium hydrogen carbonate for neutralisation. The solid formed was filtered off and dried in a desiccator yielding a yellow solid (0.0726 g). HPLC analysis was undertaken.

HPLC; found 11.48 mins (100% *trans*-stilbene (**49**))

Experiment 2 using three molar equivalents of N₂O₅

trans-Stilbene (0.0990 g, 0.55 mmol) was dissolved in PP6 and N_2O_5 (2.8 cm³, 1.17 mol dm⁻³) was added. The solution was stirred for 3 hours at ambient temperature. Water was added to quench the reaction followed by potassium hydrogen carbonate for neutralisation. The solid formed was filtered off and dried in a desiccator yielding a yellow solid (0.1229 g). HPLC analysis was undertaken.

HPLC; found 11.48 mins (*trans*-stilbene (**49**)) and unknown at 8.36 mins and 1.40 mins. 8.36 mins separated and gave EIMS 315 m/z

Experiment 3 using six molar equivalents of N₂O₅

trans-Stilbene (0.1094 g, 0.60 mmol) was dissolved in PP6 and N_2O_5 (2.0 cm³, 1.03 mol dm⁻³) was added. The solution was stirred for 3 hours at ambient temperature. Water was added to quench the reaction followed by potassium hydrogen carbonate for neutralisation. The solid formed was filtered off and dried in a desiccator yielding a yellow solid (0.1215 g). HPLC analysis was undertaken.

HPLC; found 11.48 mins (*trans*-stilbene (**49**)) and unknown at 8.43 mins, 4.37 and 1.37 mins. 8.36 mins separated and gave EIMS 315 m/z.

6.6 Chapter four experimental

Nitration of 4-chloroanisole (56)
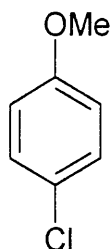
(56)

N_2O_5 was carefully dissolved in PP6 (**see section 6.3**). The solution of N_2O_5 in PP6 (10 cm^3, 0.5 mol dm^{-3}) was added to a solution of 4-chloroanisole (0.2 g, 1.4 mmol) in PP6 (20 cm^3) using a glass syringe at ambient temperature and left to stir for 3 hours. The resulting reaction mixture contained a ratio of 1 molar equivalent of 4-chloroanisole to 4 molar equivalents of N_2O_5. On the addition of distilled water to the reaction mixture a solid was formed. This was filtered under vacuum to give a solid (0.14 g, 48 %). The composition of the solid, determined by integration of the ^{1}H NMR peaks, was 4-chloro-2-nitroanisole 54% and 4-chloro-2,6-dinitroanisole 46%.
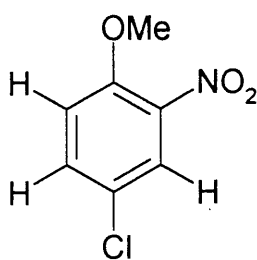
(78)   (79)
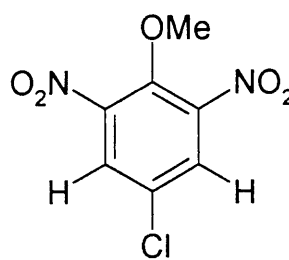
δ_H (d$_6$-DMSO) 8.02 (1H, s, H3), 7.72 (1H, d, J_{56} = 9 Hz, H5), 7.39 (1H, d, J_{65} = 9 Hz, H6), 3.91 (3H, s, C$\underline{H}_3$); 4-chloro-2-nitroanisole (**78**) (54 %)

-228-

δ_H (d$_6$-DMSO) 8.51 (2H, s, H3,H5), 3.92 (3H, s, C$\underline{H}_3$); 4-chloro-2,6-dinitroanisole (**79**) (46 %)

The above experiment was repeated using the same conditions but the solution was allowed to stir for only two minutes before quenching by adding distilled water. The resulting solid composition was determined to be 4-chloro-2-nitroanisole (67 %) and 4-chloro-2,6-dinitroanisole (33 %).

δ_H (d$_6$-DMSO) 8.02 (1H, s, H3), 7.72 (1H, d, J_{56} = 9Hz, H5), 7.39 (1H, d, J_{65} = 9 Hz, H6), 3.91 (3H, s, C$\underline{H}_3$); 4-chloro-2-nitroanisole; (**78**) (67 %)

δ_H (d$_6$-DMSO) 8.51 (2H, s, H3, H5), 3.92 (3H, s, C$\underline{H}_3$); 4-chloro-2,6-dinitroanisole (**79**) (33 %)

UV/Visible absorption of product in PP6 showed λ_{max} = 316 nm, ε = 1913 dm^{3}mol^{-1}cm^{-1} (lit. λ_{max} = 314nm).

Calculation of rate constants assuming two reactions were involved in the nitration of 2-chlorophenol

The rate constant from the first reaction was determined using the data obtained in the first 25 seconds and the second reaction was determined using the data from 100-300 seconds.

Nitration of 2-chlorophenol (57)
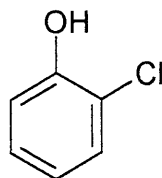
(57)

The solution of N$_2$O$_5$ in PP6 (1 cm^3, 1.155 mol dm^{-3}) was added to a solution of 2-chlorophenol (0.0359g, 0.28 mmol) in PP6 (30 cm^3) at ambient temperature. The resulting

mixture contained a ratio of 1 molar equivalent of 2-chlorophenol to 4 molar equivalents of N_2O_5. An aliquot was taken after 20 seconds and upon the addition of distilled water a solid formed which was collected by filtration. The remainder of the reaction mixture was left for a further 20 minutes before adding distilled water. Filtration under vacuum yielded a solid (0.0159 g, 26 %).

For the sample taken after 20 seconds;

(78)   (79)
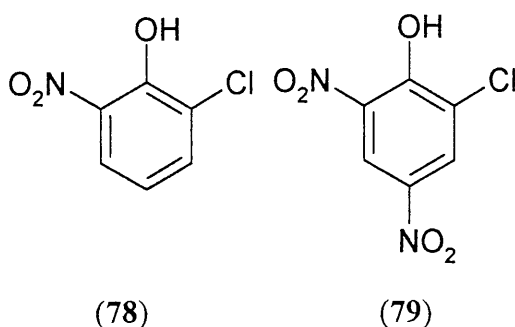
δ_H (d$_6$-DMSO) 6.90 (1H, m, H4), 7.20 (1H, m, H3), 7.35 (1H, m, H5); 2-chloro-6-nitrophenol (**78**) (30 %)

δ_H (d$_6$-DMSO) 8.54 (1H, d, J_{35} = 3 Hz, H5), 8.05 (1H, d, J_{53} = 3 Hz, H3); 2-chloro-4,6-dinitrophenol (**79**) (70 %)

For the product after 20 minutes;
δ_H (d$_6$-DMSO) 8.54 (1H, d, J_{35} = 3 Hz, H5), 8.07 (1H, d, J_{53} = 3 Hz, H3); 2-chloro-4,6-dinitrophenol (**79**) (100 %)

Nitration of 4-chlorophenol (60)

OH

Cl
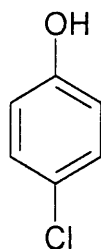
(60)

N_2O_5 in PP6 (1 cm^3, 0.575 mol dm^{-3}) was added to a solution of 4-chlorophenol (0.020 g, 0.156 mmol) in PP6 (20 cm^3) and left to stir for 10 minutes at ambient temperature. The resulting reaction mixture contained a ratio of 1 molar equivalent of 4-chlorophenol to 4 molar equivalents of N_2O_5. On the addition of distilled water to the solution a solid was formed and was collected by filtration to give an orange crystalline solid (0.030g, 89 %).

OH
NO$_2$

Cl

(84)
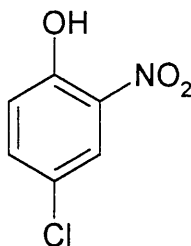
δ_H (d$_6$-DMSO) 7.15 (1H, d, J_{65} = 9 Hz, H6), 7.56 (1H, d, J_{56} = 9 Hz, H5), 7.95 (1H, s, H3); 2-nitro-4-chlorophenol **(84)**

Nitration of 2,4,6-trichlorophenol (63)

OH
Cl   Cl

Cl
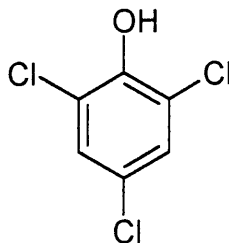
(63)

N_2O_5 in PP6 (1 cm^3, 1.12 mol dm^{-3}) was added to a solution of 2,4,6-trichlorophenol (0.0495 g, 0.25 mmol) in PP6 (30 cm^3) and left to stir for 1 hour at ambient temperature. The resulting reaction mixture contained a ratio of 1 molar equivalent of 2,4,6-trichlorophenol to 4 molar equivalents of N_2O_5. The reaction mixture was left open so that the PP6 and the N_2O_5 would evaporate, resulting in a solid (0.010 g, 17 %). Previous attempts to isolate the product by adding distilled water were not successful.

EIMS m/z= 241 (mononitrotrichlorophenol)

Nitration of 4-bromophenol (64)
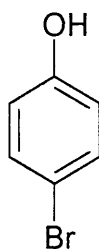
(64)

N_2O_5 in PP6 (0.54 cm^3, 1.02 mol dm^{-3}) was added to a solution of 4-bromophenol (0.0318 g, 0.18 mmol, in PP6 (40 cm^3) at ambient temperature and was left to stir for 1 minute. The resulting reaction mixture contained a ratio of 1 molar equivalent of 4-bromophenol to 6 molar equivalents of N_2O_5. The product was extracted with dichloromethane and neutralised using potassium hydrogen carbonate. The potassium hydrogen carbonate was removed by decanting the solution. The dichloromethane was removed under reduced pressure to give a brown solid (1.15 g, 64 %).

(80)
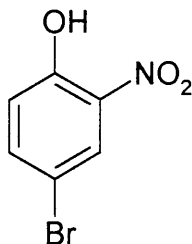
δ_H (d$_6$-DMSO) 8.04 (1H, s, H3), 7.76 (1H, d, J_{56} = 9 Hz, H5), 7.10 (1H, d, J_{65} = 9 Hz, H6); 4-bromo-2-nitrophenol

Nitration of phenol (69)

(69)

Using three equivalents of N$_2$O$_5$

A solution of N$_2$O$_5$ in PP6 (1 cm^3, 0.575 mol dm^{-3}) was added to a solution of phenol (0.02 g, 0.213 mmol) in PP6 (20 cm^3) at ambient temperature and was left to stir for 10 minutes. The resulting reaction mixture contained a ratio of 1 molar equivalent of phenol to 3 molar equivalents of N$_2$O$_5$. On the addition of distilled water to the solution a solid formed and was filtered off under vacuum (0.030 g). ^{1}H NMR spectroscopy was used to determine the composition of the product.

(81)   (82)   (83)   (70)
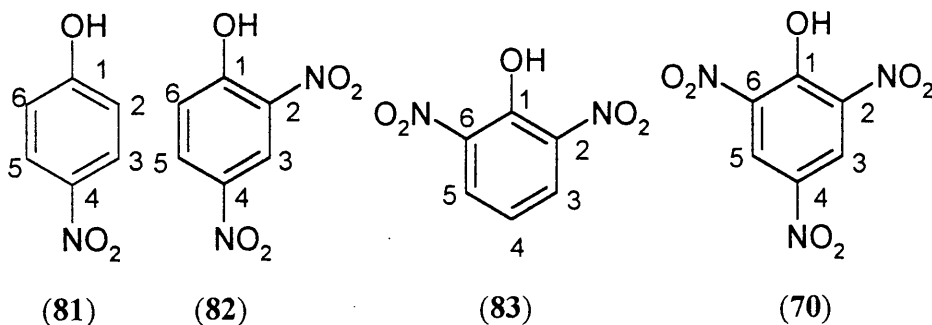
δ_H (d$_6$-DMSO) 6.92 (2H, d, J = 9 Hz, H2 H6), 8.11 (2H, d, J = 9 Hz, H3, H5); 4-nitrophenol (**81**) (24 %)

δ_H (d$_6$-DMSO) 7.28 (1H, d, J_{65} = 9 Hz, H6), 8.37 (1H, dd, J_{53} = 3 Hz, J_{56} = 9 Hz, H5) 8.71 (1H, d, J_{35} = 3 Hz, H3); 2,4-dinitrophenol (**82**) (24 %)

δ_H (d_6-DMSO) 7.17 (1H, t, H4), 8.22 (2H, d, $J_{34\ 54}$ = 8 Hz, H3, H5); 2,6-dinitrophenol (**83**) (8 %)

δ_H (d_6-DMSO) 8.58 (2H, s, H3, H5); 2,4,6-trinitrophenol (**70**) (44 %)

Using seven equivalents of N$_2$O$_5$

A solution of N_2O_5 in PP6 (1.5 cm^3, 1.00 mol dm^{-3}) was added to a solution of phenol (0.02 g, 0.213 mmol) in PP6 (30 cm^3) at ambient temperature and was left to stir for 10 minutes. The resulting reaction mixture contained a ratio of 1 molar equivalent of phenol to 7 molar equivalents of N_2O_5. On the addition of distilled water to the solution a solid formed and was filtered off under vacuum, (0.0475 g, 94 %). ^{1}H NMR spectroscopy was used to determine the composition of the product.

δ_H (d_6-DMSO) 8.58 (2H, s, H3, H5); 2,4,6-trinitrophenol (**70**) (100 %)

Attempted nitration of chlorobenzene

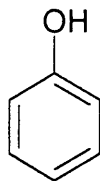A solution of N_2O_5 in PP6 (2 cm^3, 0.575 mol dm^{-3}) was added to a solution of chlorobenzene (0.02 g, 0.178 mmol), in PP6 (20 cm^3) at ambient temperature and was left to stir for 1 hour. The resulting reaction mixture contained a ratio of 1 molar equivalent of chlorobenzene to 6 molar equivalents of N_2O_5. Distilled water was added to the reaction mixture but no solid was formed, the water was removed under vacuum but nothing remained. The PP6 layer was also removed but nothing remained.

Synthesis of deuterated 4-chlorophenol (72)

Phenol (1.0 g, 0.01 mol) was dissolved in acetic acid (12 ml) and was placed in an ice bath. Chlorine gas was bubbled through and the weight increase was measured. We calculated that a 0.75 g increase would correspond to monochlorination. The experiment was repeated

using deuterated phenol (1.0 g, 0.01 mol). Once the required weight increase had occurred the acetic acid was evaporated to give a liquid (0.35 g, 26 %).

GCMS gave 606 (165, 7.8%, dichlorophenol), 630 (132, 87.4%, monochlorophenol), 636 (165, 4.2%, dichlorophenol), 775 (198, 0.67 %, trichlorophenol).

Theoretical ^{13}C NMR shift for 2-chlorophenol[3]

δ_c 155.6 (1C, s, C1), 122.2 (1C, s, C2), 130.1 (1C, m, C3), 122.4 (1C, m, C4), 128.1 (1C, m, C5), 117.0 (1C, m, C6)

Theoretical ^{13}C NMR shift for 4- chlorophenol[3]

δ_c 153.4 (1C, s, C1), 116.8 (1C, m, C2), 130.1 (1C, m, C3), 127.6 (1C, s, C4)

^{13}C NMR for deuterated 4-chlorophenol

^{13}C NMR δ_c 157.1 (1C, s, C1), 118.5 (1C, m, C2), 130.0 (1C, m, C3), 123.0 (1C, s, C4)

6.7 Chapter five experimental

Attempted nitration of morpholine (85)
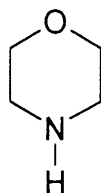
(85)

Experiment 1 using nitric acid

A solution of morpholine (2.58 g, 0.03 mol) in PP6 (20 cm^3) and 100% concentrated nitric acid (1.5 cm^3, 0.03 mol) were allowed to stir at ambient temperature over night. On the addition of nitric acid a white gas was given off and caution had to be taken whilst adding the nitric acid. A white solid was formed and was separated by filtration. The solid was washed with a small amount of water but care was taken because the product was soluble in water.
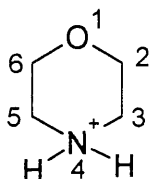
(89)

^{1}H NMR spectrum of product;

δ_H (d$_6$-DMSO) 3.08 (4H, m, H3, H5), 3,72 (4H, m, H2, H6); protonated morpholine **(89)**

Comparison with literature and authentic samples for N-nitromorpholine

A ^{1}H NMR spectrum was recorded on a sample of morpholine with DCl added in D$_2$O to confirm the signals of the product were due to protonated morpholine;

δ_H (D$_2$O) 3.02 (4H, m, H3, H5), 3,73 (4H, m, H2, H6); protonated morpholine **(89)**
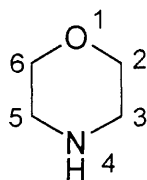
(**85**)

The ^{1}H NMR spectrum of morpholine (**85**) was recorded;

δ_H (d$_6$-DMSO) 2.74 (4H, m, H3, H5) 3.58 (4H, m, H2, H6); morpholine (**85**)
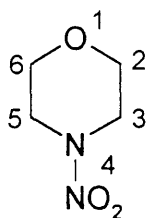
(**87**)

The literature ^{1}H NMR spectrum of *N*-nitromorpholine (**87**) is given by R.W. Millar *et al*; [4]

δ_H (CDCl$_3$) 3.80 (8H, s, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

An authentic sample of *N*-nitromorpholine was supplied by the DERA and the ^{1}H NMR spectrum was recorded on the sample;

δ_H (d$_6$-DMSO) 3.72 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

The M.pt. of the product was 139-140.5°C, (literature[5] M.pt. for *N*-nitromorpholine is 52-54°C)

Experiment 2 using N$_2$O$_5$

A solution of N$_2$O$_5$ in PP6 (5 cm^3, 1 mol dm^{-3}) was added to a solution of morpholine (0.5 g, 0.005 mol) in PP6 (40 cm^3) and stirred at −5 °C for 1 hour. The solution was allowed to reach ambient temperature before being washed with HCl solution (5 cm^3, 10 % by weight), a white solid was formed and was separated using filtration.

^{1}H NMR spectrum of product;

δ_H (d$_6$-DMSO) 3.07 (4H, m, H3, H5), 3.30 ((s) H$_2$O) 3,72 (4H, m, H2, H6); protonated morpholine (**89**)

N-Acetylmorpholine(86)
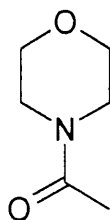
(**86**)

(The solubility of *N*-acetyl morpholine in PP6 was found to be 0.044 moldm^{-3} compared to a value for morpholine of 0.60 mol dm^{-3}.)

Experiment 1 using nitric acid

A solution of *N*-acetylmorpholine (0.17g, 1.32 mmol) in PP6 (35cm^3) and 100% concentrated nitric acid (0.3cm^3, 7.14 mmol) were allowed to for 48 hours. The solution was heated for two hours at 70°C. Distilled water was added and the aqueous layer was separated. The aqueous layer was washed with dichloromethane. The dichloromethane was left to evaporate giving a solid (0.001g, 0.6%). There was only enough product to characterise using ^{1}H NMR spectroscopy

δ_H (d$_6$-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

Experiment 2 using nitric acid

A solution of *N*-acetylmorpholine (1.00 g, 7.5 mmol) in PP6 (30 cm^3) and 100 % concentrated nitric acid (2 cm^3, 46.5 mmol) was added. The solution was heated for 2 hours at 70°C and was left for a further 1 hour at ambient temperature. Distilled water was added and the aqueous layer was separated. The aqueous layer was washed with dichloromethane.

The dichloromethane was left to evaporate and the resulting liquid was examined by ^{1}H NMR spectroscopy.

δ_H (d_6-DMSO) 2.74 (4H, m, H3, H5) 3.58 (4H, m, H2, H6); morpholine (**85**)

Experiment 3 using PP2 – perfluoromethylcyclohexane.

A solution of *N*-acetylmorpholine (0.2 g, 1.5 mmol) in PP2 (50 cm^3) and 100% concentrated nitric acid (0.5 cm^3, 9.3mmol) were allowed to stir for 24 hours. Distilled water was added and the aqueous layer was separated. The aqueous layer was washed with dichloromethane. The dichloromethane was left to evaporate and the resulting product was examined by ^{1}H NMR spectroscopy.

δ_H (d_6-DMSO) 2.74 (4H, m, H3, H5) 3.58 (4H, m, H2, H6); morpholine (**85**)

Experiment 4 using nitric acid

A solution of *N*-acetylmorpholine (0.2 g, 1.55 mmol) in PP2 (50 cm^3) and 100 % concentrated nitric acid (0.5 cm^3, 9.3 mmol) were allowed to stir for one week. Distilled water was added and the aqueous layer was separated. The aqueous layer was washed with dichloromethane. The dichloromethane was left to evaporate resulting in a liquid (0.005 g, 2.6 %).

δ_H (d_6-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

Experiment 5 using N_2O_5

A solution of *N*-acetylmorpholine (0.17 g, 1.3 mmol) in PP6 (35cm^3) and N_2O_5 in PP6 (4.5 cm^3, 2.6 mmol) were allowed to stir for 24 hours and samples were taken after 2 hours and 4 hours. Distilled water was added and the aqueous layer was separated. The aqueous layer was neutralised with potassium hydrogen carbonate and left to evaporate. The organic layer

was also left to evaporate. The resulting product from the aqueous layer was a liquid (0.005 g, 3 %)

δ_H (d$_6$-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

Experiment 6 using mixed acid and ZnCl$_2$ as catalyst

A solution of *N*-acetylmorpholine (0.2285 g, 1.74 mmol) in PP6 (30 cm^3), 100% concentrated nitric acid (0.5 cm^3, 9.3 mmol) and 98% sulfuric (0.5 cm^3, mmol) were added. ZnCl$_2$ (1 g) was weighed out under argon and the added to the reaction mixture. The reaction mixture was stirred for 3 hours at ambient temperature. Distilled water was added and the aqueous layer was separated and neutralised with potassium hydrogen carbonate. The aqueous layer was washed with dichloromethane and the dichloromethane was left to evaporate. Small amount of brown solid resulted enough for only determination by ^{1}H NMR spectroscopy.

δ_H (d$_6$-DMSO) 2.74 (4H, m, H3, H5) 3.58 (4H, m, H2, H6); morpholine (**85**)

The experiment was repeated but the reaction mixture was heated to 50°C for 3 hours giving the same result.

Experiment 7 using N$_2$O$_5$ and using no water in extraction

N-Acetylmorpholine (0.200 g, 1.55 mmol) was dissolved in PP2 (35 cm^3). N$_2$O$_5$ in PP2 (4.5 cm^3 1.03 mol dm^{-3}) was added and the solution was stirred for 3 hours at ambient temperature. The product was extracted using dichloromethane, neutralised with potassium hydrogen carbonate and the dichloromethane was decanted off and evaporated *in vacuo*. The product was a clear liquid (0.2155 g, 105 %).

δ_H (d$_6$-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**) and δ_H (d$_6$-DMSO) 1.90 (unknown (s))

GCMS: Found at 595s m/z 132 (Mr of *N*-nitromorpholine 132)

Ethanol trituration did not yield a solid.

N-Trimethylsilylmorpholine (88)
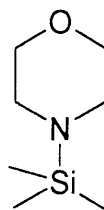
(**88**)

Experiment 1 using N_2O_5

A solution of *N*-trimethylsilylmorpholine (0.200 g, 0.13 mmol) in PP6 (30 cm^3) and N_2O_5 in PP6 (5 cm^3, 0.8175 mol dm^{-3}) was added, the solution was allowed to stir for 1 hour at ambient temperature. Distilled water was added and the aqueous layer was separated. The aqueous layer was washed with dichloromethane. The dichloromethane was left to evaporate yielding a solid (0.001 g, 5 %). The product was characterised using ^{1}H NMR spectroscopy.

δ_H (d$_6$-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

Experiment 2 using N_2O_5 and using no water in extraction

The above experiment was repeated using different extraction procedure. A solution of *N*-trimethylsilylmorpholine (0.2201 g, 1.4 mmol) in PP6 (30 cm^3) and N_2O_5 in PP6 (7 cm^3, 0.5875 mol dm^{-3}) were added together. After the reaction had been allowed to stir at ambient temperature for 1 hour the PP6 was distilled leaving a liquid (0.099 g). The crude yield was 54 %. The ^{1}H NMR spectrum gave signals corresponding to *N*-nitromorpholine and protonated morpholine.

(89)   (87)
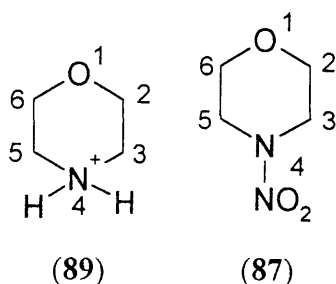
^{1}H NMR spectrum of product;

δ_H (d_6-DMSO) 3.08 (4H, m, H3, H5), 3,72 (4H, m, H2, H6); protonated morpholine (**89**) and δ_H (d_6-DMSO) 3.73 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

Experiment 3 using N_2O_5 and using no water in extraction

N-trimethylsilylmorpholine was dissolved in PP2 (0.2075g, 1.3 mmol) and N_2O_5 in PP2 (4cm^3, 1.03 mol dm^{-3}) was added immediately and the solution was stirred for 3 hours at ambient temperature.

The product was extracted using dichloromethane and neutralised with potassium hydrogen carbonate. The dichloromethane was decanted off and evaporated *in vacuo*, leaving a clear liquid (0.1488g). The crude yield was 87% but the product contained morpholine salt (25%) determined by ^{1}H NMR spectroscopy and ESMS.

δ_H (d_6-DMSO) 3.10 ((m) morpholine salt) 3,72 ((m), morpholine salt (25%) and *N*-nitromorpholine (75%))

From the ^{1}H NMR spectrum the yield of *N*-nitromorpholine could be estimated as 75% of 87%, which is 65%.

Ethanol was added to the product and a small amount of white solid was separated by filtration. The spectrum of the white solid gave signals at δ3.10 ppm and δ3.75 ppm which

are consistent with the formation of a morpholine salt, possibly morpholine nitrate, determined using ESMS.

(89)   (90)
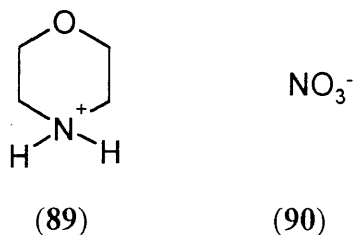
ESMS; Found m/z (+) 88 (89) and m/z (-) 62 (90)

δ_H (d_6-DMSO) 3.10 (4H, m, H2, H6), 3,75 (4H, m, H3, H5); protonated morpholine (89)

3-trimethylsilyl-2-oxazolidinone (91)

(91)
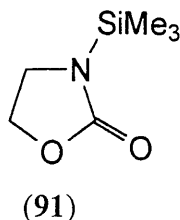
3-trimethylsilyl-2-oxazolidinone (0.2289 g , 1.4 mmol)was dissolved in PP6 (30 cm^3) and N_2O_5 in PP6 (5 cm^3 of 0.8175 mol dm^{-3}) was added. The reaction mixture was stirred for 1 hour at ambient temperature. The reaction mixture was quenched with water, the aqueous layer was separated and neutralised, a white solid formed (0.0316 g, 16 %), which was separated by filtration.

The experiment was repeated but without using water in the separation step. The reaction mixture was left to evaporate after being stirred for 1 hour at ambient temperature resulting in a white solid (0.1222g, 73%). M.pt. was 106 –107.8 °C (lit.[6] 108-109.5°C) of *N*-nitro-1,3-oxazolidin-2-one(92).

(92)
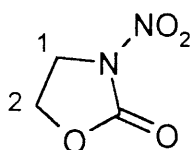
δ_H (d$_6$-DMSO) 3.53 (s, H$_2$O), 4.32 (4H, m, H1, H2); *N*-nitro-1,3-oxazolidin-2-one (92) CIMS; found m/z 133-1 = 132 (Mr of (92) is 132)

N-Trimethylsilylpyrrolidine (93)
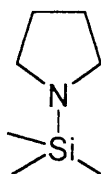
(93)

Experiment 1

N-Trimethylsilylpyrrolidine (0.3266g, 2.3 mmol) was dissolved in PP6 (30cm^3) and N$_2$O$_5$ in PP6 was added (4.5 cm^3 of 0.9600 moldm^{-3}). The reaction mixture was stirred for 1 hour at ambient temperature. The reaction mixture was quenched with water, the aqueous layer was separated and the product was extracted using dichloromethane yielding a yellow oil. There was only enough product to characterize using ^{1}H NMR spectroscopy.

(94)
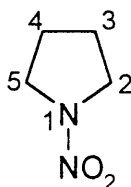
δ_H (d$_6$-DMSO) 3.29 (s, H$_2$O), 1.93 (4H, m, H3, H4) 3.74 (4H, m, H2, H5) in (94)

Comparison to literature and authentic samples for N-nitropyrrolidine

The literature ^{1}H NMR spectrum of *N*-nitropyrrolidine (**94**) is given by R.W. Millar *et al*; [4] δ_H (CDCl$_3$) 2.00 (4H, m) 3.70 (4H, m); *N*-nitropyrrolidine (**94**).

An authentic sample of *N*-nitropyrrolidine was supplied by the DERA and the ^{1}H NMR spectrum was recorded on the sample;
δ_H (d$_6$-DMSO) 1.93 (4H, m, H3, H4) 3.74 (4H, m, H2, H5)

The literature M.pt. for *N*-nitropyrrolidine is 58°C [7]

Experiment 2

Trimethylsilylpyrrolidine (0.2055 g, 1.4 mmol) was dissolved in PP6 (30 cm^3) and N$_2$O$_5$ in PP6 was added (7 cm^3 of 0.8175 mol dm^{-3}). The reaction mixture was stirred for 3 hours at ambient temperature. The product was extracted using dichloromethane, neutralised with potassium hydrogen carbonate. The dichloromethane was filtered then evaporated leaving an oil (0.0685 g, 42 %).

δ_H (d$_6$-DMSO) 3.29 (s, H$_2$O), 1.93 (4H, m, H3, H4) 3.74 (4H, m, H2, H5); *N*-nitropyrrolidine (**94**)

N-BOC-morpholine (95)

(**95**)
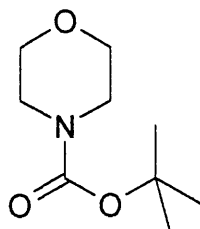
Synthesis of N-BOC-morpholine

Morpholine (1.002 g, 0.012 mol) was dissolved in dichloromethane (20 cm^3) and triethylamine (0.1g, 0.001 mol) was added. BOC-anhydride (2.488 g, 0.012 mol) was dissolved in dichloromethane (20 cm^3), this was added slowly with stirring to the morpholine mixture. The solution was left for 3 hours with stirring at ambient temperature. The dichloromethane and triethylamine was evaporated off under vacuum leaving a white solid.

(95)
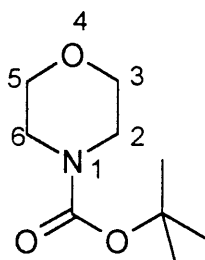
δ_H (d$_6$-DMSO) 1.38 (9H, s, 3CH$_3$) 3.28 (4H, m, H2, H6) 3.50 (4H, m, H3, H5); *N*-BOC-morpholine (95)

Nitration of N-BOC-morpholine

Experiment 1

N-BOC-morpholine (0.2103 g, 1.13 mmol) was dissolved in PP2 (40 cm^3). N$_2$O$_5$ in PP2 (1 cm^3, 1.03 mol dm^{-3}) was added and the solution was stirred for 3 hours at ambient temperature. The product was extracted using dichloromethane, neutralised with potassium hydrogen carbonate and the dichloromethane was decanted and evaporated under vacuum. The product was a clear liquid (0.1118g, 76 %).

δ_H (d$_6$-DMSO) 3.74 (8H, m, H2, H3, H5, H6) in *N*-nitromorpholine (87)

EIMS; found m/z 132 (Mr *N*-nitromorpholine is 132)

Experiment 2

N-BOC-morpholine (0.1018 g, 0.65 mmol) was dissolved in PP6 (30 cm^3). N$_2$O$_5$ in PP6 (2 cm^3, 1.00 mol dm^{-3}) was added and the solution was stirred for 3 hours at ambient temperature. The product was extracted using dichloromethane, neutralised with potassium hydrogen carbonate and the dichloromethane was decanted and evaporated *in vacuo*. The product was a clear liquid (0.0634 g, 83 %).

δ_H (d$_6$-DMSO) 3.74 (8H, m, H2, H3, H5, H6); *N*-nitromorpholine (**87**)

HPLC; found 1.217 minutes (100% *N*-nitromorpholine (**87**))

N-BOC-pyrrolidine (97)

(**97**)
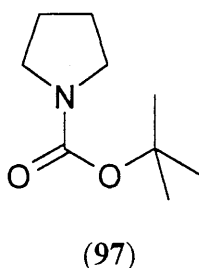
Synthesis of N-BOC-pyrrolidine

The *N*-BOC-pyrrolidine was generously supplied by Mr B.Dutton (PhD student at Durham) and was prepared in the following way;

A solution of BOC-anhydride, (27 g, 0.124 mol) in tetrahydrofuran (150 cm^3) was added drop wise over an hour to a stirred mixture of pyrrolidine (8.0 g, 0.112 mol) in tetrahydrofuran (180 ml) and sodium hydroxide (15 M, 82 cm^3, 0.124 mol). After 1 hour, the reaction mixture was extracted with ether. The extract was washed with water. The organic extract was dried (MgSO$_4$) and concentrated *in vacuo*. Vacuum distillation yielded the title product (17.65 g, 92 %).

(97)
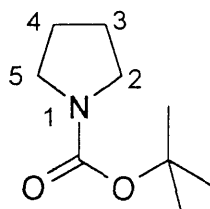
δ_H (d$_6$-DMSO) 1.44 (9H, s, 3CH$_3$) 1.50 (s, H$_2$O), 1.80 (4H, m, H3, H4) 3.25 (4H, m, H2, H5); *N*-BOC-pyrrolidine (97)

Nitration of N-BOC-pyrrolidine

Experiment 1

N-BOC-pyrrolidine (0.3423 g, 2.0 mmol) was dissolved in PP6 (30 cm^3). N$_2$O$_5$ (7.5 cm^3 0.955 mol dm^{-3}) in PP6 was added. The solution was stirred for 2 hours at ambient temperature. The solution was extracted with dichloromethane. Potassium hydrogen carbonate was added to the dichloromethane layer to neutralise excess acid. The dichloromethane was decanted from the solid. The dichloromethane was evaporated *in vacuo*, leaving a yellow liquid (0.097 g, 42 %).

δ_H (CDCl$_3$) 1.69 (s, H$_2$O), 2.05 (4H, m, H3, H4) 3.87 (4H, m, H2, H5) *N*-nitropyrrolidine (94) 7.00 (unknown) and 1.70 (9H, s, C$\underline{H}_3$); probably 1,1-dimethylethylnitrate (98) (20 %)

Experiment 2

N-BOC-pyrrolidine (0.5265 g, 3.08 mmol) was dissolved in PP6 (50 cm^3). N$_2$O$_5$ in PP6 (6 cm^3, 0.955 mol dm^{-3}) was added. The solution was stirred for 1 hour at ambient temperature. The solution was extracted with dichloromethane. Potassium hydrogen carbonate was added to the dichloromethane layer and the dichloromethane was decanted. The dichloromethane was evaporated *in vacuo* leaving a pale yellow crystalline solid (0.3936 g, 110 %), (M.Pt. 48-50 °C).

δ_H (CDCl$_3$) 1.54 (s, H$_2$O), 1.92 (4H, m, H3, H4) 3.73 (4H, m, H2, H5); *N*-nitropyrrolidine (**94**), 1.54 (9H, C$\underline{H}_3$) in 1,1-dimethylethylnitrate (**98**) and 6.03 (possibly HNO$_3$).

GCMS gave a signal at 627s m/z 116. (Mr of *N*-nitro-pyrrolidine is 116).

Experiment 3

N-BOC-pyrrolidine (0.5194 g, 3.04 mmol) was dissolved in PP6 (50 cm^3). N$_2$O$_5$ in PP6 (3.2 cm^3 0.955 mol dm^{-3}) was added. The solution was stirred for 1 hour at ambient temperature. The solution was extracted with dichloromethane. Potassium hydrogen carbonate was added to the dichloromethane layer and the dichloromethane was decanted and evaporated *in vacuo*. A pale yellow crystalline solid was collected (0.2168 g, 62 %), (M.Pt. 50-54°C).

δ_H (d$_6$-DMSO) 1.93 (4H, m, H3, H4) 3.74 (4H, m, H2, H5) in *N*-nitropyrrolidine (**94**) and 1.56 (9H, s, C$\underline{H}_3$) in 1,1-dimethylethylnitrate (5 %)

GCMS gave a signal at 624s m/z 116. (Mr of *N*-nitro-pyrrolidine is 116).

HPLC at 1.26 minutes gave 100% *N*-nitropyrrolidine)

N-BOC-piperidine (99)

(**99**)
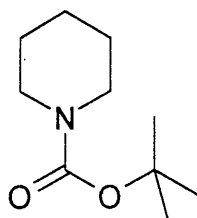
Synthesis of N-BOC-piperidine

Piperidine (1.0780 g, 0.012 mol) was dissolved in dichloromethane (20 cm^3) and triethylamine (0.1 g, 0.001 mol) was added. BOC-anhydride (2.348 g, 0.011 mol) was dissolved in dichloromethane (20 cm^3), this solution was added slowly with stirring to the piperidine mixture. The solution was left for 3hours with stirring at ambient temperature. The dichloromethane and triethylamine were evaporated *in vacuo*. The product was dissolved in dichloromethane and washed with a small amount of water. MgSO$_4$ was added as a drying agent then filtered off. The dichloromethane was evaporated off *in vacuo* leaving the title product (0.3g, 14 %)

δ_H (CDCl$_3$) 1.50 (9H, s, CH3), 1.58 (6H, m, H3, H4, H5), 3.36 (4H, m, H2, H6); *N*-BOC-piperidine

Nitration of N-BOC-piperidine

N-BOC-piperidine (0.245 g, 1.3 mmol) was dissolved in PP6 (30 cm^3). N$_2$O$_5$ in PP6 (4mls, 0.955 mol dm^{-3}) was added. The solution was stirred for 2 hours at ambient temperature. The product was extracted using dichloromethane, neutralised using potassium hydrogen carbonate and decanted and evaporated *in vacuo*, leaving a brown oil (0.225 g, 133 %).

(100)
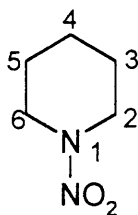
δ_H (d$_6$-DMSO) 1.65 (6H, m, H3, H4, H5) 3.88 (4H, m, H2, H6); *N*-nitropiperidine (100) and 1.58 (9H, s, C$\underline{H}_3$); 1,1-dimethylethylnitrate (30 %)

GCMS found signal at 643s m/z 130. (Mr of *N*-nitropiperidine is 130).

Literature values for *N*-nitropiperidine are oil, ^{1}H NMR spectrum giving signals at δ1.65 ppm (m, 6) and δ3.85 ppm (m, 4).[4]

Di-N-BOC-hexahydropyrimidine (101)
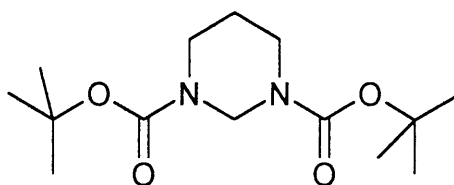
(**101**)

Synthesis of hexahydropyrimidine

1,3-Diaminopropane (1.2577 g, 0.017 mol) was dissolved in H_2O (7.5 cm^3). HCl (1 M) was added until neutralised (methyl orange). 1,3 diaminopropane (1.2536 g, 0.017 mol) was added. Formaldehyde (28.3 cm^3, 0.034mol) was added very slowly with agitation. The solution was cooled and NaOH (10 g) was added, the oil was extracted with dichloromethane. The product was left in dichloromethane because it was known to be unstable.

Synthesis of di-N-BOC-hexahydropyrimidine

BOC-anhydride (14.84g, 0.068 mol) was added to the solution of hexahydropyrimidine (0.034 mol) in dichloromethane (20 cm^3). NEt$_3$ (0.34g, 0.0068 mol) was added to the dichloromethane solution. The reaction was stirred for 3 hours at ambient temperature. The dichloromethane was evaporated and ^{1}H NMR spectroscopy determined the product (0.1075 g).

$δ_H$ (d$_6$-DMSO) 1.40 (18H, s, CH$_3$), 3.30 (4H, m, H4, H6), 3.40 (2H, t, H5), 4.82 (2H, s, H2); di-*N*-BOC-hexahydropyrimidine

Nitration of di-N-BOC-hexahydropyrimidine

Di-*N*-BOC-hexahydropyrimidine (0.0805 g, 0.28 mmol) was dissolved in PP6 (30 cm^3). N_2O_5 in PP6 (1.7 cm^3, 1.0 mol dm^{-3}) was added and the solution was stirred for 3 hours at ambient temperature. The product was extracted with dichloromethane and neutralised with potassium hydrogen carbonate. The dichloromethane was evaporated. The product (oil), (0.0576g, 86%)was characterised by ^{1}H NMR spectroscopy and mass spectroscopy.

(**102**)   (**107**)
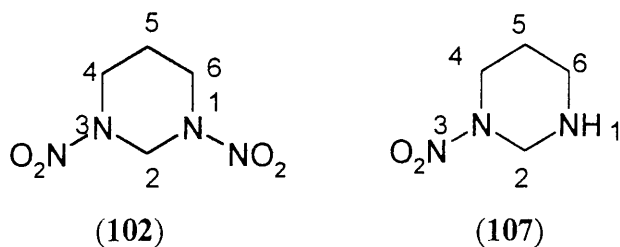
δ_H (d$_6$-DMSO) 1.82 (2H, m, H5) 3.95 (4H, m, H6, H4) 5.75 (2H, s, H2); di-*N*-nitrohexahydropyrimidine (**102**) and 5.25 (2H, s, H2); monohexhydropyrimidine (**107**) Impurities could also be seen in the ^{1}H NMR spectrum.

The mass spectrum gave a signal at 130m/z, which could correspond to the loss of one NO_2 from the dinitroderivative.

Nitration of butyl-pyrrolidine by chloride catalysis

(**106**)
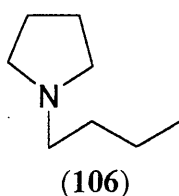
1-Butylpyrrolidine (0.4311 g, 3.4 mmol) was dissolved in PP6 (30 cm^3). Tetra-methylammoniumchloride (0.4 g, 3.4 mmol) and HNO_3 (1 cm^3, 0.024 mol) were added. After reaction for 3 hours at 70° C, the solution was extracted using dichloromethane and characterised using ^{1}H NMR spectroscopy. The ^{1}H NMR spectrum gave signals that could be assigned to the product *N*-nitropyrrolidine, but also contained other impurities.

6.8 References

1.   Lewis, R. and Moodie, R. B., *J. Chem. Soc., Perkin Trans. II,* **1996**, 1315.

2.   Lewis, R. and Moodie, R. B., *J. Chem. Soc., Perkin Trans. II,* **1997**, 563.

3.   Ewing, D. F. , *Org. Mag. Res.* **1979** 12, 499.

4.   Millar, R.W., and Philbin, S.P., *Tetrahedron*, **1997**, 53, 4371.

5.   Emmons, W. D., Pagano, A. S., and Stevens, T E., *J. Org. Chem.,* **1958** 23, 311, organic synthesis collected Vol 5, 839.

6.   White, E. H., Chen, M. C., and Dolak, L. A., *J. Org. Chem.,* **1966**, 70, 3038.

7.   Lamberton, A.H., *Q. Rev.,* **1951,** 5, 75.

Chapter Seven

7 Conferences and Colloquia

7.1 Conferences attended

1.   2nd Chemical Synthesis Symposium (DERA, Fort Halstead, 13-14th July 1998).

2.   Postgraduate Winter School on Organic Reactivity –WISOR IX (Bressanone. Italy, 7-15th January 2000).
        Poster Presentation 'Nitration in Inert Fluids'.

3.   Royal Society of Chemistry Organic Reaction Mechanistic Group Annual seminars attended-
        (i)   Zeneca (Huddersfield, 18th Sepetember 1998)
        Poster Presentation 'Nitration in Inert Fluids'.
        (ii)   Roche (Welwyn Garden City, 17th September 1999)
        Poster Presentation 'Nitration in Inert Fluids'

4.   16th International Symposium in Fluorine Chemistry (University of Durham, 16-2 1st July 2000)
        Poster Presentation 'Nitration in Inert Fluids'.

5.   7th European Symposium of Organic Reactivity, (ESOR-7), (Ulm, Germany, August 1999)
        Poster Presentation 'Nitration in Inert Fluids'.

7.2 First year Induction Course, October 1997

The course consists of a series of one hour lectures on the services available in the department.

1. Introduction, research resources and practicalities
2. Safety matters
3. Electrical appliances and hands-on spectroscopic services
4. Departmental computing
5. Chromatography and high pressure operations
6. Elemental analysis
7. Mass spectrometry
8. Nuclear magnetic resonance spectroscopy
9. Glassblowing techniques

7.3 Colloquia

<u>1997</u>

October 8   Professor E Atkins, Department of Physics, University of Bristol
Advances in the control of architecture for polyamides: from nylons to
genetically engineered silks to monodisperse oligoamides

October 15   Dr R M Ormerod, Department of Chemistry, Keele University
Studying catalysts in action

October 21   Professor A F Johnson, IRC, Leeds
Reactive processing of polymers: science and technology

October 22   Professor R J Puddephatt (RSC Endowed Lecture), University of Western
Ontario Organoplatinum chemistry and catalysis

October 23   Professor M R Bryce, University of Durham, Inaugural Lecture
New Tetrathiafulvalene Derivatives in Molecular, Supramolecular and
Macromolecular Chemistry: controlling the electronic properties of organic
solids

October 29   Professor R Peacock, University of Glasgow
Probing chirality with circular dichroism

October 28   Professor A P de Silva, The Queen's University, Belfast
Luminescent signalling systems"

November 5   Dr M Hii, Oxford University
Studies of the Heck reaction

November 11   Professor V Gibson, Imperial College, London
Metallocene polymerisation

November 12   Dr J Frey, Department of Chemistry, Southampton University
Spectroscopy of liquid interfaces: from bio-organic chemistry to
atmospheric chemistry

November 19   Dr G Morris, Department of Chemistry, Manchester Univ.
Pulsed field gradient NMR techniques: Good news for the Lazy and DOSY

November 20   Dr L Spiccia, Monash University, Melbourne, Australia
Polynuclear metal complexes

November 25   Dr R Withnall, University of Greenwich
Illuminated molecules and manuscripts

November 26   Professor R W Richards, University of Durham, Inaugural Lecture
A random walk in polymer science

December 2   Dr C J Ludman, University of Durham
Explosions

December 3   Professor A P Davis, Department. of Chemistry, Trinity College Dublin.
Steroid-based frameworks for supramolecular chemistry

December 10   Sir G Higginson, former Professor of Engineering in Durham and retired
Vice-Chancellor of Southampton Univ.
1981 and all that.

December 10   Professor M Page, Department of Chemistry, University of Huddersfield
The mechanism and inhibition of beta-lactamases

October 27   Professor W Roper FRS. University of Auckland, New Zealand

1998

January 14   Professor D Andrews, University of East Anglia
Energy transfer and optical harmonics in molecular systems

January 20   Professor J Brooke, University of Lancaster
What's in a formula? Some chemical controversies of the 19th century

January 21   Professor D Cardin, University of Reading

January 27   Professor R Jordan, Dept. of Chemistry, Univ. of Iowa, USA.
Cationic transition metal and main group metal alkyl complexes in olefin
polymerisation

January 28   Dr S Rannard, Courtaulds Coatings (Coventry)
The synthesis of dendrimers using highly selective chemical reactions

February 3   Dr J Beacham, ICI Technology
The chemical industry in the 21st century

February 4   Professor P Fowler, Department of Chemistry, Exeter University
Classical and non-classical fullerenes

February 11   Professor J Murphy, Dept of Chemistry, Strathclyde University

February 17   Dr S Topham, ICI Chemicals and Polymers
                Perception of environmental risk; The River Tees, two different rivers

February 18   Professor G Hancock, Oxford University
                Surprises in the photochemistry of tropospheric ozone

February 24   Professor R Ramage, University of Edinburgh
                The synthesis and folding of proteins

February 25   Dr C Jones, Swansea University
                Low coordination arsenic and antimony chemistry

March 4   Professor T C B McLeish, IRC of Polymer Science Technology, Leeds
                University.
                The polymer physics of pyjama bottoms (or the novel rheological
                characterisation of long branching in entangled macromolecules)

March 11   Professor M J Cook, Dept of Chemistry, UEA
                How to make phthalocyanine films and what to do with them.

March 17   Professor V Rotello, University of Massachusetts, Amherst
                The interplay of recognition & redox processes - from flavoenzymes to
                devices

March 18   Dr J Evans, Oxford University
                Materials which contract on heating (from shrinking ceramics to bullet proof
                vests

October 7   Dr S Rimmer, Ctr Polymer, University of Lancaster
                New Polymer Colloids

October 9   Professor M F Hawthorne, Department Chemistry & Biochemistry, UCLA,
                USA,RSC Endowed Lecture

October 21   Professor P Unwin, Department of Chemistry, Warwick University
                Dynamic Electrochemistry: Small is Beautiful

October 23   Professor J C Scaiano, Department of Chemistry, University of Ottawa,
                Canada
                In Search of Hypervalent Free Radicals, RSC Endowed Lecture

October 26   Dr W Peirs, University of Calgary, Alberta, Canada
                Reactions of the Highly Electrophilic Boranes $HB(C6F5)2$ and $B(C6F5)3$
                with Zirconium and Tantalum Based Metallocenes

October 27   Professor A Unsworth, University of Durham

What's a joint like this doing in a nice girl like you?
In association with The North East Polymer Association

October 28   Professor J P S Badyal, Department of Chemistry, University of Durham
              Tailoring Solid Surfaces, Inaugural Lecture

November 4   Dr N Kaltscoyannis, Department of Chemistry, UCL, London
              Computational Adventures in d & f Element Chemistry

November 3   Dr C J Ludman, Chemistry Department, University of Durham
              Bonfire night Lecture

November 10   Dr J S O Evans, Chemistry Department, University of Durham
              Shrinking Materials

November 11   Dr M Wills, Department of Chemistry, University of Warwick
              New Methodology for the Asymmetric Transfer Hydrogen of Ketones

November 12   Professor S Loeb, University of Windsor, Ontario, Canada
              From Macrocycles to Metallo-Supramolecular Chemistry

November 17   Dr J McFarlane
              Nothing but Sex and Sudden Death!

November 18   Dr R Cameron, Department of Materials Science & Metallurgy, Cambridge
              University
              Biodegradable Polymers

November 24   Dr B G Davis, Department of Chemistry, University of Durham
              Sugars and Enzymes

December 1   Professor N Billingham, University of Sussex
              Plastics in the Environment - Boon or Bane
              In association with The North East Polymer Association.

December 2   Dr M Jaspers, Department of Chemistry, University of Aberdeen
              Bioactive Compounds Isolated from Marine Inverterates and Cyanobacteria

December 9   Dr M Smith Department. of Chemistry, Warwick University
              Multinuclear solid-state magnetic resonance studies of nanocrystalline
              oxides and glasses

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January 19   Dr J Mann, University of Reading
              The Elusive Magic Bullet and Attempts to find it?

January 20   Dr A Jones, Department of Chemistry, University of Edinburgh
              Luminescence of Large Molecules: from Conducting Polymers to Coral
              Reefs

January 27   Professor K Wade, Department of Chemistry, University of Durham
              Foresight or Hindsight? Some Borane Lessons and Loose Ends

February 3   Dr C Schofield, University of Oxford
              Studies on the Stereoelectronics of Enzyme Catalysis

February 9   Professor D J Cole-Hamilton, St. Andrews University
              Chemistry and the Future of life on Earth

February 10   Dr C Bain, University of Oxford
              Surfactant Adsorption and Marangoni Flow at Expanding Liquid Surfaces

February 17   Dr B Horrocks, Department of Chemistry, Newcastle University
              Microelectrode techniques for the Study of Enzymes and Nucleic Acids at
              Interfaces

February 23   Dr C Viney, Heriot-Watt
              Spiders, Slugs And Mutant Bugs

February 24   Dr. A-K Duhme, University of York
              Bioinorganic Aspects of Molybdenum Transport in Nitrogen-Fixing
              Bacteria

March 3   Professor B Gilbert, Department of Chemistry, University of York
              Biomolecular Damage by Free Radicals: New Insights through ESR
              Spectroscopy

March 9   Dr Michael Warhurst, Chemical Policy issues, Friends of the Earth
              Is the Chemical Industry Sustainable?

March 10   Dr A Harrison, Department of Chemistry, The University of Edinburgh
              Designing model magnetic materials

March 17   Dr J Robertson, University of Oxford
              Recent Developments in the Synthesis of Heterocyclic Natural Products

May 11   Dr John Sodeau, University of East Anglia
              Ozone Holes and Ozone Hills

May 12   Dr Duncan Bruce, Exeter University
                The Synthesis and Characterisation of Liquid-Crystalline Transition Metal
                Complexes

October 12   Dr. S. Beckett (Nestle)
                Chocolate for the next Millennium

October 13   Professor G. Fleet, University of Oxford
                Sugar Lactone and Amino Acids

October 19   Professor K. Gloe, TU Dresden, Germany
                Tailor Made Molecules for the Selective binding of Metal Ions

October 20   Professor S. Lincoln, University of Adelaide
                Aspects of Complexation and Supramolecular Chemistry

October 25   Professor S. Collins, University of Waterloo, Canada
                Methacrylate Polymerization Using Zirconium Enolate Initiators:
                Polymerization Mechanisms and Control of Polymer Tacticity

October 26   Dr. D. Hughes (Astra Zeneca)
                Perspectives in Agrochemistry

October 27   Dr. C. Braddock, Imperial College
                Novel catalysts for Atom Economic Transformations

November 3   Professor D.W. Smith, University of Waikato, NZ
                The Strengths of C-C and C-H Bonds in Organic and Organometallic
                Molecules: Empirical, Semi-empirical and Ab Initio Calculations

November 10   Dr. I. Samuel, Department of Physics, University of Durham
                Improving Organic Light Emitting Diodes by Molecular, Optical and Device
                Design

November 16   Professor A. Holmes
                Conjugated Polymers for the Market Place

November 17   Dr. J. Rourke, University of Warwick
                C-H Activation Induced by Water

November 18   Dr. G. Siligardi, Kings College London
                The Use of Circular Dichrosim to Detect and Characterise Biomolecular
                Interactions in Solution.

November 23   Professor B. Caddy

Trace evidence - a challenge for the forensic scientist

November 24 Professor T. Jones, Imperial College
Atomic and Molecular Control of Inorganic and Organic Semiconductor
Thin Films

November 30 Rev. R. Lancaster
Fireworks: Principles and Practice

December 8 Professor D. Crout, Department of Chemistry, University of Warwick
More than Simply Sweet: Carbohydrates in Medicine and Biology

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January 12 Professor D. Haddleton, Department of Chemistry, University of Warwick
Atom Transfer Polymerisation - What's all the Hype About?

January 19 Dr. P.R. Fielden, UMIST
Miniaturised Chemical Analysis (Lab-on-a-Chip): Functional or Merely
Fashionable?

January 25 Professor B. Meijer
From Supramolecular Architecture Towards Functional Materials

January 26 Professor S. Flisch, University of Edinburgh
The challenges involved in protein glycosylation - synthesis of glycan
chains and selective attachment to proteins

February 2 Chick Wilson, Head of Crytallography, ISIS, Rutherford Appleton Lab
Protons in motion? Neutron diffraction studies of hydrogen atoms in
organic crystal structures.

February 9 Dr. S. Moratti, University of Cambridge
Shape and Stereoselectivity in Polymer

February 15 Professor D. Phillips
A Little Light Relief

February 16 Professor Kocienski, University of Glasgow
Asymmetric Synthesis Using Planar Chiral TT-Allyl Cationic Complexes

February 23 Dr. N. Clarke, UMIST
The Flow of Polymer Blends

February 22 Professor G. Stuart
Brewing - Evolution from a Craft into a Technology

March 1   Professor D. Tildsley, Unilever (Head of Research)
Computer Simulation of Interfaces: Fact and Friction

March 7   Prof. Motherwell, University College, London
Curiosity and Simplicity - Essential Ingredients for the Discovery of New Reactions

March 8   Professor J. Courtieu, Universite de Paris-Sud, Orsay
Chiral Recognition through NMR in Liquid Crystal Solvents: an Order Affair

March 9   Dr. Antony Fairbanks, Dyson-Perrins Laboratory, Oxford
Selectivity in Glycoside Formation"

March 20   Professor S Marder, Professor of Chemistry and Optical Sciences, University of Arizona
Design of Molecules for Two-Photon Absorption and their Application to 3D Polymerization and Imaging

March 21   Professor E. Rizzardo, CSIRO Mol. Sci. Victoria, Australia
Designed Polymers by Free Radical Addition-Fragmentation Processes

May 5   Professor R. Hochstrasser, University Pennsylvania, USA
Ultrafast Molecular and Protein Dynamics seen through their Vibrations