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SYNTHETIC AND MECHANISTIC STUDIES IN POLYNITROAROMATIC CHEMISTRY

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ABSTRACT

This project developed from an industrial need for a plasticiser for explosives formulations which is easier to manufacture, more stable than those presently employed, but still based on a polynitroaromatic nucleus. The major aim of this programme was to produce new liquid or low melting polynitroaromatic compounds by simple routes.

A literature search highlighted various molecular features which appeared to produce a low melting temperature in polynitroaromatic compounds. Using these features, four categories of compounds were identified as target compounds for a synthetic programme to produce low melting polynitroaromatic compounds. (A : Alkyltrinitrobenzenes; B : trinitrophenylpropanoate esters; C : 3-alkylpicryl ethers; D : 3-alkyltrinitrobenzoate esters).

2,4,6-Trinitrotoluene (the preferred starting material for category A and B compounds) forms an anion in basic solution, which has been suggested as having nucleophilic characteristics[3]. In fact, this work has shown that it displays very poor nucleophilic qualities, though reaction with p-nitrobenzyl bromide was successful. An ultraviolet and nmr spectroscopic study of this reaction provided evidence to suggest that σ-adduct formation facilitates an ionic substitution reaction; whereas in other cases such σ-complex formation is not favoured and radical decomposition of TNT occurs.

Three 3-alkylpicryl chlorides have been prepared from 3-alkylphenols as precursors for category C and D compounds. Attempts to prepare such compounds from TNT were unsuccessful. Partial reduction of TNT, to 2,4-diamino-6-nitrotoluene was achieved, but bromination of this compound proved to be uncontrollable, with 2,4-diamino-3,5-dibromo-6-nitrotoluene being the only product. The mechanism of this reaction is discussed.

The preparation of 3-alkylpicryl ethers (category C compounds) was successfully achieved and numerous liquids or low melting solids were produced. 3-t-Butylpicryl chloride in reaction with certain alkoxides, displayed a competition between nitro group and halogen substitution, with up to 30% nitro group substitution being observed; a novel reaction in systems of this type. A series of low melting compounds have been prepared from 3-alkylpicryl halides using various sulphur and nitrogen nucleophiles.

ACKNOWLEDGEMENTS

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My parents have been a sound pillar of support during the writing of this thesis and without their encouragement I would not have made it this far.

Mrs. Ann Ching has been extremely patient with my writing and has typed an excellent job.

Finally Mrs.K.Salter, whose aid in the final stage was greatly appreciated.

ABBREVIATIONS

t-Bu	- Tertiary butyl
CT	- Charge transfer (complex)
DABCO	- 1,4-Diaza-(2:2:2)-bicyclooctane
DMF	- N,N-Dimethylformamide
DMSO	- Dimethylsulphoxide
DNT	- 2,4-Dinitrotoluene
ESR or esr	- Electron spin resonance (spectroscopy)
Et	- Ethyl
HNBB	- 2,2',4,4',6,6',-Hexanitrobibenzyl
HNS	- 2,2',4,4',6,6',-Hexanitrostilbene
HSE	- Health and Safety Executive
IR or ir	- Infrared (spectroscopy)
Me	- Methyl
ms	- Mass spectroscopy
NMR or nmr	- Nuclear magnetic resonance (spectroscopy)
PCNBBr	- p-Cyanobenzyl bromide
PERME	- Propellants, Explosives and Rocket Motor Establishment
PNBBr	- p-Nitrobenzyl bromide
R	- Alkyl
RARDE	- Royal Armaments Research and Development Establishment
SET	- Single electron transfer
THF	- Tetrahydrofuran
TLC	- Thin layer chromatography
TNB	- 1,3,5-Trinitrobenzene
TNBB	- 2,4,4',6-Tetranitrobibenzyl
TNBCL	- 2,4,6-Trinitrotoluene
UV or uv	- Ultraviolet (spectroscopy)

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CHAPTER 1

APPROACHES TO NOVEL LOW MELTING POLYNITROAROMATIC COMPOUNDS

The work presented in this thesis was stimulated by an industrial need for an energetic liquid which could be used as a plasticiser in explosives formulations. Plasticisers used at present, require for their manufacture processes involving nitrations with oleum, which are not favourably regarded in the industry, and their volatility is much greater than desired. Other available energetic liquids are either too low in explosive power or too sensitive to be used for this purpose. The collaborating establishment, the Ministry of Defence, Propellants, Explosives and Rocket Motor Establishment (P.E.R.M.E.), have specified a number of criteria (not quoted here) as important for the required type of liquid. In this project, emphasis was placed upon the aims of synthesising new liquid or low melting polynitroaromatic compounds from readily available starting materials (such as 2,4,6-trinitrotoluene), by relatively simple routes which do not involve hazardous operations.

1.1 LITERATURE REVIEW

A literature search was carried out to obtain information on known liquid or low melting polynitroaromatic compounds. This search was concentrated on four main categories of compounds because previous work completed at P.E.R.M.E., suggested these as potentially useful types. These categories were:

(a) alkyltrinitrobenzenes;
(b) nitroalkyldi-(or tri-) nitrobenzenes;
(c) difluoroamine containing compounds;
(d) esters of trinitrobenzoic acids, and esters and ethers of picric acid.

In excess of one hundred compounds were retrieved from the literature[1], and within the compounds discovered, certain structure/melting point correlations were recognised. During this study, there was no evidence of any previous work on structure/melting point correlations in organic compounds. Most of the correlations can be explained on the basis of an interference in crystal structure formation, or due to decreases in the change in entropy for the process of crystallation, but there is no work in the literature which describes these effects. Examples of the correlations found are shown in Schemes 1-14.

Type (c) compounds were not at all well reported in the literature, and those that were reported were described as highly explosive and very shock sensitive. It was concluded therefore that difluoroamines were probably not suitable for the application in question and they were not further considered.

There is one report of esters of 3-(2,4-dinitrophenyl) propanoic acid (LXXX)[2], in which thirteen esters are described. With three exceptions, they are light yellow, rather viscous oils or glassy solids at room temperature and seemed to be quite stable for at least six months under these conditions.

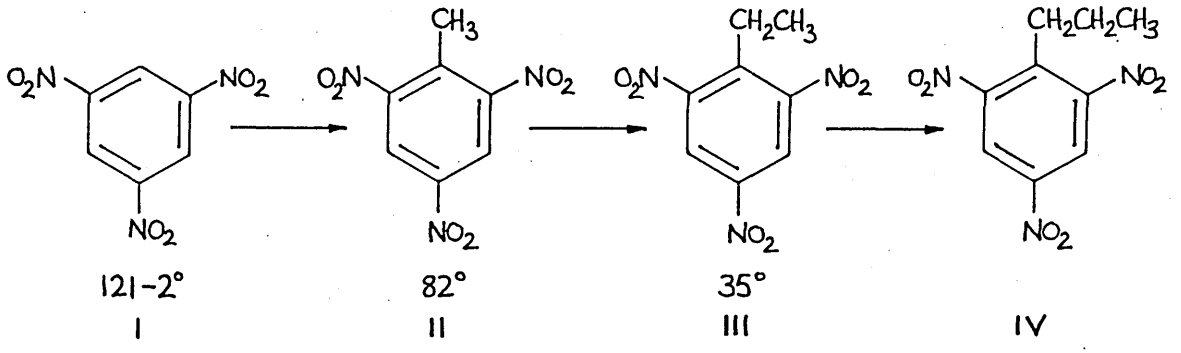
From the data collected, four basic factors emerged as links between the structure and the melting point of polynitroaromatic compounds. These were:

(i) the nature of the functional groups in the molecule;

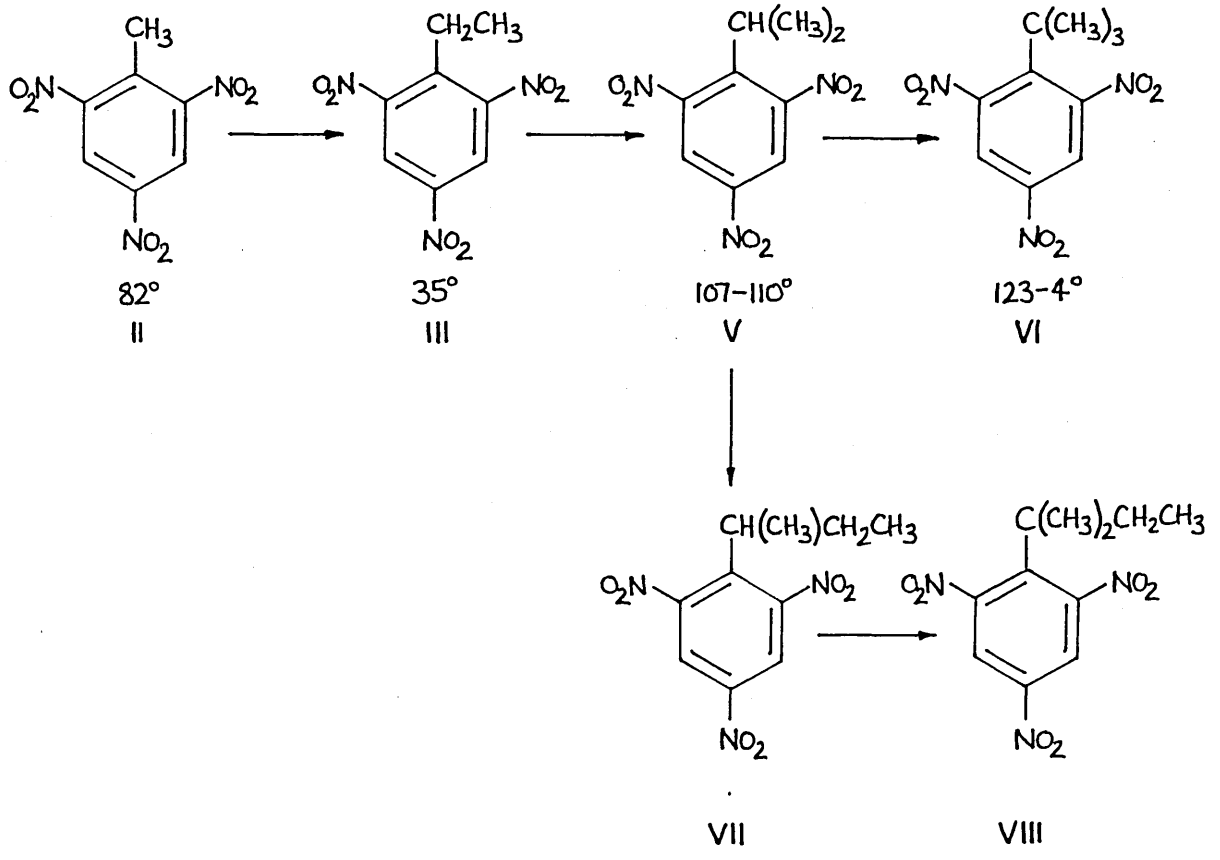
(ii) the length of any aliphatic side chains;

(iii) the degree of asymmetry of the molecule; particularly the pattern of benzene ring substitutions;

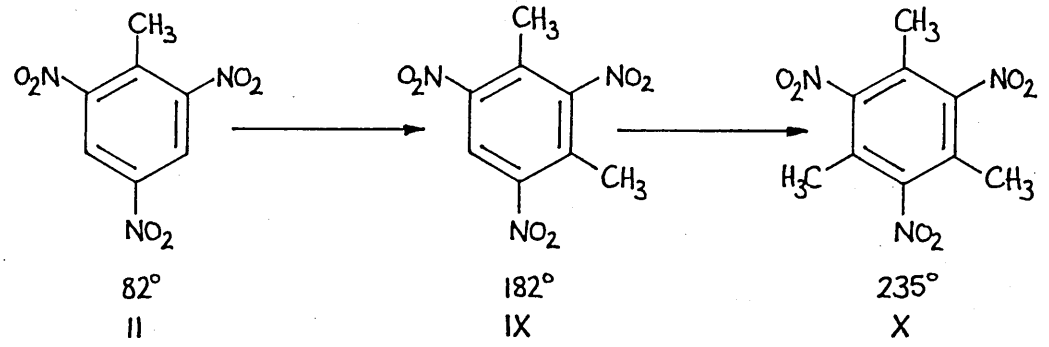
(iv) the number of nitro groups.



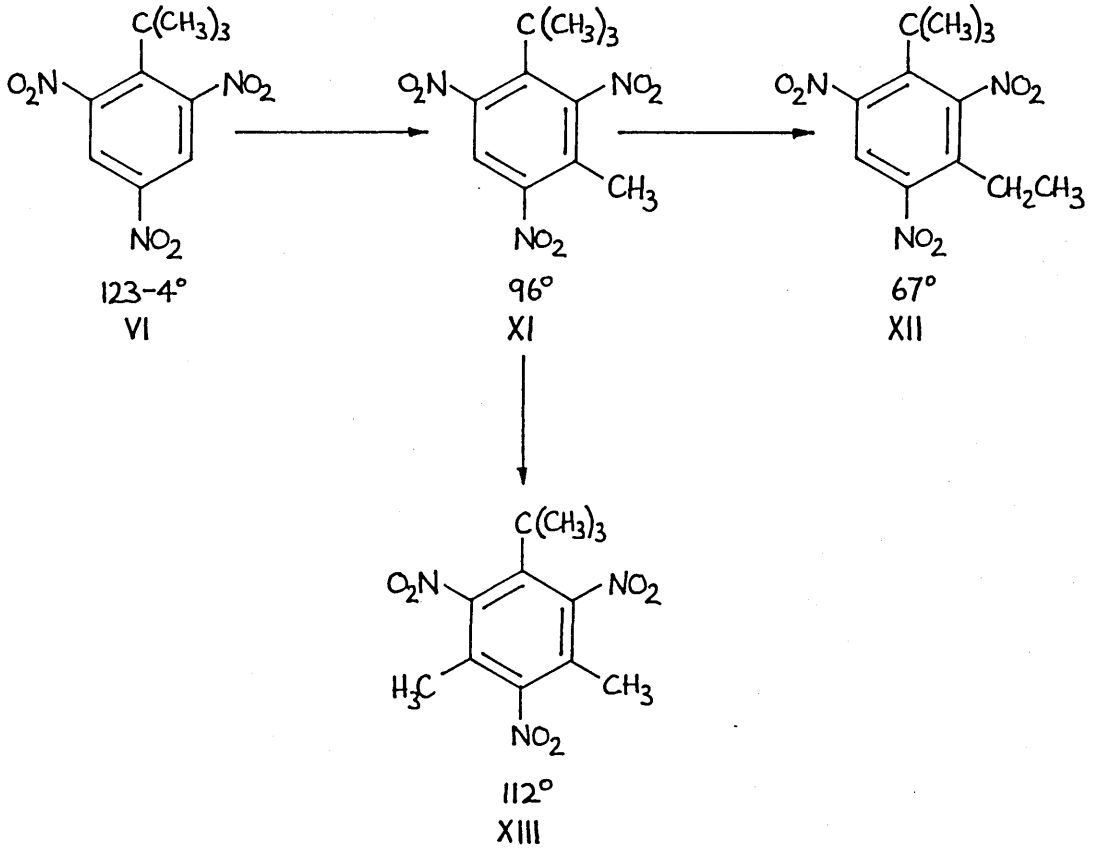
Scheme 1: n-Alkyl substituted trinitrobenzenes.



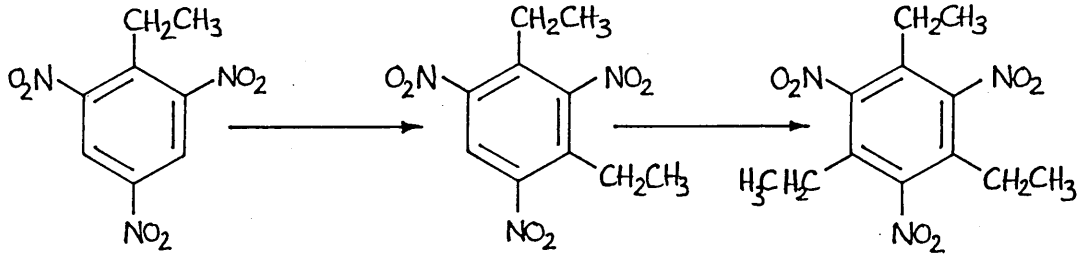
Scheme 2: Branched alkyl substituted trinitrobenzenes.



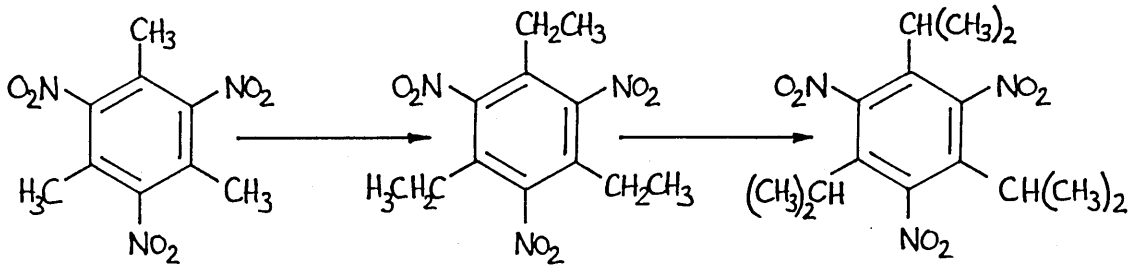
Scheme 3: Methyl substituted trinitrobenzenes.



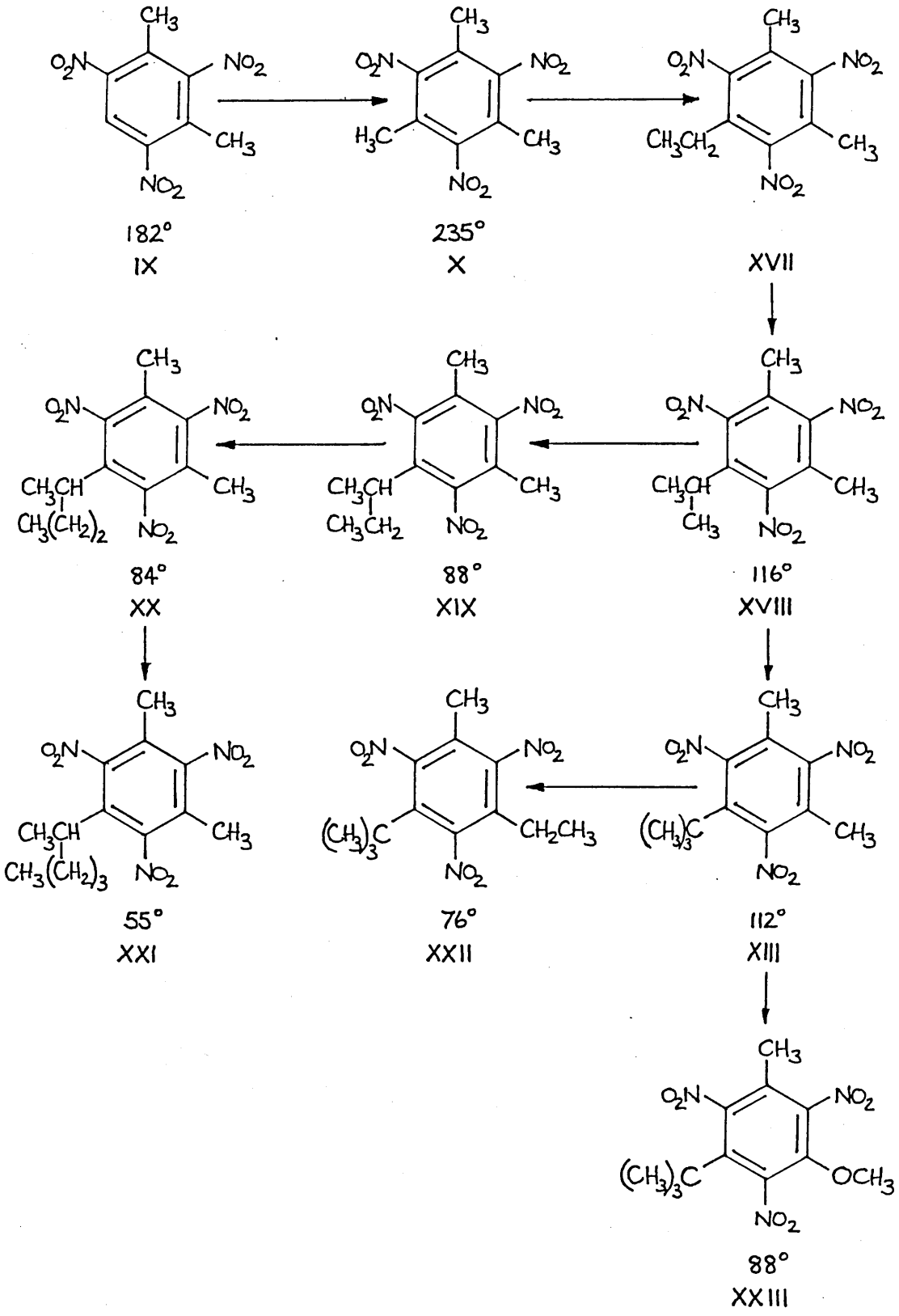
Scheme 4: Alkyl substituted t-butyltrinitrobenzenes.



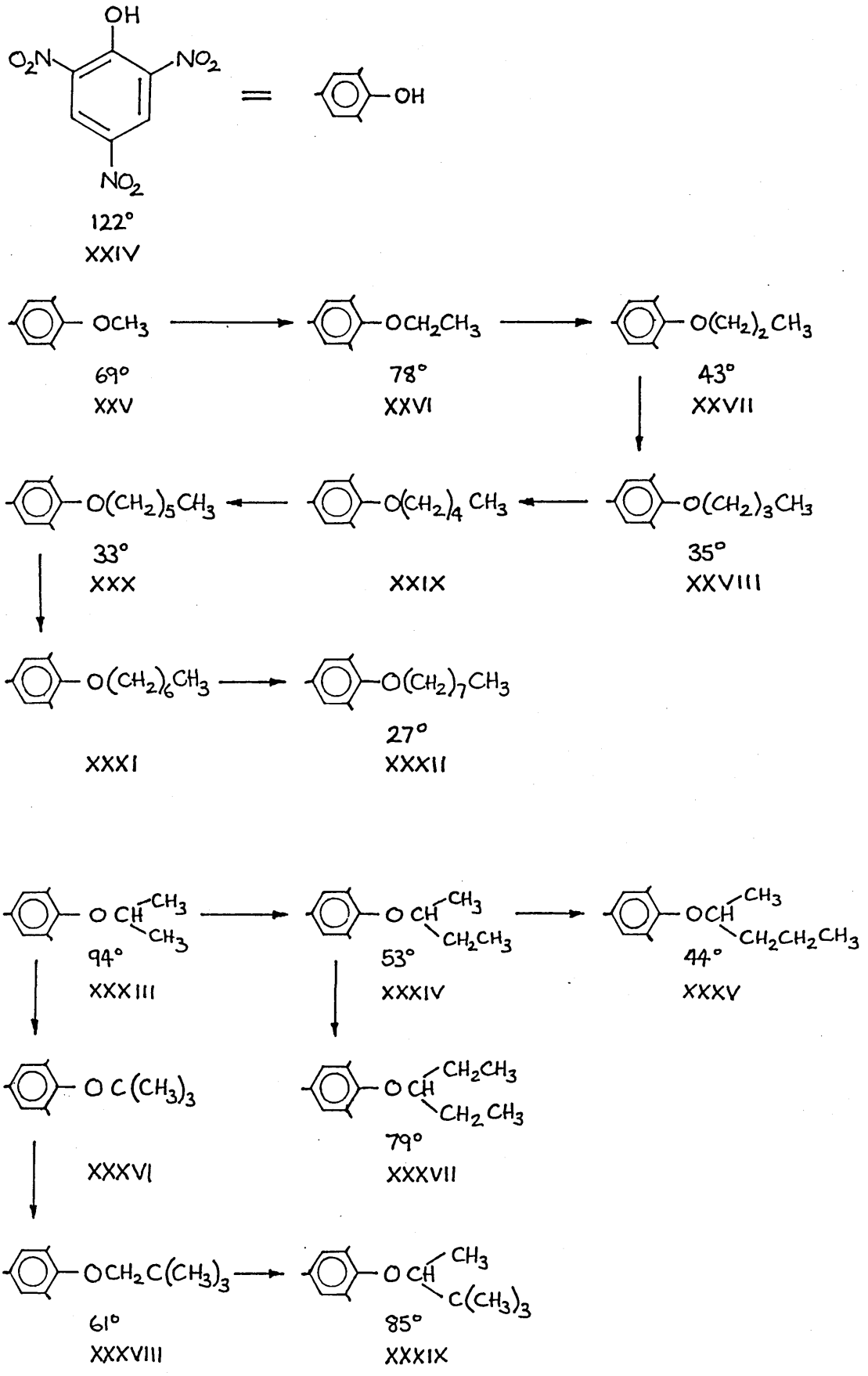
Scheme 5: Ethyl substituted trinitrobenzenes.



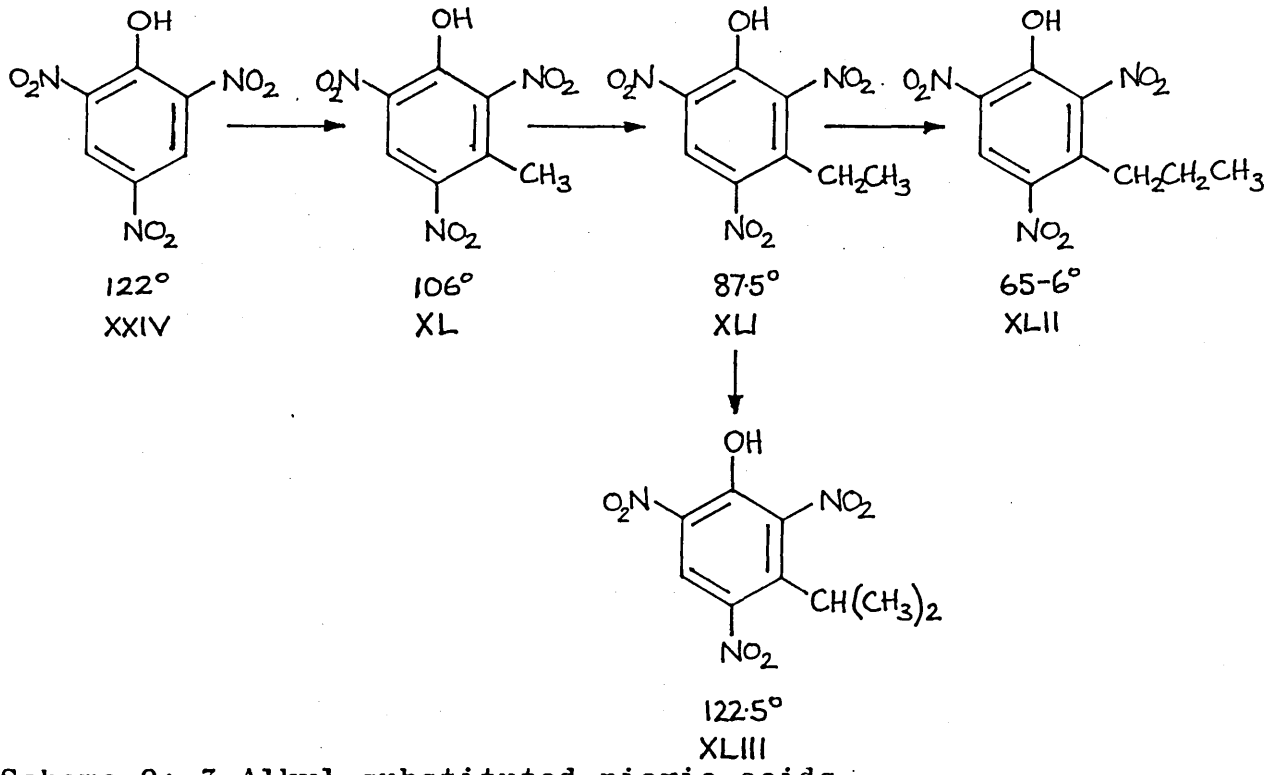
Scheme 6: Trialkyl substituted trinitrobenzenes.



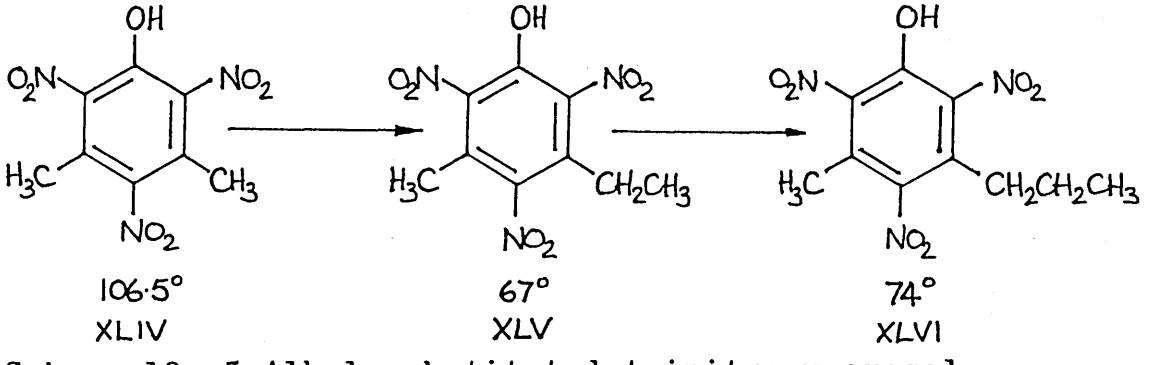
Scheme 7: 5-Alkyl substituted trinitro-m-xylenes.



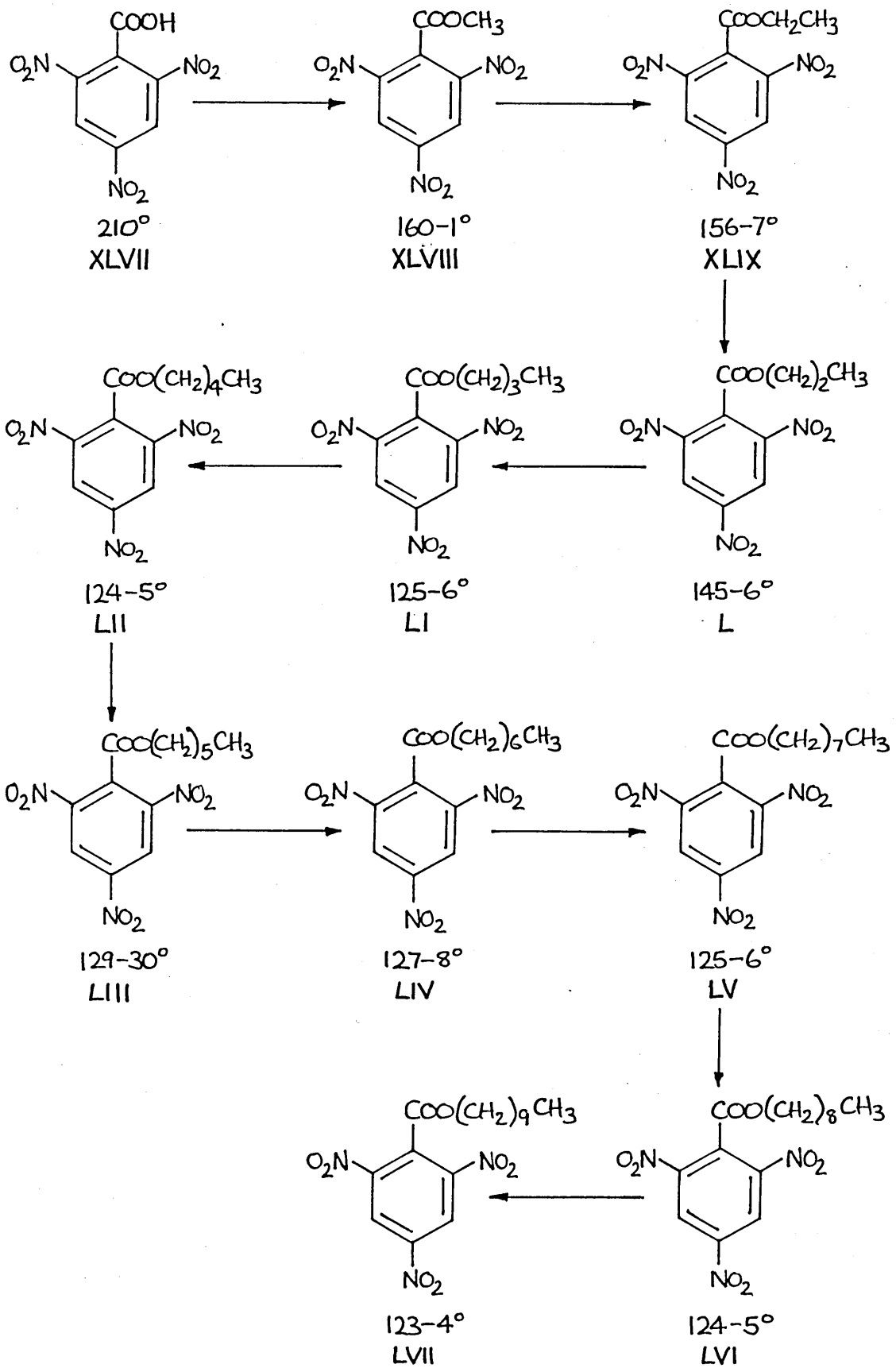
Scheme 8: Ethers of picric acid.



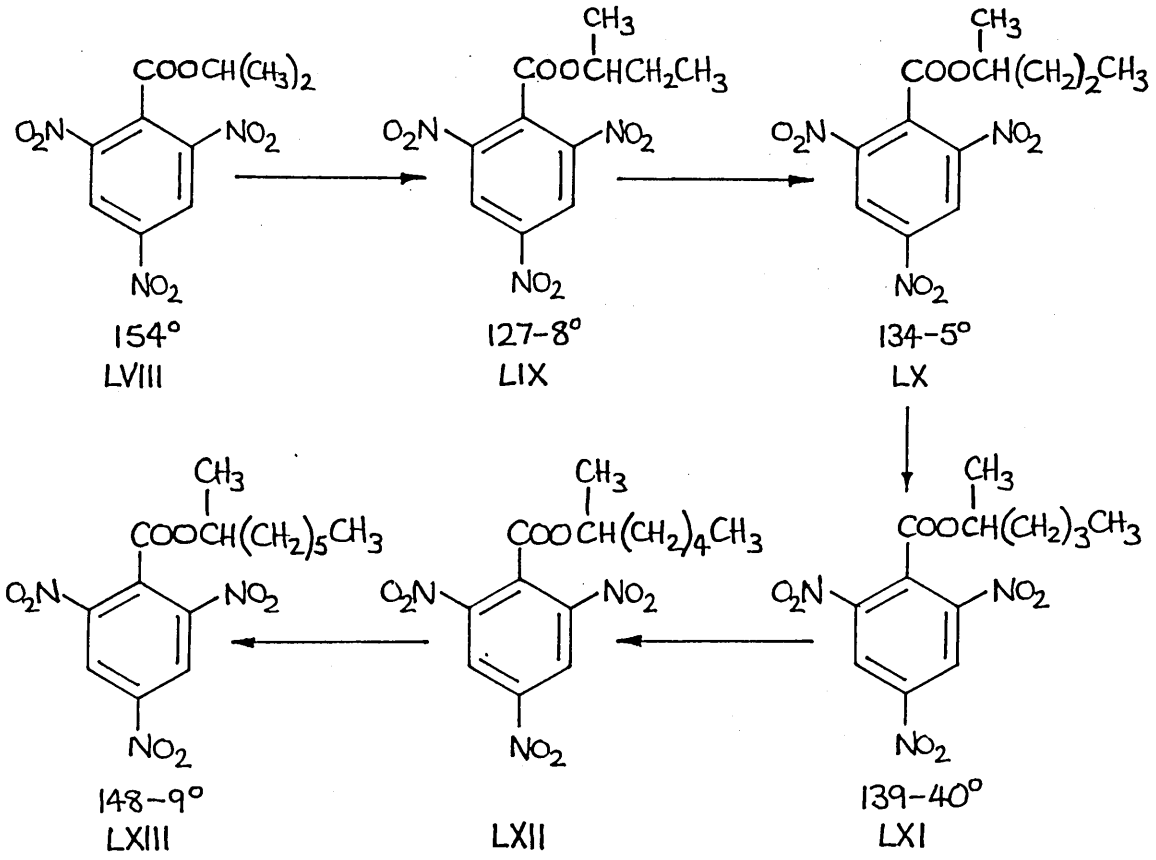
Scheme 9: 3-Alkyl substituted picric acids.



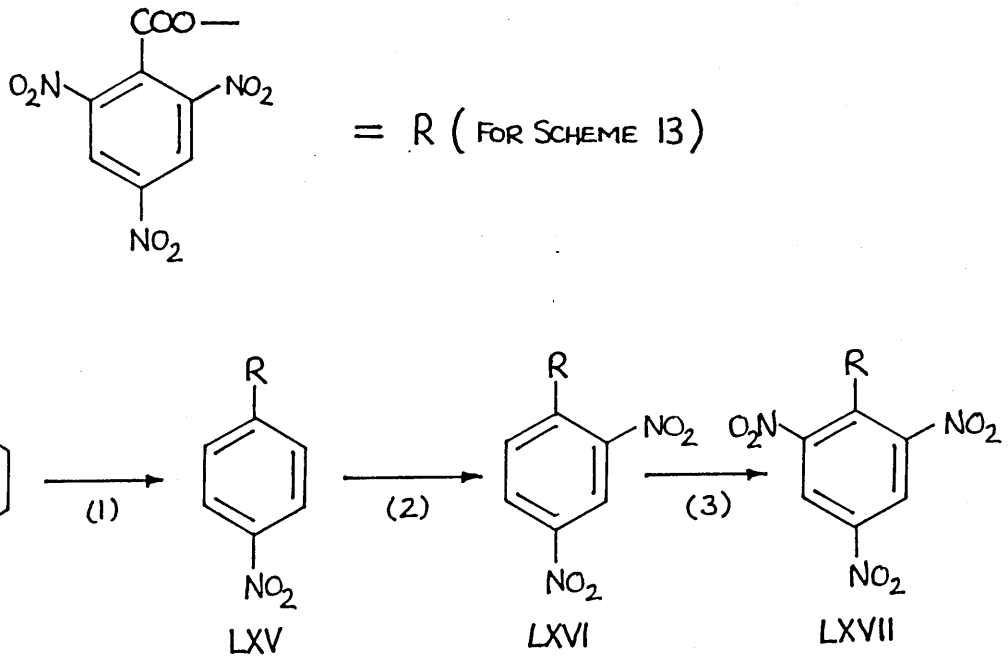
Scheme 10: 5-Alkyl substituted trinitro-m-cresol.



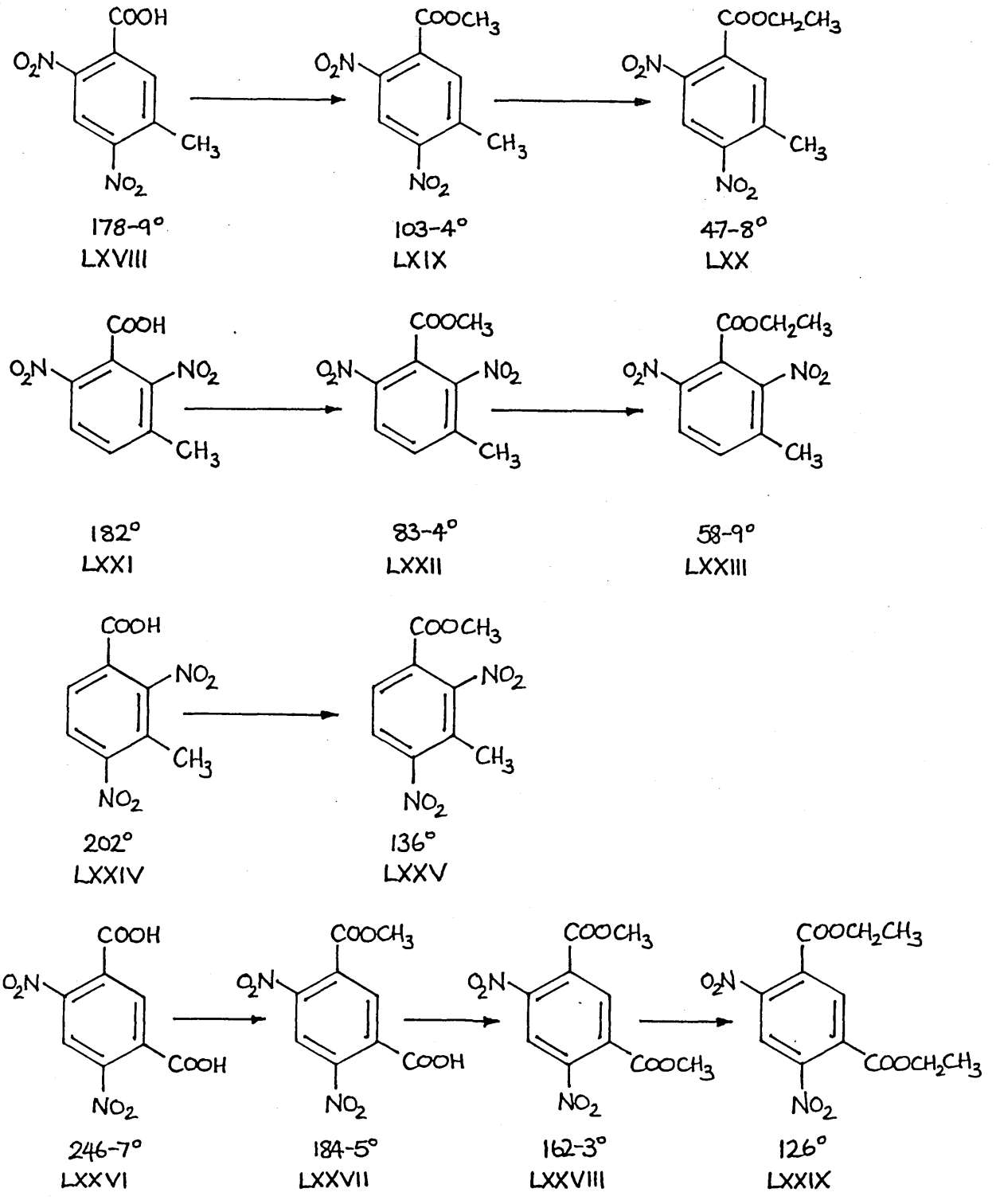
Scheme 11: n-Alkyl esters of trinitrobenzoic acid.



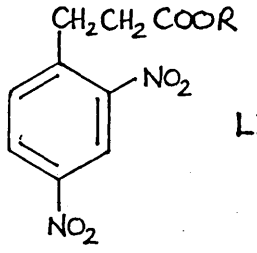
Scheme 12: 2-Alkyl esters of trinitrobenzoic acid.



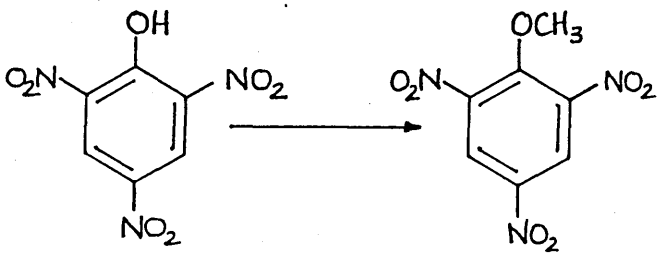
Scheme 13: Nitrophenyl esters of trinitrobenzoic acid.



Scheme 14: Dinitro isophthalic and m-toluic acids and esters.

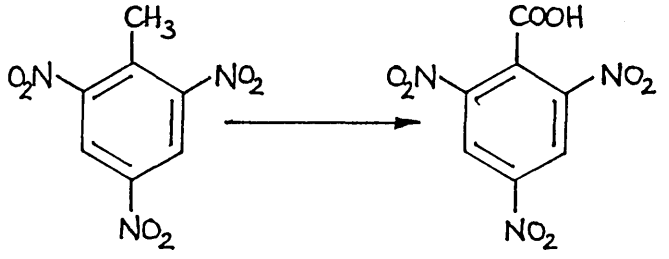


LXXX



122°
XXIV

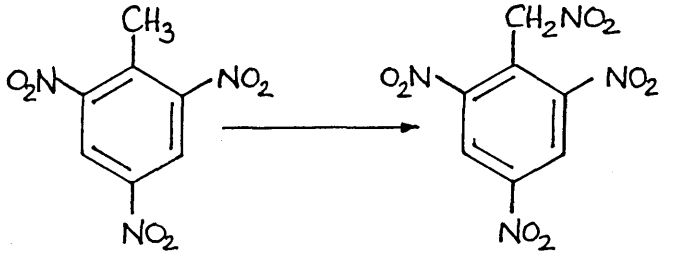
69°
XXV



82°
II

210°
XLVII

Scheme 15: Examples of the change in melting point with functional group.



82°
II

118°
LXXXI

Scheme 16: The effect of the number of nitro groups on the melting point.

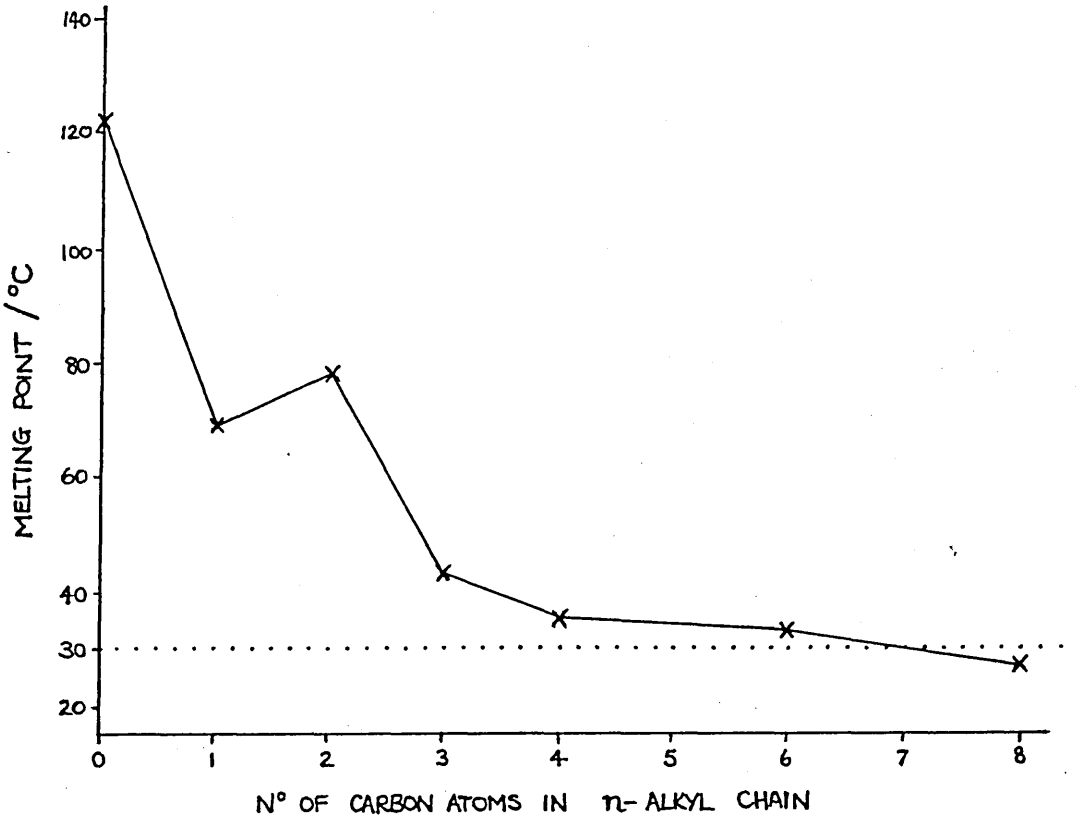


Figure 1: A graphical representation of Scheme 8.

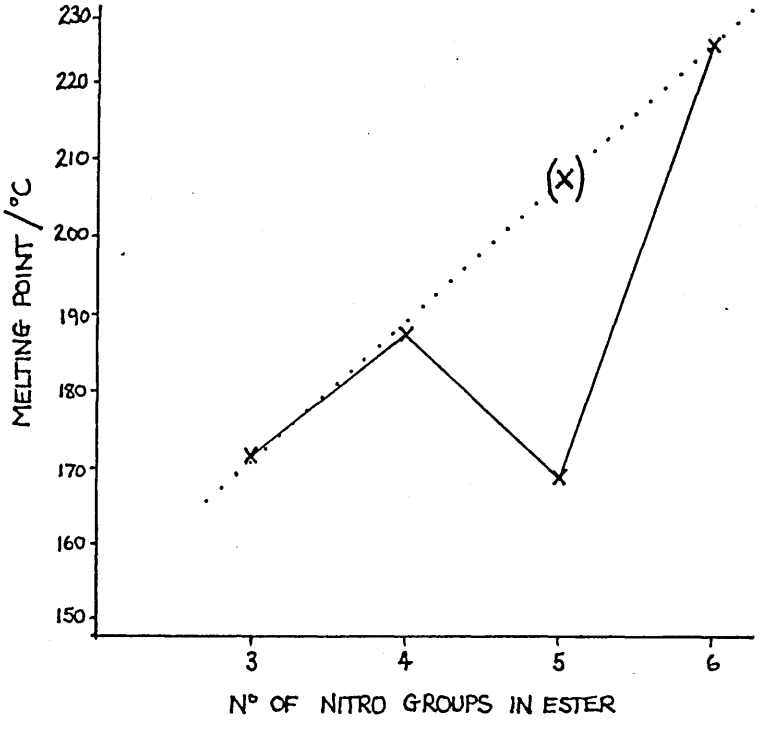
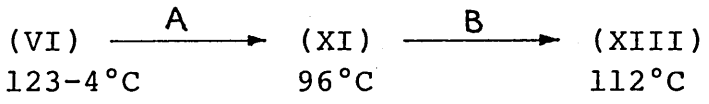


Figure 2: A graphical representation of Scheme 13.

It is generally accepted that a change of functional group significantly affects the melting point of any organic compound due to major alterations to intermolecular forces, in particular hydrogen bonding, as shown in Scheme 15.

Most correlations show that increasing the length of any aliphatic side chains directly decreases the melting point, though this decrease seems to show an asymptotic low, i.e. at a certain chain length, an additional increase would not substantially decrease the melting point any more. In fact, if the chain length was increased further the melting points would very likely start to rise again due to increasing mass effects. An example of this can be seen in Scheme 8 and Figure 1. This series of compounds has an asymptotic low of approximately 30°C.

Of the previously mentioned factors, direct exemplification of (iii) and (iv) is much more difficult than for (i) and (ii), because in many cases all four factors are inter-connected. However, Scheme 4 shows an example of how asymmetry in the molecule affects the melting point (factor (iii)). Step A decreases the symmetry of (VI) and therefore decreases



Recap Scheme 4: The affect on melting point of molecular asymmetry.

the melting point of the compound. Step B increases the symmetry again and the melting point increases. Schemes 3 and 5 also show that increasing the symmetry of the molecule can vastly increase the melting point.

(II) ⟶ (IX) ⟶ (X)
82°C 182°C 235°C

Recap Scheme 3: The affect of molecular symmetry on melting point.

(III) ⟶ (XIV) ⟶ (XV)
35°C 62.3°C 108°C

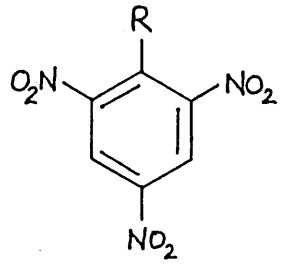
Recap Scheme 5: The affect of molecular symmetry on melting point.

The relationship shown in Scheme 16 is an example of the influence of the number of nitro groups on the melting point (factor (iv)). Addition of nitro groups, aliphatic or aromatic, increases the melting point, although aromatic nitro groups seem to affect this to a greater extent. Scheme 13 illustrates the inter-relationship of factors (iii) and (iv). Step (1) shows that addition of a nitro group results in an increase in the melting point. In Step (2), addition of a nitro group affects the symmetry and gives an overall drop in melting point. Step (3) shows that greater symmetry together with addition of a nitro group leads to a very sharp increase in the melting point. If the graphical representation of Scheme 13 is considered (Figure 2), it can be seen that the only asymmetrically substituted compound has quite a drop in melting point compared to the rest. Thus if it were possible to add an aromatic nitro group, without loss of symmetry, a melting point of approximately 205°C should be obtained. Therefore, in this case, it appears that the asymmetry produces a drop of approximately 40°C in melting temperature.

1.2 TARGET COMPOUNDS

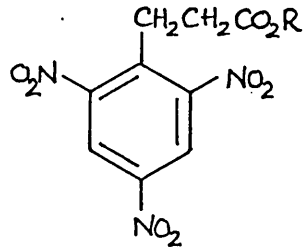
Consideration of the above melting point data led to the conclusion that there were four main categories of compound (Figure 3: A-D), within which low melting points should be obtained. Category A type compounds were chosen because increasing the alkyl chain length would seem likely

Category A:



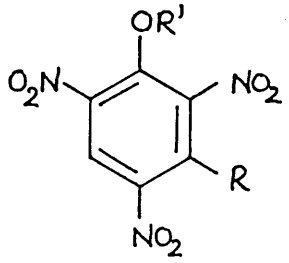
ALKYLTRINITROBENZENES

Category B:



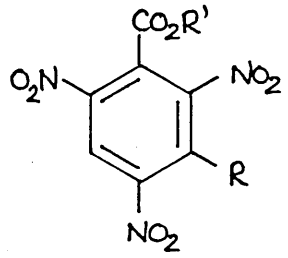
3-(TRINITROPHENYL)PROPANOATE ESTERS

Category C:



3-ALKYLPICRYL ETHERS

Category D:



3-ALKYLTRINITROBENZOATE ESTERS

Figure 3: Target compounds.

to lower the melting point, and since ethyltrinitrobenzene (III) has a melting point of 35°C, higher homologs would presumably be liquids. Category B type compounds were chosen because, as previously mentioned, their 2,4 -dinitro analogs have been reported as liquids. Picryl ethers have fairly low melting characteristics and category C compounds are picryl ethers with an asymmetric substitution pattern, and therefore should have even lower melting points. Also the longer this alkyl substituent, the lower the melting points should become. Similarly, category D compounds have the asymmetry which should bring down the melting point compared to those of the trinitrobenzoate esters.

These categories thus became the target compounds of a synthetic programme which would confirm the hypothesis that the four factors previously mentioned do influence melting points, and also provide new low melting polynitroaromatic compounds for the application discussed earlier.

1.3 SYNTHETIC ROUTES

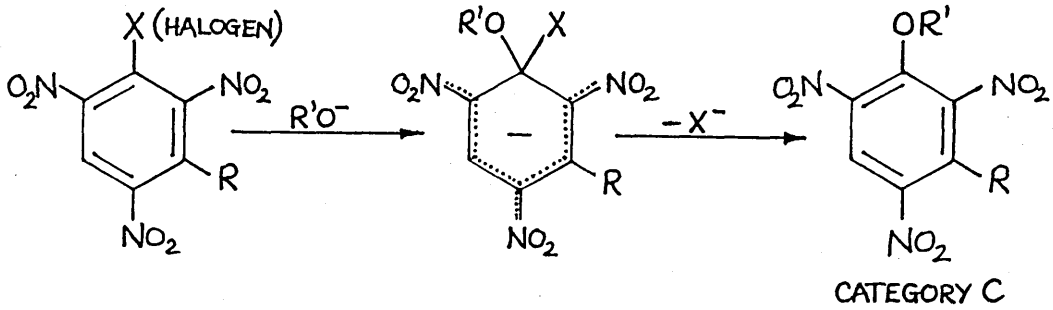
In line with the aims mentioned previously, an appropriate general approach to the synthesis of the target polynitroaromatic compounds given above, would be to start with 2,4,6-trinitoluene (TNT) wherever possible. Alternatively, another approach could be to prepare an appropriately substituted aromatic ring and then to trinitrate this product. TNT is a starting material which was readily available from P.E.R.M.E.; is easily purified; would eliminate the need for oleum nitrations; and was therefore preferred as a starting material.

When TNT is treated with base in a dipolar aprotic solvent, a TNT anion can be produced by abstraction of a proton from its methyl group. It was proposed that this anion could be used as a nucleophile in reactions with organic halides, thus extending the alkyl side chain to

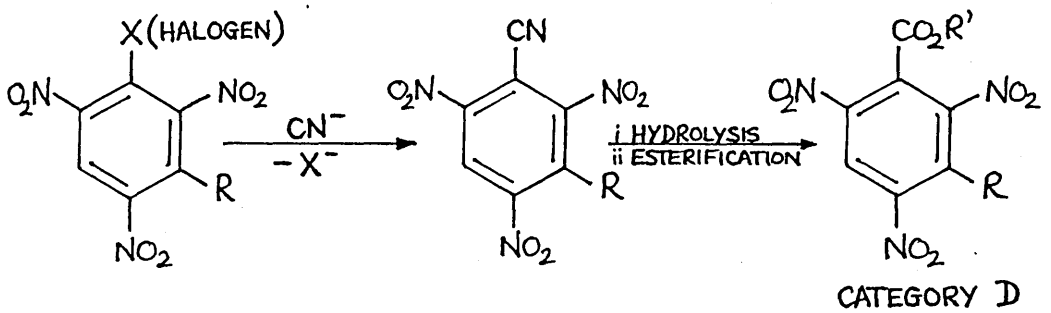
yield category A and B target compounds. Shipp et.al. have indeed shown the TNT anion to act as a nucleophile in both aliphatic and aromatic substitution.[3]

A proposed route to category C and D compounds involved nucleophilic aromatic substitution, as shown in Schemes 17 and 18. Both of these schemes require a 3-alkylpicryl chloride as starting material. Two synthetic routes were proposed to prepare these compounds, starting either from TNT (Scheme 19) or from the appropriate phenol (Scheme 20).

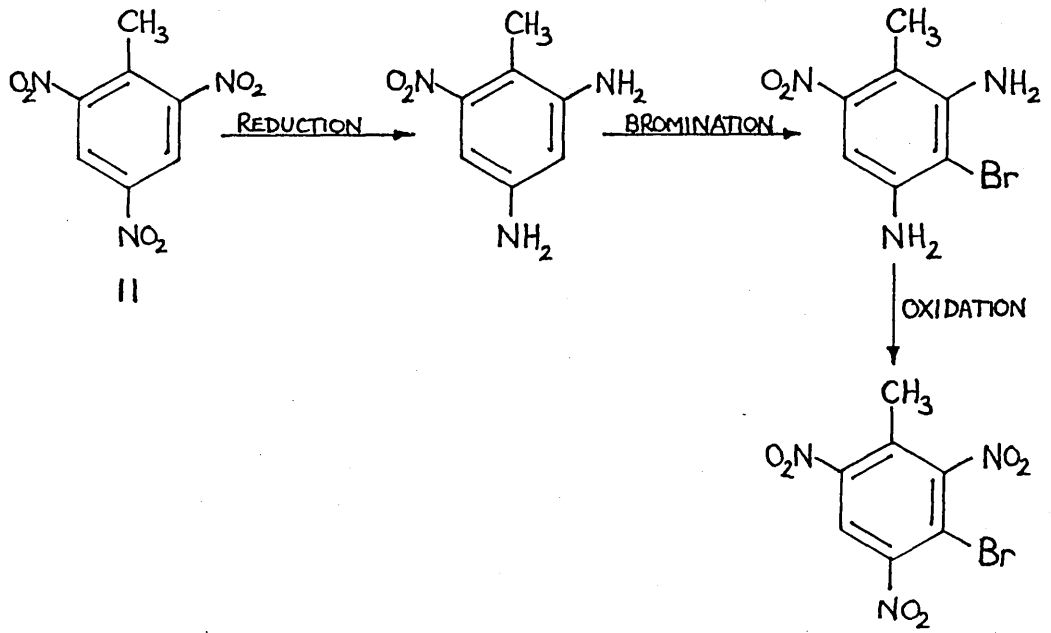
Scheme 20 involves nitration, but does not necessitate the use of oleum because of the activating effect of the hydroxy group on electrophilic aromatic substitution reactions. Trinitration of the parent halobenzene would require the use of oleum and it was therefore not considered as a possible route.



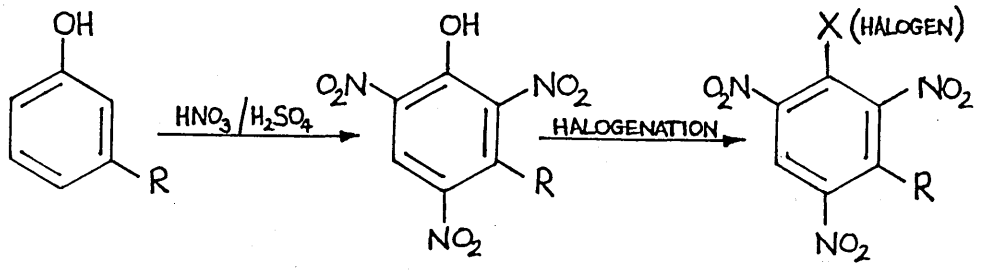
Scheme 17: Proposed preparation of category C compounds.



Scheme 18: Proposed preparation of category D compounds.



Scheme 19: Proposed preparation of category C precursors.



Scheme 20: Alternative route to 3-alkylpicryl halides.

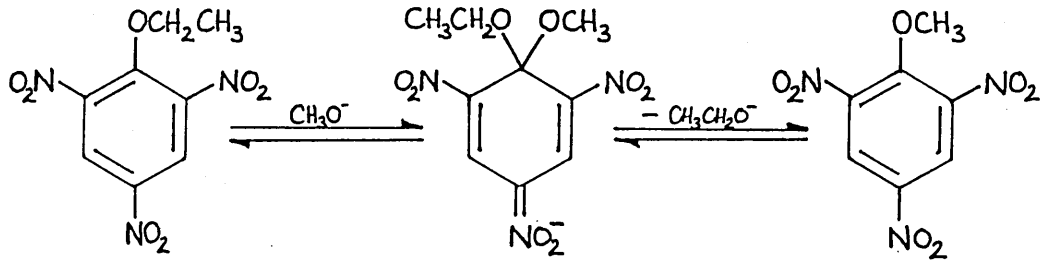
CHAPTER 2

THE TNT ANION IN SYNTHESIS

2.1 TNT AND BASES

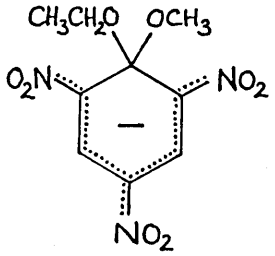
For over one hundred years chemists have been intrigued by the intense colours produced when polynitroaromatic compounds are treated with base. Reports of these reactions first appeared around 1880[4], when it was noticed that the initial reactions that occurred could be reversed by acid, and that these initial reactions were followed by a slower irreversible reaction. It was not until 1902 that any convincing chemical evidence appeared to explain the processes involved in these reactions. This evidence was provided by Meisenheimer[5] who observed that identical species were obtained when potassium methoxide was added to 2,4,6-trinitrophenetole (XXVI), and when potassium ethoxide was added to 2,4,6-trinitroanisole (XXV) (equation 1). Also when each reaction mixture was acidified, identical mixtures of 2,4,6-trinitrophenetole and 2,4,6-trinitroanisole were obtained. He concluded that the species observed in solution must be an addition complex of the type (LXXXII) shown in equation 1. Today with modern analytical methods, the structure (LXXXIII) has been assigned to this intermediate in which the negative charge is delocalised around the benzene ring and is essentially shared between the 3-nitro groups.

This type of intermediate is called a σ-adduct. If the addition complex is formed by attack of a carbon nucleophile on a polynitroaromatic compound it is often called a Janovsky complex[6] (so named after Janovsky, who noticed a colour formed in the reaction of dinitrobenzene with alkaline acetone); when the reaction is with an oxygen, nitrogen or any other nucleophile the complex is called a Meisenheimer complex. σ-Adducts have been the subject of many papers[7] and reviews,[8] mainly because they have been recognised as intermediates in nucleophilic aromatic substitution reactions.

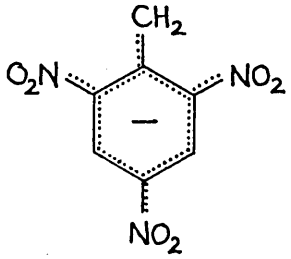


XXVI LXXXII XXV

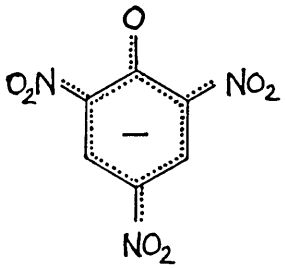
Equation 1: The formation of σ-adducts.



LXXXIII



LXXXIV



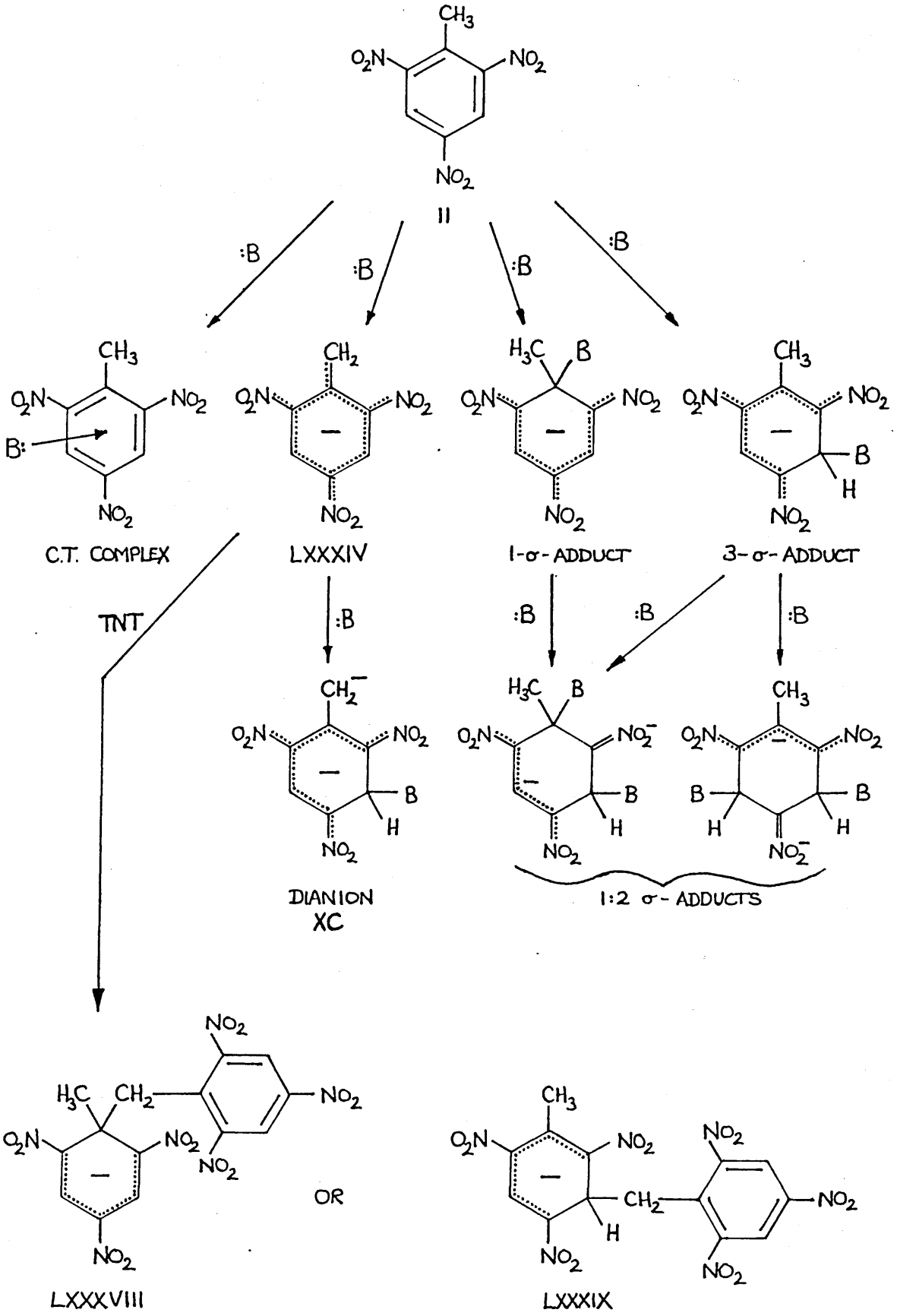
LXXXV

The reactions of 2,4,6-trinitrotoluene (TNT) with base have been thoroughly investigated over the past thirty years. These reactions are extremely complex with many reactive intermediates having been observed. TNT, in common with most polynitroaromatic compounds, when treated with base undergoes a fast, acid-reversible reaction, followed by a slower irreversible reaction. Scheme 21 shows some of the species which have been identified during the initial reversible reaction of TNT with various bases. Most of these primary species formed are susceptible to oxidation from molecular oxygen, another polynitroaromatic molecule, their own nitro groups, or any other oxidising species present. This results in a general degradation involving a variety of oxidised species, radicals and radical ionic species; this is the nature of the slower irreversible reaction. This slower reaction is so complicated that a full study of it has never been reported. The initial reaction though has received a lot of attention and a large amount of interest has developed concerning the existence of the 2,4,6-trinitrobenzyl anion (LXXXIV) (TNT anion) and the mechanism of its formation.

2.2 THE TNT ANION

The 2,4,6-trinitrobenzyl anion was first postulated by Caldin and Long[9] in 1955. They attributed the structure (LXXXIV) to a purple colour formed by the reaction of ethoxide ions with TNT. This seemed likely as this species would be isoelectronic with the picrate ion (LXXXV). Since then this species has been the subject of many kinetic studies, and substantial evidence for the existence of this anion has been sought. Initially, the results obtained appeared to be conflicting.

Large primary isotope effects were observed when TNT-d^3 was treated in various bases in deuterated solvents.[10,11,12,13] That is, when the methyl group on TNT is fully deuterated, the rate of reaction with base becomes slower; this suggests that proton (or deuteron) abstraction by base is the major process, which is indicative of TNT anion formation.

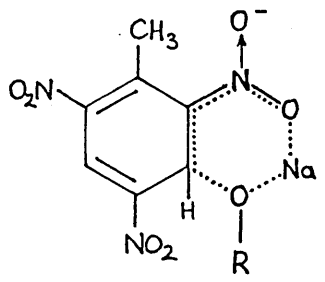


Scheme 21: The species produced by the action of base upon TNT.

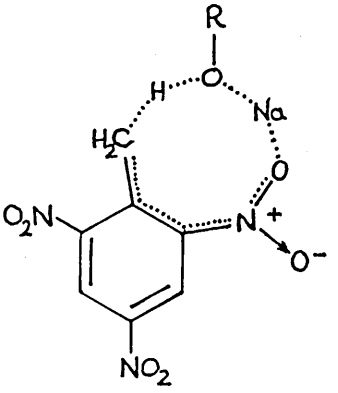
Deuterium isotopic exchange experiments were not so convincing. When normal TNT is treated with a base in a deuterated solvent a proton (or deuteron) exchange equilibrium is set up and deuterium is incorporated into the acidic site of the molecule. Exchange was observed in D_2O/pyridine but only to 23% of the theoretical value after 2-3 weeks.[14] Negligible exchange was observed in 10% DMSO/D_2O with NaOD as the base,[15] but rapid exchange in 90% DMF/D_2O/NaOD.[16]

Bernasconi[17], using temperature jump experiments observed the TNT anion in 50% dioxan/water, but not in 10% dioxan/water. He concluded that to produce the purple anion, a reasonable base strength and a low ratio of water : dipolar aprotic solvent was necessary, as σ-adduct formation is favoured in water rich solvents. With this conclusion he could explain the previous exchange experiments; that is, in pyridine/D_2O slow exchange is observed because pyridine is a weak base; in 10% DMSO/D_2O negligible exchange is observed because the TNT anion is not the major species; rapid exchange in 90% DMF/D_2O/NaOD is observed because conditions are correct for anion formation.

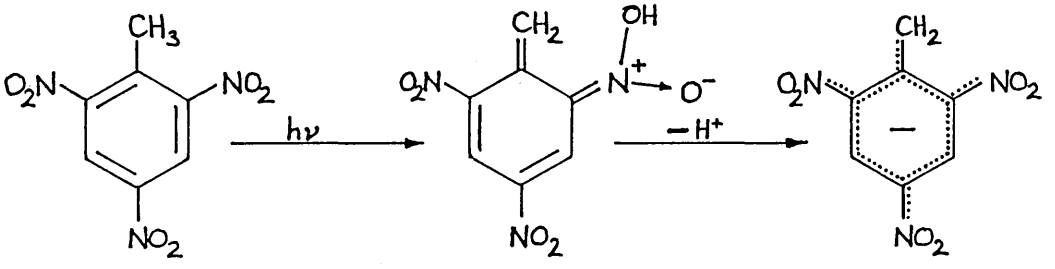
Bernasconi also observed a rapid pre-equilibrium which was followed by slower TNT anion formation. This he tentatively attributed to a 3-σ-adduct being the kinetic product and the TNT anion being the thermodynamic product : an idea postulated by Caldin on observation of a transient brown colour prior to the formation of the anion. Buncel and co-workers[11] studying the action of isopropoxide ions on TNT supported this idea of pre-equilibrium and proposed that an ion pairing effect stabilised 3-σ-adduct formation by producing a cyclic 6-membered transition state (LXXXVI) as opposed to an 8-membered cyclic transition state (LXXXVII) for proton abstraction. Bernasconi also discovered the existence of Janovsky type complexes (LXXXVIII - LXXXIX) shown in scheme 21, but he was unsure of the position of addition.



LXXXVI

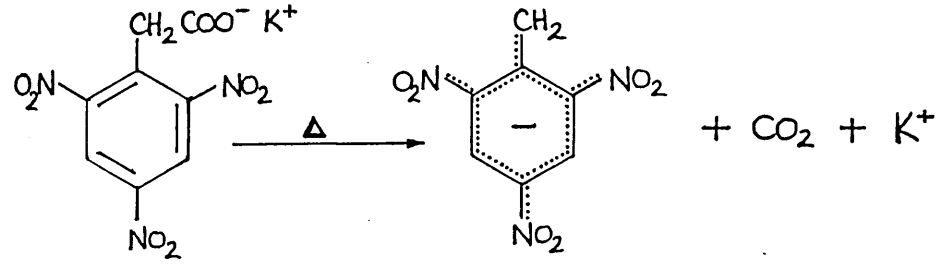


LXXXVII



II aci-TNT $pK_a < 1$ LXXXIV

Equation 2: The photochemical production of the TNT anion.



LXXXIV

Equation 3: The decarboxylation of 2,4,6-trinitrophenyl-ethanoic acid, potassium salt.

Servis[18] on the other hand argued against the TNT anion because in his study of the action of methoxide on 2,4,6-trinitroaniline, only σ-adducts were produced. He proposed that since the aniline protons should be 10^{10} times more acidic than the analogous hydrocarbon (TNT) protons, the TNT anion should not exist.

Until 1976, nmr investigations had only been able to observe σ-adducts; nmr evidence for the TNT anion had been impossible to obtain due to the accompanying production of a variety of free radicals. Fyfe and co-workers[19] succeeded by employing a flow cell in their investigations. They observed the fast formation of a brown species (the σ-adduct) followed by a slower appearance of the TNT anion. They also realised the importance of efficient mixing and the amount of base added. The mixing is optimised when flow techniques are used, and it was noted that amounts of base below equimolar, to TNT, produced vast quantities of radicals whereas greater than equimolar quantities of base produced new species. In their studies the nmr spectrum of the dianion (XC) was observed. During this work, Fyfe and co-workers prepared potassium and tetraphenylarsonium salts of the TNT anion. These salts were prepared at -70^{o}c in an inert atmosphere and were unstable at ambient temperatures. Fyfe also carried out electron spin resonance studies in which substantial quantities of radicals were observed, which seemed to increase with the disappearance of the TNT anion. This observation conflicted with a prior esr study[20], where only weak signals were observed.

More recently the TNT anion has been produced by photochemical means (equation 2) in solutions of low pH[21]; and also by the decarboxylation of 2,4,6-trinitrophenylethanoic acid (equation 3).[22]

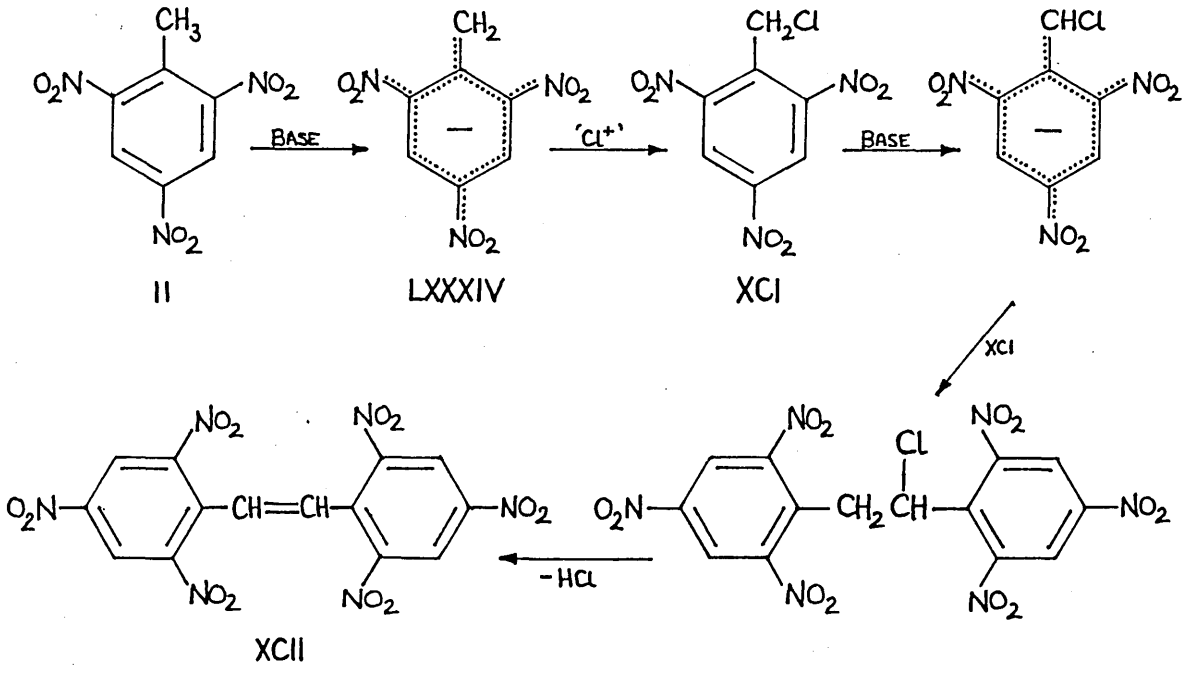
In summary, the evidence is now overwhelming, that when TNT in a dipolar aprotic solvent is treated with reasonably strong base,

the primarily formed σ-complex (kinetic product) will give way to production of the TNT anion (thermodynamic product). Though it must be said that many authors have commented on concentration effects upsetting this process, e.g. [Base]>[TNT] produces other species (dianion and 1:2 σ-complexes), and the decomposition rate is increased; [TNT]>[Base] leads to a high degree of decomposition, Janovsky complex formation and vast quantities of radicals. In high equimolar concentrated solutions of TNT and base, radical formation predominates over all other processes.

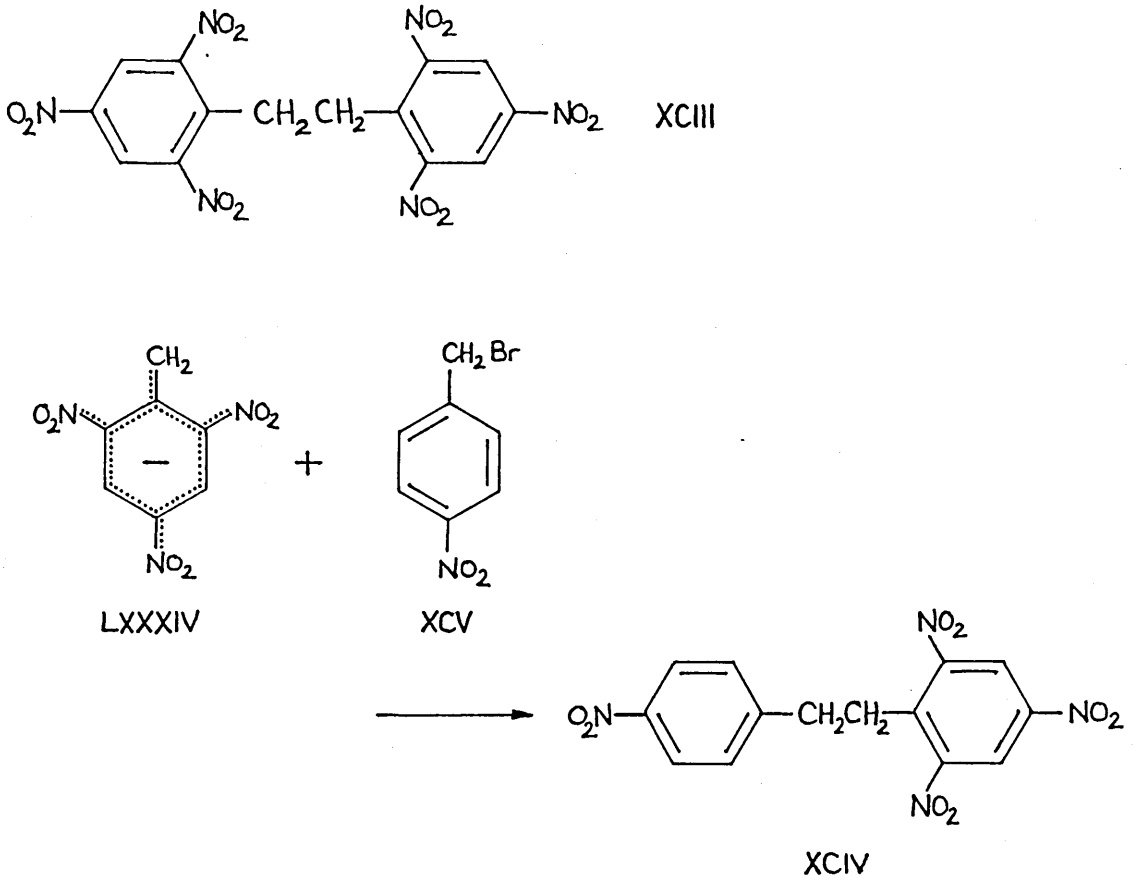
2.3 SYNTHETIC UTILITY OF THE TNT ANION

Only Shipp and co-workers have used the TNT anion in synthetic chemistry. Their initial interest was in the preparation of the industrially important explosive 2,2',4,4',6,6'-hexanitrostilbene (HNS)[23] (XCII), which they obtained from the reaction of 2,4,6-trinitrobenzyl chloride (TNBCl,XCI) with alcoholic potassium hydroxide. It was found that TNBCl could be prepared from TNT by using sodium hypochlorite to trap the TNT anion; "Cl^+" being the trapping agent. HNS could thus be produced from TNT in a "one pot" reaction (equation 4).[24] This reaction could also be modified to produce 2,2',4,4',6,6'-hexanitrobibenzyl (HNBB,XCIII) by varying the conditions. Mechanistically it was suggested that TNBCl yielded an anion by basic proton abstraction from the methylene group. This anion then reacted with another TNBCl molecule followed by ready dehydrohalogenation of the α-chlorobibenzyl (equation 4).

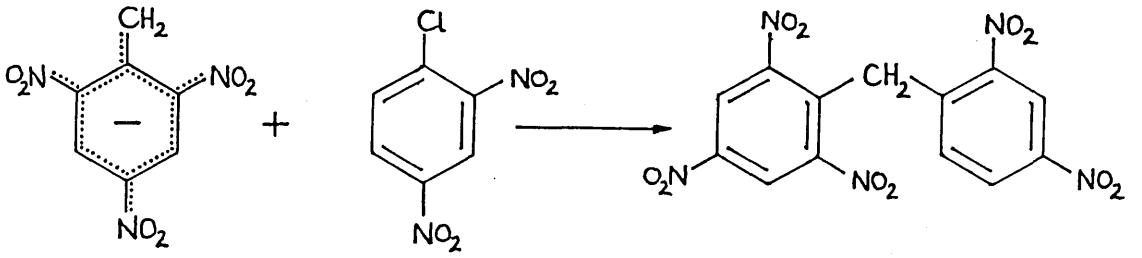
This work directed their attentions to the possibility of utilising the TNT anion as a nucleophile.[3] They reported >80% yields of 2,4,4'6-tetranitrobibenzyl (TNBB,XCIV) by the reaction of TNT anion with p-nitrobenzyl bromide (XCV) (equation 5). In addition, they carried out a range of nucleophilic aromatic substitutions with the TNT anion to produce a variety of nitrated diphenylmethanes (equation 6).



Equation 4: Reaction of TNT with alkaline hypochlorite.

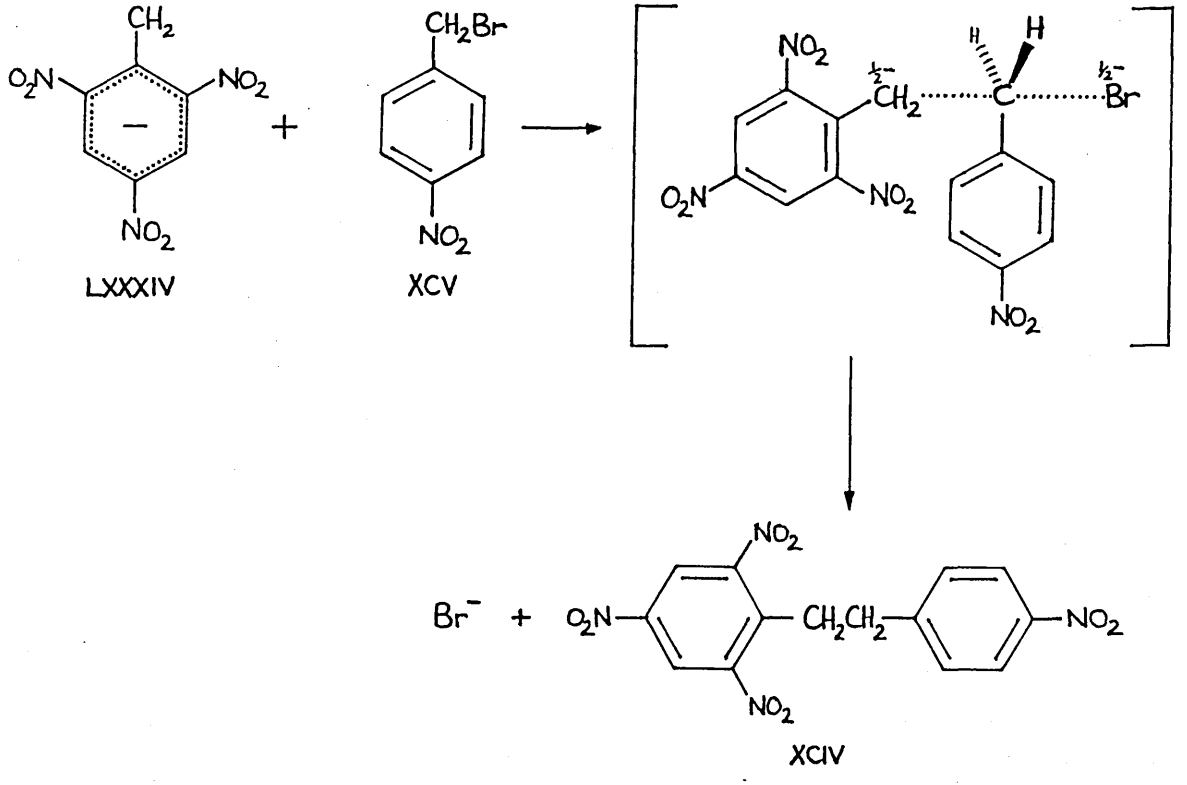


Equation 5: Reaction of TNT with p-nitrobenzyl bromide, an example of aliphatic substitution.



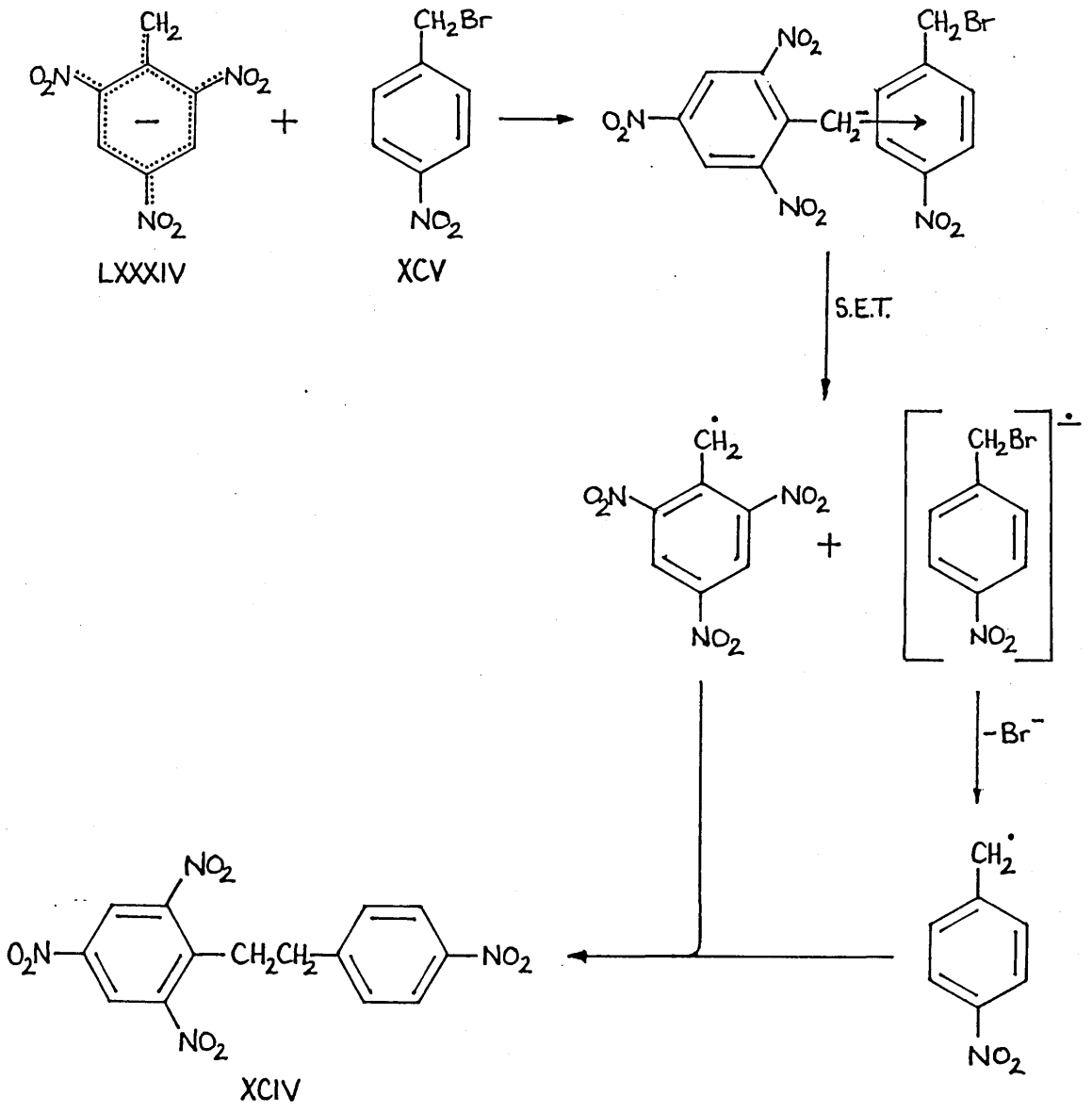
LXXXIV

Equation 6: Reaction of TNT anion giving aromatic substitution.

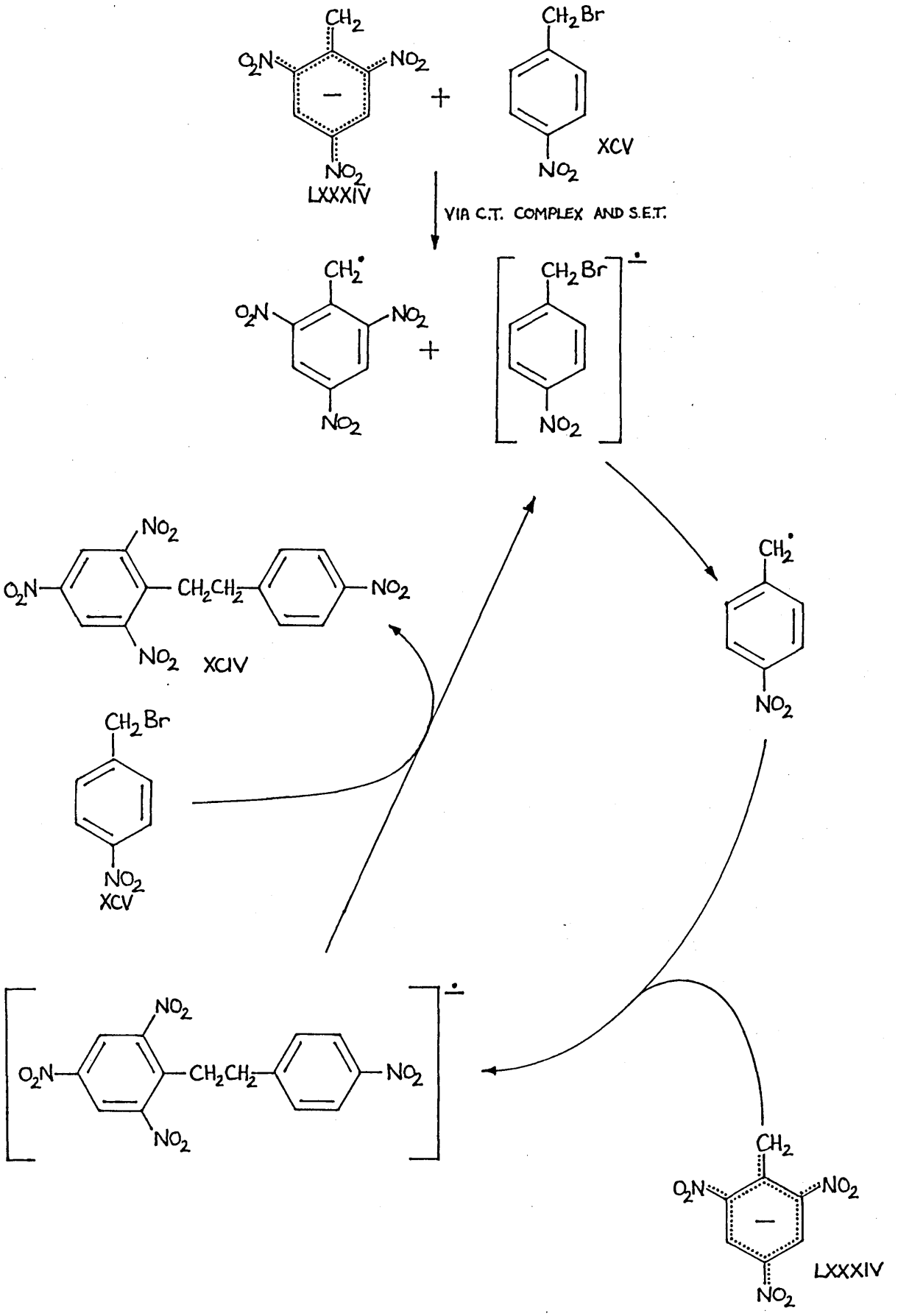


LXXXIV XCV XCIV

Scheme 22: The S_N2 mechanism pathway of the reaction of TNT with p-nitrobenzyl bromide.



Scheme 23: The reaction of TNT anion with p-nitrobenzyl bromide by radical mechanism.



Scheme 24: Radical chain mechanism applied to the reaction of TNT and p-nitrobenzyl bromide.

There are two possible mechanisms for the reaction in equation 5; ionic or radical. The ionic mechanism, or nucleophilic aliphatic substitution, could be, for example, S_N2 (Scheme 22). Two radical mechanisms are possible as shown in Schemes 23 and 24.[3,25]

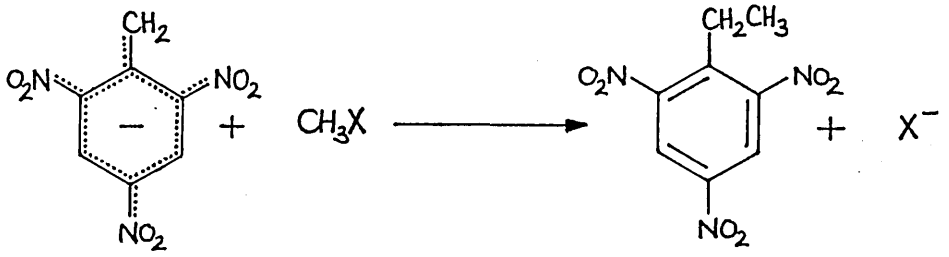
Shipp et. al. argued in favour of an ionic mechanism because a significant leaving group effect was observed. When the TNT anion was reacted with p-nitrobenzyl bromide an 83% yield was found, whereas reaction with p-nitrobenzyl chloride afforded only an 8% yield. Also Kornblum and co-workers,[26] who studied the alkylation of the 2-nitropropyl anion with p-nitrobenzyl halides, found that with carbon alkylations (radical mechanism), very little leaving group effect was observed, but that other oxygen alkylations (ionic mechanism) exhibited a substantial leaving group effect. Further to this, in aromatic substitution experiments that Shipp et. al. carried out, they again found a substantial leaving group effect which is consistent with an ionic mechanism.

Thus, the above work provided a basis for the idea of utilising the TNT anion as a nucleophile to react with various substrates for the synthesis of the target compounds of categories A and B, as described earlier.

2.4 PHASE TRANSFER CATALYSIS

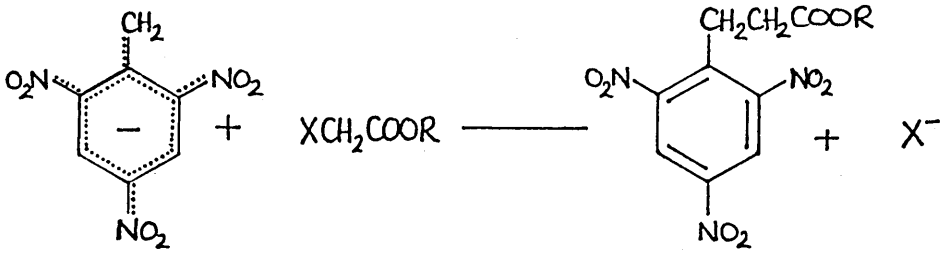
As discussed above, the TNT anion has been used as the nucleophile in what appear to be aliphatic and aromatic nucleophilic substitution reactions. It was on this basis that investigations were started into the synthesis of target compounds by reactions such as illustrated in equations 7 and 8.

The essential requirement for success in these reactions was considered to be production of the TNT anion in the presence of the required alkyl halide or haloacetate ester. Nucleophilic substitution under phase transfer catalysis conditions[28] was the initial approach adopted.

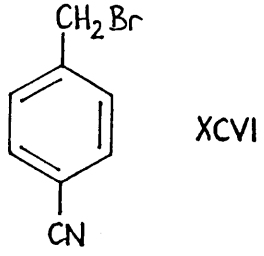


LXXXIV

Equation 7: The synthesis of category A compounds.



Equation 8: The synthesis of category B compounds.



XCVI

There are a number of important factors to consider when attempting reactions of this type.

(i) Choice of catalyst. The catalyst must have the ability to partition itself equally between the aqueous and organic phases, e.g. the tetramethylammonium cation is too hydrophilic and the tetra-n-hexylammonium is lipophilic. It also must not be too surface active e.g. the cetyltrimethylammonium cation ($[N(nC_{16}H_{33})(CH_3)_3]^+$). The ideal choice is the tetra-n-butylammonium cation.

(ii) Choice of catalyst counter ion. This must be hydrophilic, so as not to interfere with the reaction process. The bisulphate ion (HSO_4^-) is a very hydrophilic anion and therefore a good choice of catalyst would be tetra-n-butylammonium hydrogen sulphate.

(iii) Choice of halogen leaving group. The halide ion produced in the substitution must be hydrophilic to provide a driving force for the reaction. Iodide ions are too lipophilic; bromide ions are evenly partitioned, but chloride ions are hydrophilic and thereby chosen as the best leaving group to use in this situation

Addition of an aqueous solution of base, containing phase transfer catalyst, to a solution of TNT in dichloromethane, containing an appropriate substrate, gave a burgundy coloured organic phase, which eventually with vigorous stirring became completely opaque. The aqueous phase turned slightly pink. On leaving the solution overnight, the organic layer became an opaque brown colour and the aqueous phase, too, had turned dark brown, though not opaque. The phase boundary was lined both sides with small solid particles. This was the pattern of events for every substrate chosen, with one exception. The intense purple colour which is characteristic of the TNT anion, was not observed in any of these experiments.

Thin layer chromatography (TLC) showed that many products were formed during these reactions. Figure 5 shows the chromatogram obtained from the reaction in which ethyl chloroacetate was the substrate.

This chromatogram is quite typical of those obtained. The only exception was when p-nitrobenzyl bromide (PNBBr) was the substrate. Figure 6 shows the thin layer chromatogram from the reaction of TNT with PNBBr. This chromatogram shows the reaction to be quite clean but not complete. Perhaps this is because of the nature of the leaving group (Br^-) which is not the preferred leaving group for phase transfer catalysis conditions. However, this reaction does show the formation of the required substitution product. Again, the TNT anion was not observed. Either the presence of water, albeit as a separate phase, did not favour its formation, or, it was consumed as soon as it was formed.

It is possible that, with all of these reactions, phase transfer catalysis of the hydroxide ions is slow and the TNT anion, as produced, reacted with neutral TNT or other nitro aromatic compounds to yield a variety of Meisenheimer or Janovsky type species which could lead to a range of products. Clearly, phase transfer catalysis was not providing a means of producing the desired target compounds.

2.5 SINGLE SOLVENT SYSTEMS

Shipp, Kaplan and Sitzmann[3] used a mixed solvent system in their preparation of TNBB, comprising tetrahydrofuran/methanol with aqueous sodium hydroxide as base. With 50% water present in the reaction mixture they observed 80% yields of TNBB. This method was repeated in our studies both with PNBBr and other substrates. With PNBBr as substrate, > 80% yield of TNBB was obtained, as a yellow solid, melting point of 181-2^{o}C after recrystallisation from ethanol/water. On adddition of aqueous sodium hydroxide, the reaction mixture again became burgundy in colour: not the colour

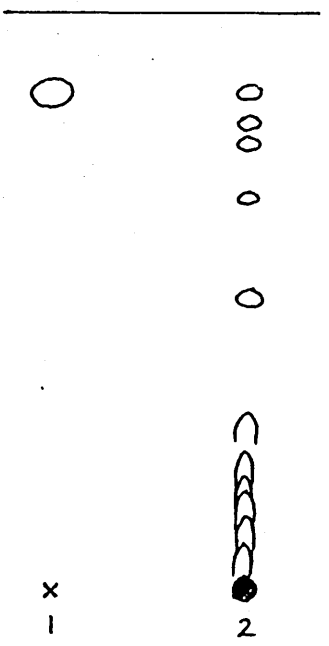


Figure 5: Thin layer chromatography from the reaction of TNT with ethyl chloroacetate under phase transfer catalysis conditions.

1 = TNT
2 = Reaction Mixture
Eluent = 40% Ethyl acetate
60% Petroleum spirit (40-60°)

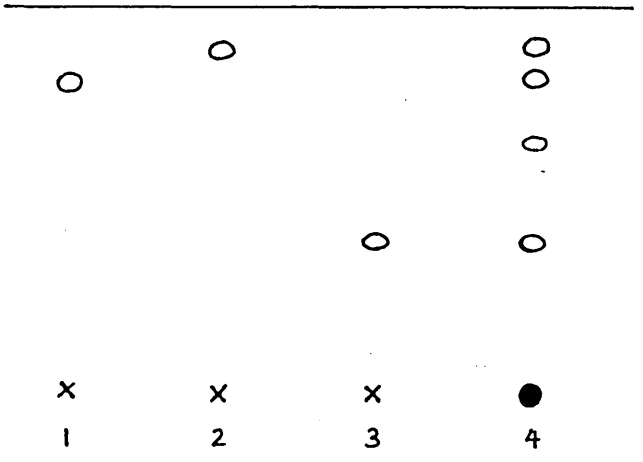


Figure 6: TLC of TNT reacted with p-nitrobenzyl bromide.

1 = TNT
2 = p-nitrobenzyl bromide
3 = 2,4,4',6-tetranitrobibenzyl,
4 = reaction product
Eluent = 50% ethyl acetate
50% petroleum spirit (40-60°)

expected on formation of TNT anion. One minute after the addition of the aqueous base, product began to precipitate and the reaction was effectively complete after thirty minutes.

If PNBBr was replaced by another substrate (ethyl chloroacetate, allyl bromide, allyl chloride, benzyl bromide, methyl iodide, 1-chlorobutane, 1-bromobutane were used) a complex product mixture was obtained similar to that observed in the earlier experiments (Figure 5). The fact that these other substrates did not participate in what has been described as a nucleophilic substitution reaction is perhaps not surprising, since the presence of 50% water in the system is not conducive to TNT anion formation. It is interesting that PNBBr does react so effectively under these conditions. Either PNBBr has a stabilizing effect on the TNT anion and precipitation of the product assists its formation, or the reaction has a different mechanism which is not favoured with other substrates.

If the TNT anion is to take part in a nucleophilic substitution reaction, then anion formation must be favoured. The elimination of water from the reaction system seemed the primary requirement. An extensive range of solvent systems and bases were studied and comparisons made between the nature and yields of product from PNBBr reactions with those obtained from other substrates under the same conditions. N,N-dimethylformamide (DMF), dimethylsulphoxide (DMSO), and tetrahydrofuran (THF) were used as solvents.

Base systems used were: potassium t-butoxide in t-butanol; solid potassium t-butoxide in the presence of a phase transfer catalyst (cetyltrimethylammonium chloride)[28] potassium hydroxide in methanol; sodium methoxide in methanol; solid sodium formate and a phase transfer catalyst (cetyltrimethylammonium chloride)[28]; solid anhydrous sodium carbonate and a phase transfer catalyst (cetyltrimethylammonium chloride)[28]; and aqueous sodium hydroxide.

In general, the t-butoxide bases, both solid and in solution were too strong and with PNBBr as substrate, produced only black tars. Methoxide as base produced a partially decomposed product, which contained some TNBB. In experiments with sodium formate and sodium carbonate as base (with a phase transfer catalyst), TNT and PNBBr were recovered quantitatively from the reaction in most cases. This reaction produced good yields of TNBB in tetrahydrofuran, dimethylformamide and dimethylsulphoxide, with potassium hydroxide in methanol and aqueous sodium hydroxide as bases. It also worked well with dimethylsulphoxide and anhydrous solid sodium carbonate (with phase transfer catalyst) as base. These systems gave 70 - 80% yields of TNBB. But if other substrates were used under similar conditions, complex mixtures of products were again observed. When potassium hydroxide/methanol was the base, the TNT anion could be observed, in all three solvents, except when PNBBr was the substrate.

It appears that the TNT anion is produced, but not taking part in reaction with the substrate (in most cases) and decaying by the numerous oxidation/reduction processes that can occur in these solutions. Allyl chloride, allyl bromide and benzyl bromide are considered to be very good alkylating agents, it is therefore surprising that they do not react with the TNT anion.

p-Cyanobenzyl bromide (PCNBBr, XCVI) was investigated as a substrate because, in an aromatic environment, the electron withdrawing ability of the cyano group is not that much less than that of the nitro group. If this is significant to the success of the nucleophilic substitution reaction, then PCNBBr should produce a bibenzyl when reacted with the TNT anion.

Surprisingly, PCNBBr does not produce a bibenzyl. It does in fact produce a complex mixture of compounds similar to those obtained with substrates other than PNBBr. In dimethylformamide solvent, with potassium hydroxide/methanol base, the system

initially exhibited the characteristic purple colour of the TNT anion, which gradually changed to a dark brown colour, from which a complex mixture of products was obtained. Thus, again the only successful reaction is that involving PNBBr as substrate. In all other cases, including reactions with PCNBBr, complex mixtures are obtained. It is interesting that with PCNBBr, there is evidence that the TNT anion is produced, but obviously not reacting to give the desired products. In the only successful system, the TNT anion was seemingly not present in any quantity. Although it would appear that as a route to the target compounds this reaction is not likely to be of interest, a number of spectroscopic studies were carried out on selected systems in an attempt to gain further understanding of the behaviour of the TNT anion.

2.6 SPECTROSCOPIC STUDIES

Figure 7 shows the well recognised U.V./visible spectrum of the TNT anion[17,29] and Figure 8 that of a typical Meisenheimer complex.[8(a)] It can be noted that λmax for the TNT anion is at 526 nm and for the Meisenheimer complex is around 441 nm. A study was carried out in which the ratio of the absorbances of these two wavelengths (A_{526}/A_{441}) were observed as PNBBr and PCNBBr reacted with basic solutions of TNT. The two reactions showed marked differences, as shown in Figures 9 and 10.

The PNBBr reaction profile shows a rapid appearance of the peak at 441 nm reading a maximum after $1^1/_2$ minutes (minimum absorbance ratio) which implies a dominant σ-adduct. This is succeeded by a slow recovery of the peak at 526nm with an equilibrium being reached at an absorbance ratio of 1.15. It was noted that the spectrum which appears during the recovery process showed an increasing blue shift in the position of λmax, which at the end of the study was at 505 nm. Thus the recovery period does not reflect the reformation of the TNT anion.

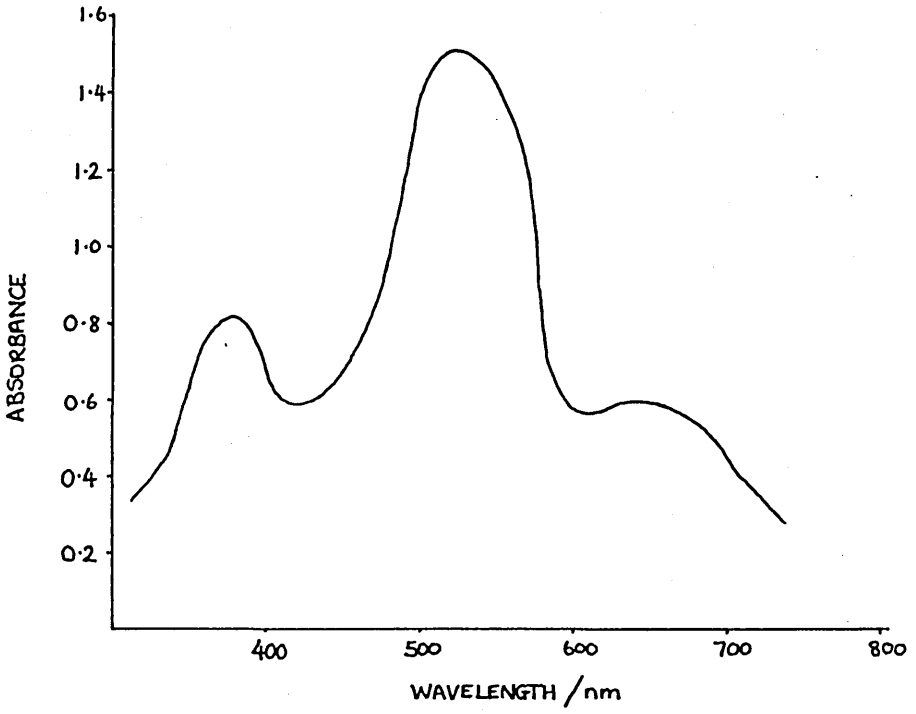


Figure 7: The ultraviolet spectrum of the TNT anion.

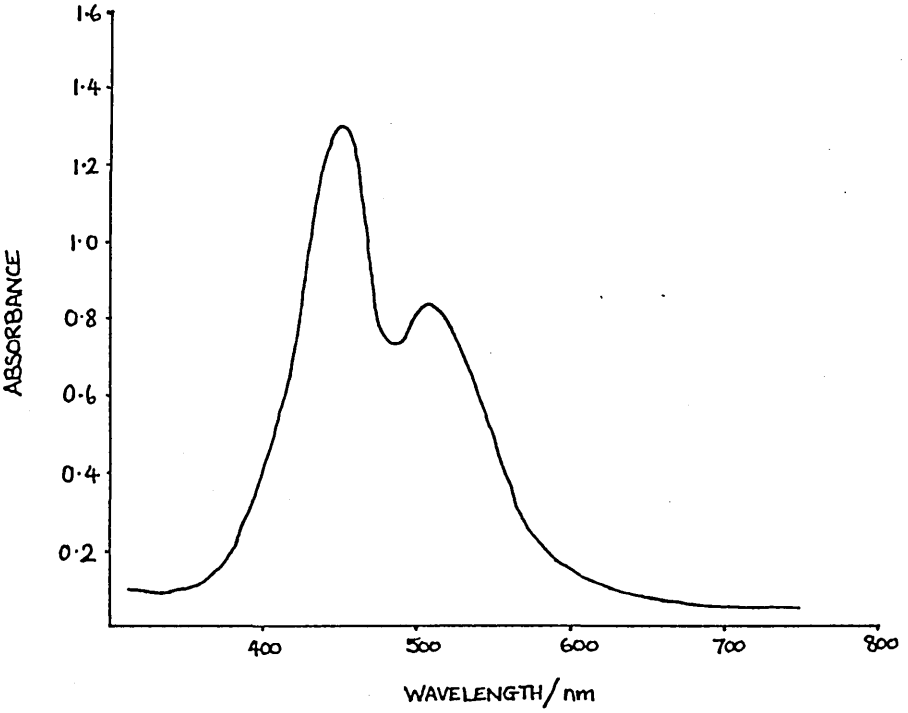


Figure 8: The ultraviolet spectrum of a 3-σ-adduct.

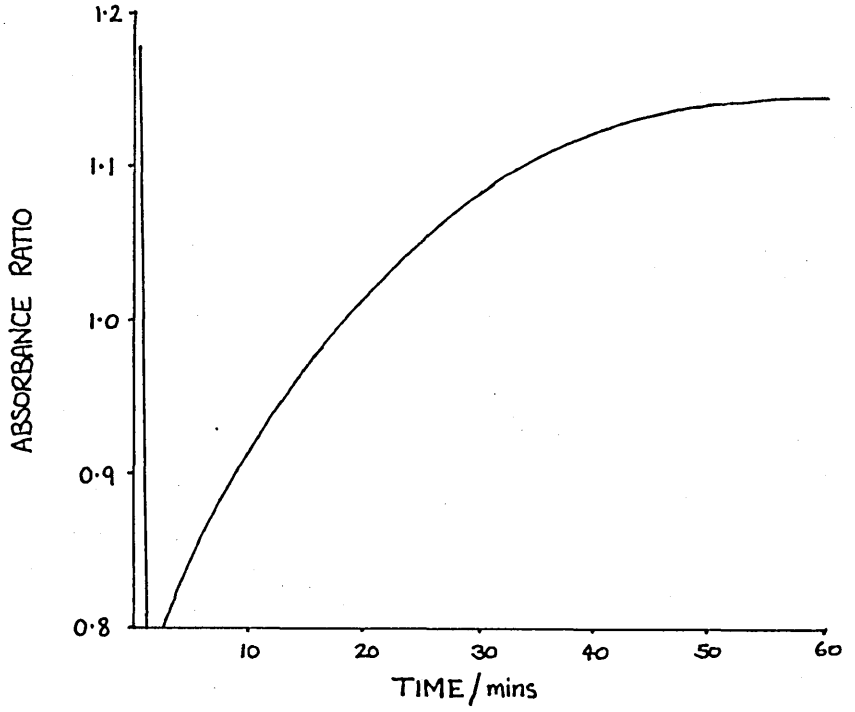


Figure 9: The U.V. profile of the PNBBr reaction (0.5g TNT, 0.48g PNBBr, 20cm^3 DMF, ambient temperature, add 0.09g KOH in 5cm^3 methanol).

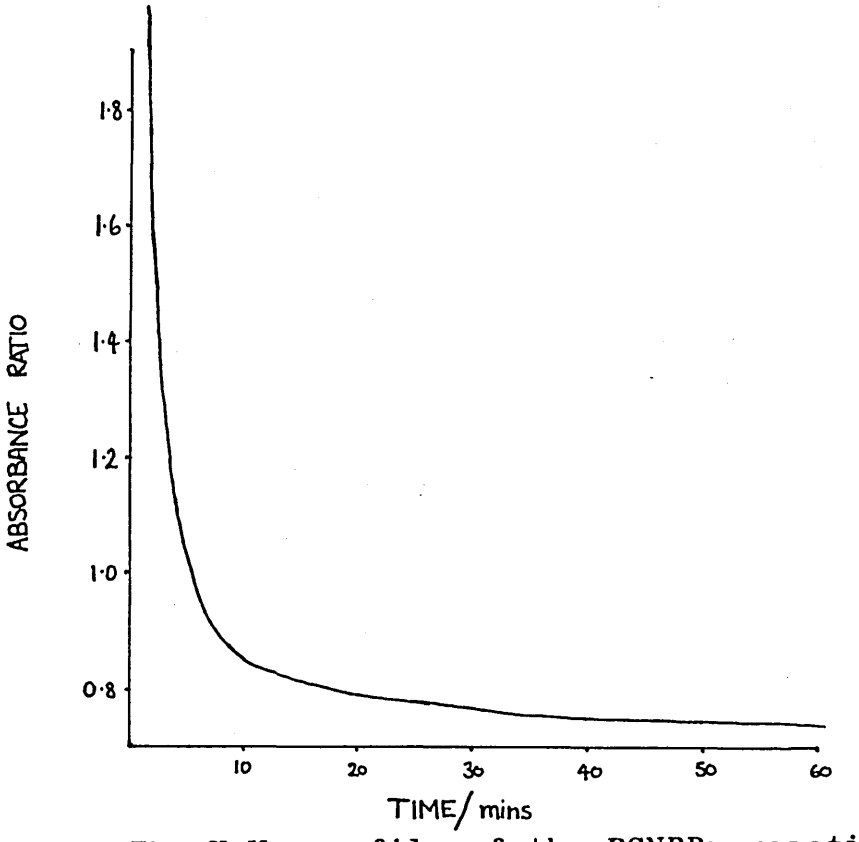


Figure 10: The U.V. profile of the PCNBBr reaction (0.5g TNT, 0.43g PCNBBr, 20cm^3 DMF, ambient temperature, add 0.09g KOH in 5cm^3 methanol).

The PCNBBr reaction profile shows that there was no significant σ-adduct formation for 6-8 minutes, after which it was dominant until quenching. The first spectrum obtained from the reaction was almost pure TNT anion with a very small, almost insignificant σ-adduct peak at 441 nm.

It seems from this information, that in the PNBBr reaction a σ-adduct is quickly formed which is not observed in the PCNBBr reaction. This could well be the significant step in the reaction. However if the PNBBr reaction is quenched after $1^{1}/_{2}$ minutes, TNBB can be seen by infrared spectroscopy although the presence of TNT and PNBBr show that the reaction is far from completed.

It would appear that the TNT anion is not a very good nucleophile, and that its involvement in a reaction with PNBBr is an exception, rather than typical. It seems unlikely that such a reaction can be solely ionic, because the TNT anion does not react with other alkylating agents. It could be that σ-adduct formation between PNBBr and TNT is a precursor to single electron transfer initiation of either of the radical mechanisms shown in schemes 23 and 24 (section 2.3). This σ-adduct could have the structure (XCVII) or (XCVIII) and may lead to the formation of a charge transfer complex. It is possible that the peak that rapidly appears at 441 nm in the PNBBr reaction is due to the charge transfer complex, rather than the σ-adduct.

Figure 11 shows the nmr spectra recorded during the decay of TNT in basic solution. It can be seen that from the point of addition of the base, the spectrum is very complex and very weak. This rapid decay of the spectrum could be due to the formation of radicals or to the formation of a variety of different compounds by any mechanism. However, it was evident that the TNT was rapidly destroyed by the base.

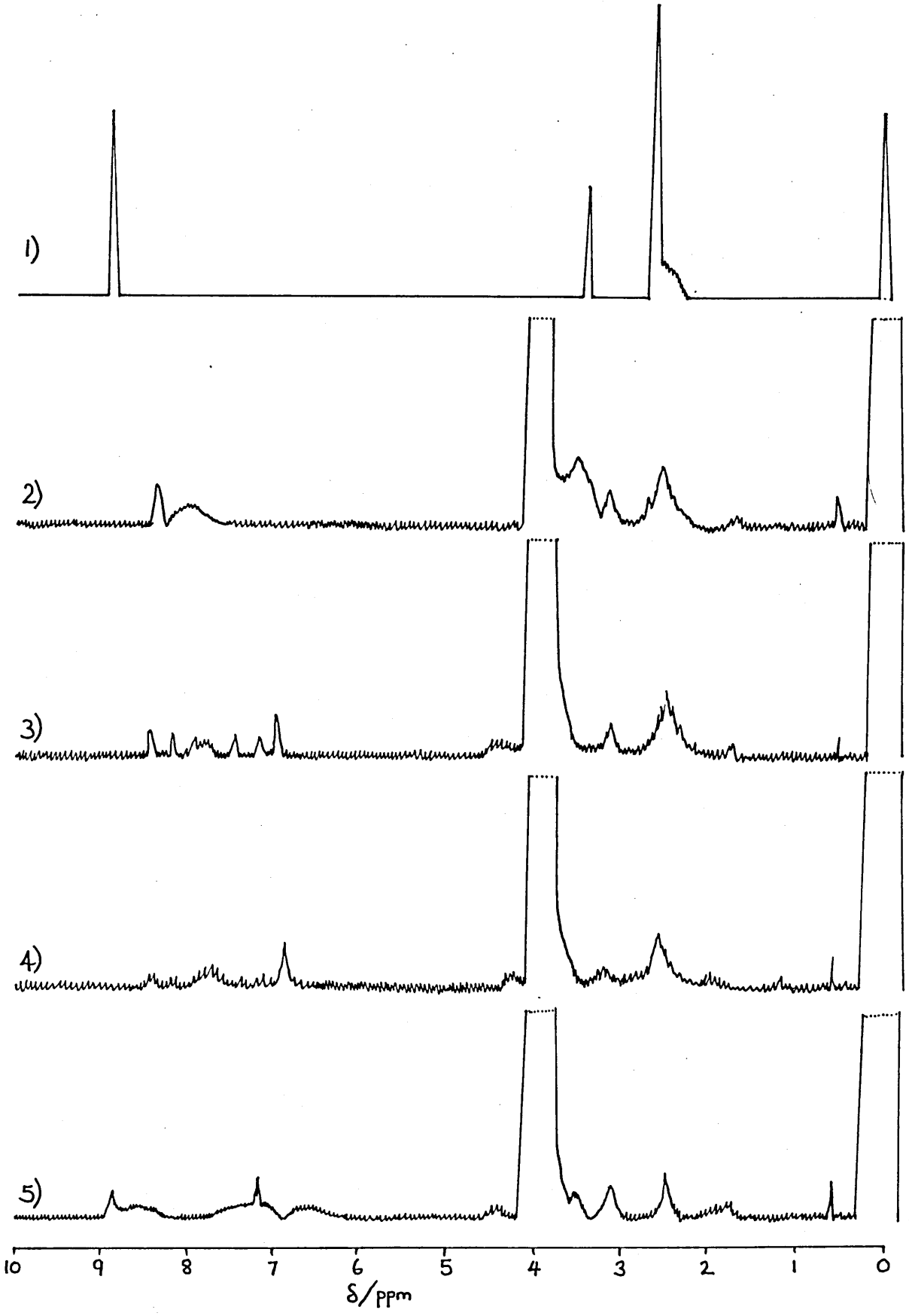


Figure 11: The nmr spectra obtained from the action of base on TNT; 1) before base addition, 2) after 60 sec., 3) after 4 mins., 4) after $10\frac{1}{2}$ mins., 5) after 40 mins.

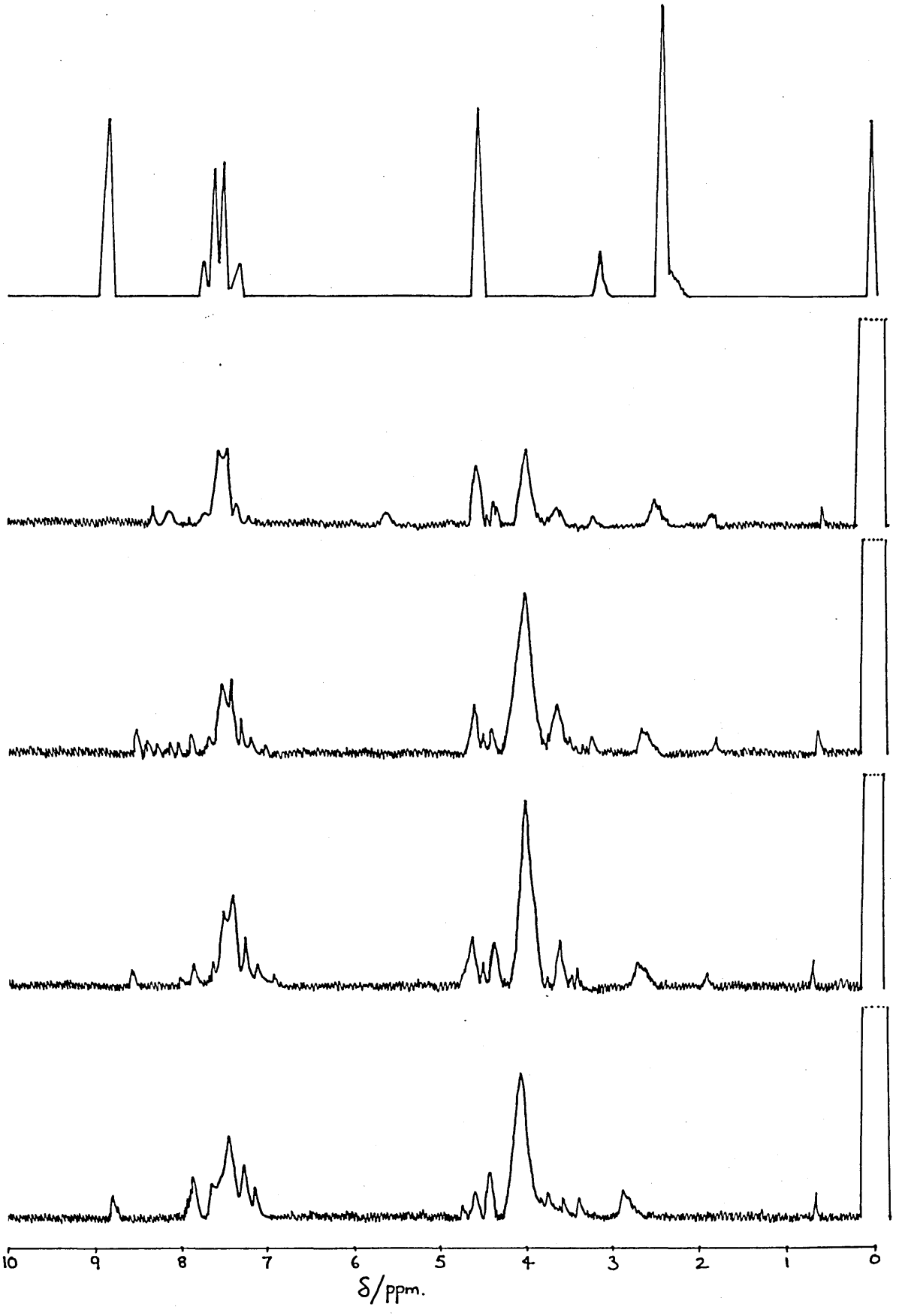


Figure 12: The nmr spectra obtained from the PCNBBr reaction; 1) before base addition, 2) after 30 sec., 3)after $3\frac{1}{2}$ mins., 4) after 11 mins., 5) after 40 mins.

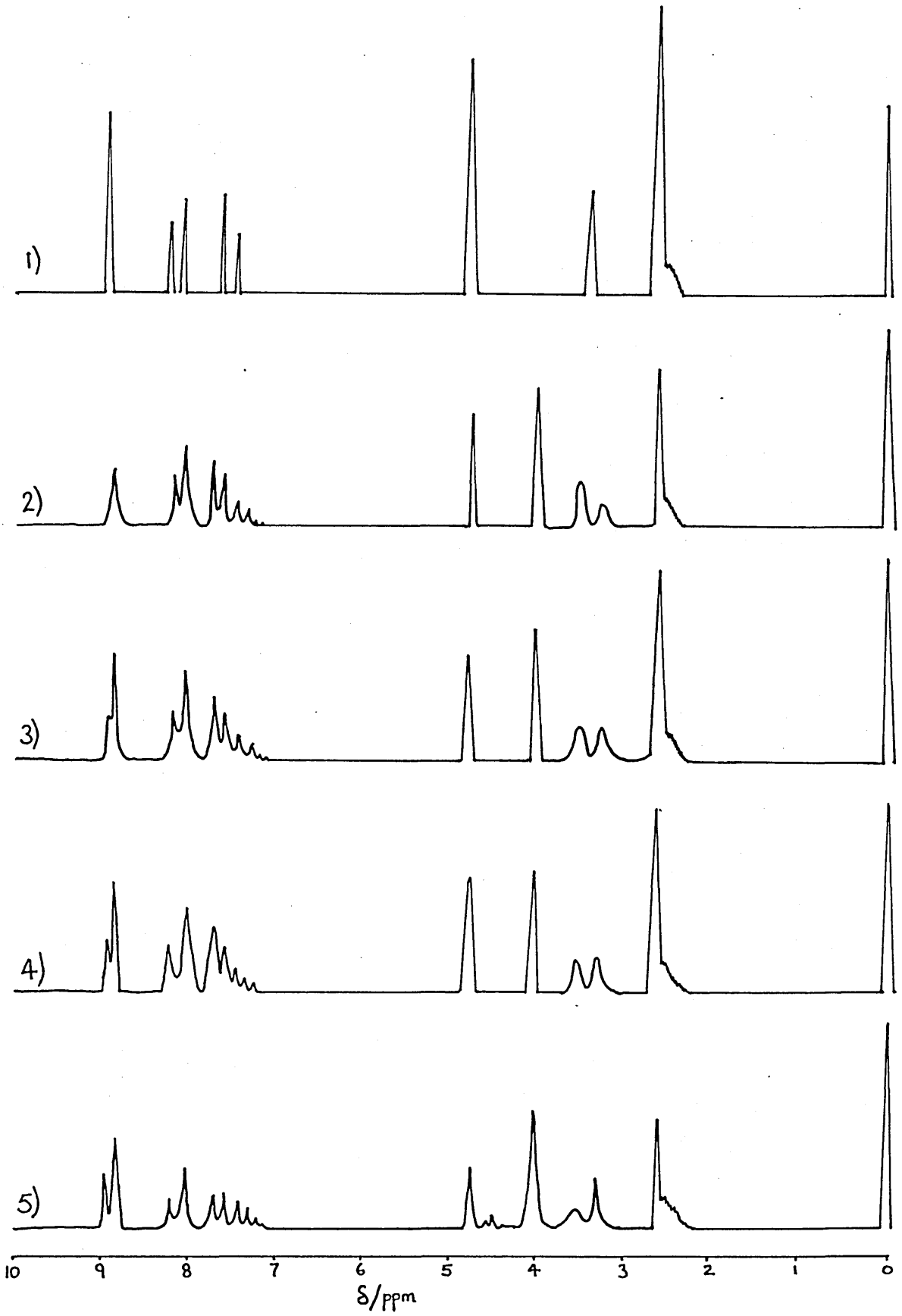


Figure 13: The nmr spectra obtained from the PNBBr reaction; 1) before base addition, 2) after 45 sec., 3) after 4 mins., 4) after $10\frac{3}{4}$ mins., 5) after 40 mins.

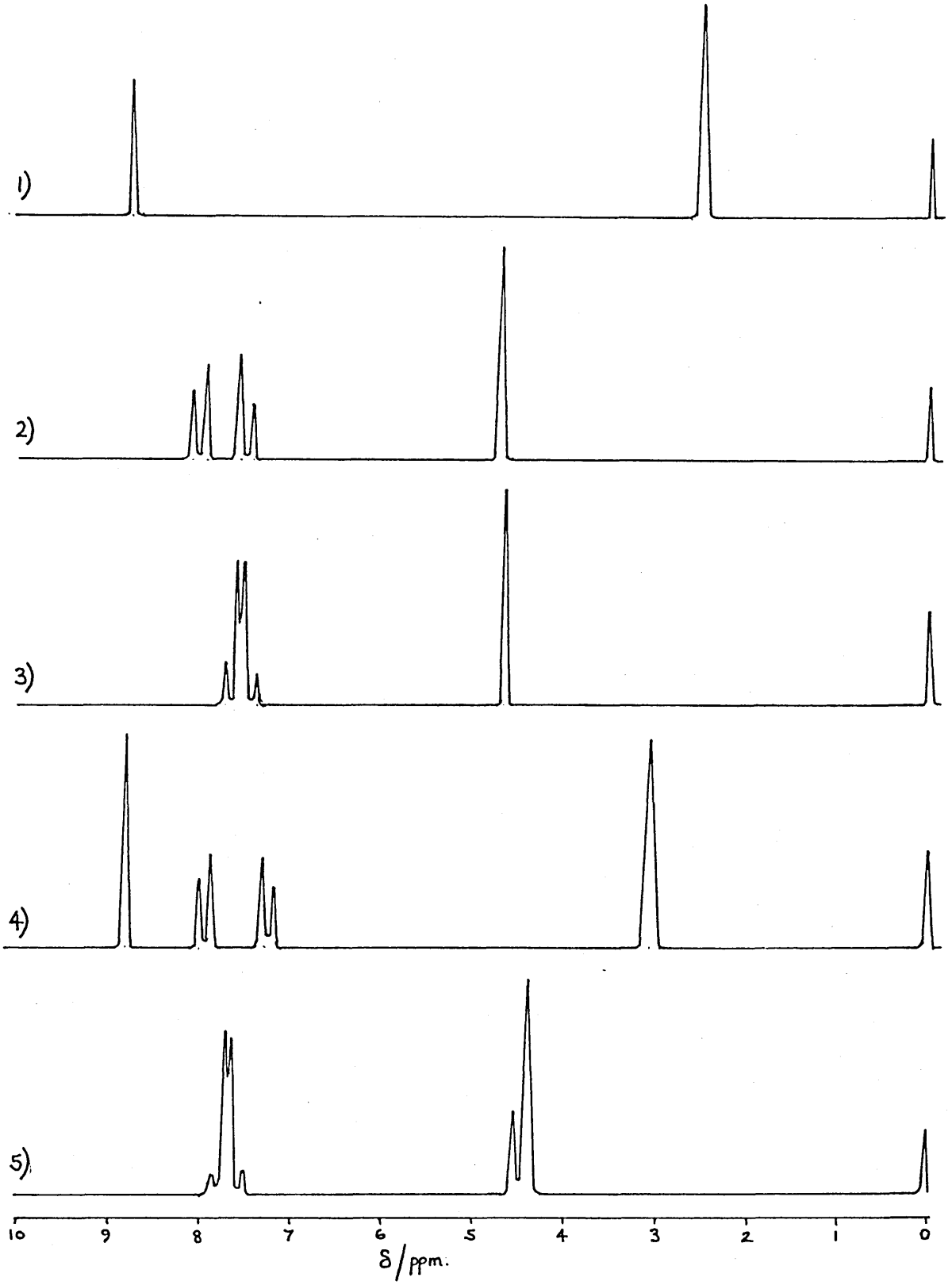


Figure 14: The nmr spectra of ; 1) TNT, 2) p-nitrobenzyl bromide, 3) p-cyanobenzyl bromide, 4) 2,4,4',6-tetranitrobibenzyl, 5) p-cyanobenzyl alcohol.

In a reaction involving PCNBBr (Figure 12) a similar pattern of decay was observed to that shown in Figure 11. It appears that the TNT is reacting with the base in a similar way despite the presence of PCNBBr. There is a noticeable change in the signal due to PCNBBr, which is probably due to its reaction with OH^- to give p-cyanobenzyl alcohol (Figure 14 cf Figure 12).

In contrast the PNBBr reaction (Figure 13) clearly showed, throughout the reaction, signals due to TNT, PNBBr and TNBB in changing proportions. The reaction was clean, the spectra were clear, and evidence for the presence of a substantial concentration of radicals not found.

Spectroscopic studies support the earlier evidence that the TNT anion is formed in the presence of base, but it is not reacting with substrates which should be susceptible to nucleophilic attack. In such systems there is evidence that a significant concentration of free radicals is produced, presumably during the oxidation of the TNT anion to a complex mixture of products. However, in the presence of PNBBr the major intermediate species observed is a σ-adduct, not free radicals, and the desired product is obtained.

2.7 CONCLUSIONS

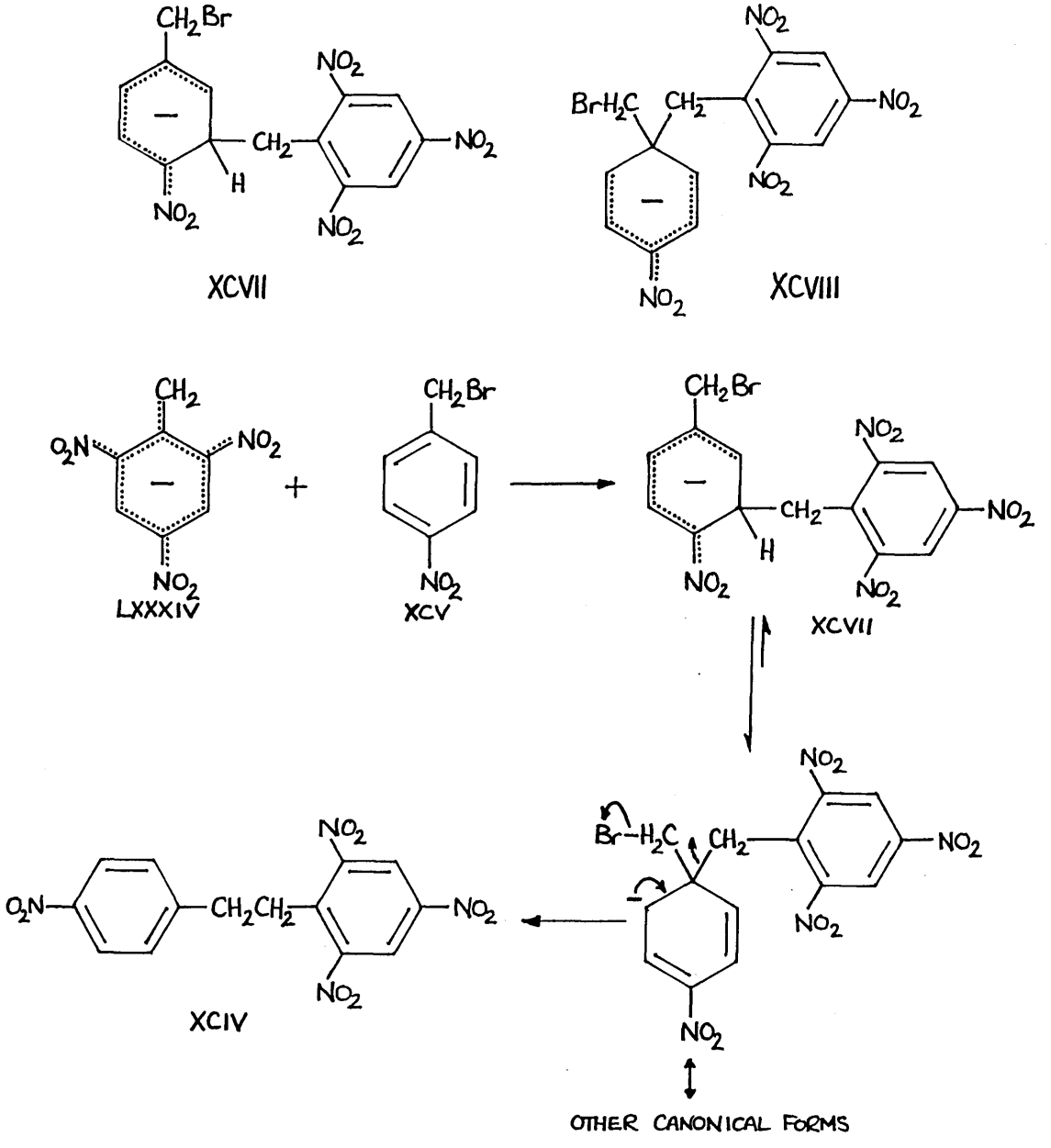
Use of TNT anion as a nucleophile for the preparation of category A and B compounds was not successful. Indeed, only PNBBr gave the required substitution product. All other substrates gave complex mixtures of products regardless of the solvent medium and initiating base. The mechanistic differences between the PNBBr reaction and the PCNBBr reaction were highlighted by the spectroscopic studies carried out. U.V./visible spectroscopy shows the critical feature of the PNBBr reaction to be σ-adduct formation, whereas in the PCNBBr reaction, the TNT anion was observed as the major intermediate.

The production of free radicals was shown by the decay observed in the nmr spectra of basic TNT solutions, with or without PCNBBr present. However, the PNBBr reaction did not show any sign of decay due to the presence of paramagnetic species.

It was suggested earlier, that the mechanism of the PNBBr reaction might be ionic, radical or radical ionic (schemes 22, 23 and 24). Shipp et. al. preferred the ionic mechanism to the radical mechanisms for a number of reasons, most importantly the leaving group effects observed. But, it has been shown in this study that the TNT anion is not a good nucleophile. However, it is known that nitro groups are efficient at promoting σ-adduct formation, and it was seen that σ-adduct formation was important in the PNBBr reaction. In the reaction of TNT anion with PNBBr, the kinetic reaction product is likely to be (XCVII), because it will be the least hindered site of ring attack, with (XCVIII) being the thermodynamic product, because σ-complex formation is preferred para to a nitro group[30,31,32]

It can be seen that (XCVIII) brings the active sites of both reactants into close proximity and could result in the required substitution product, as shown in equation 9.

This mechanism provides a better explanation of the experimental evidence found in this study and by Shipp et. al. than earlier proposals.



Equation 9: The likely mechanism for the reaction between TNT anion and p-nitrobenzyl bromide.

CHAPTER 3

SUBSTRATES FOR NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS

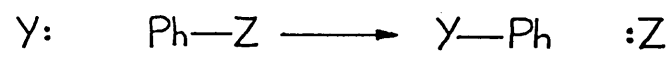
3.1 NUCLEOPHILIC AROMATIC SUBSTITUTION

Nucleophilic aromatic substitution resembles other nucleophilic substitutions at a carbon centre in so far as a bond from nucleophile Y is formed to the reaction centre and a leaving group Z is displaced with its bonding electrons, as shown in scheme 25. This scheme only gives an overall view of reactants and products; it does not consider the timing of bond formation and bond cleavage, charge distribution, reversibility of the reaction, rearrangements which may occur, or any intermediates formed.

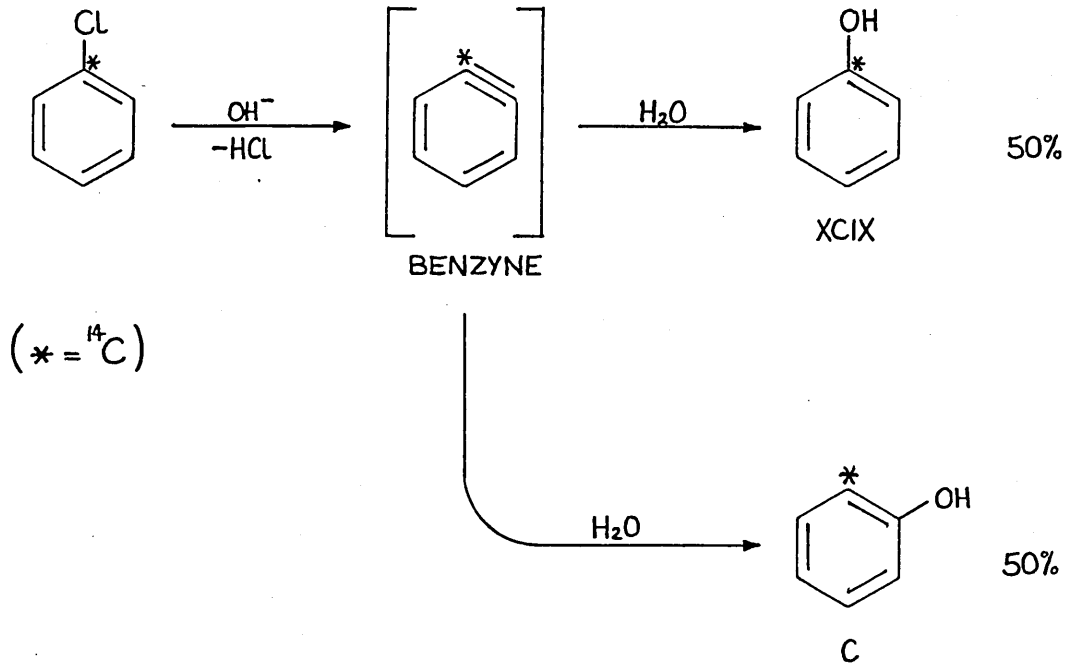
With any simple aromatic compound which contains a leaving group, nucleophilic substitution is difficult and requires strongly basic and/or rigorous conditions for reaction to proceed at all. In contrast aliphatic nucleophilic substitution is relatively easy to accomplish.

Much industrially processed phenol is made by hydrolysis of chlorobenzene using either sodium hydroxide at 370^{o}C, or water and a catalyst at 425^{o}C. Although it may appear the case, these reactions are not nucleophilic aromatic substitutions, but proceed via a benzyne mechanism (equation 10). If chlorobenzene is isotopically labelled as indicated in equation 10, this mechanism can explain the isotopic scrambling which occurs. Nucleophilic aromatic substitution would lead to 100% of XCIX as product.

When an aromatic ring is substituted with suitable functionalities, nucleophilic aromatic substitution can become relatively simple. It was reported by Pisani[33] in 1854, that both picric acid and picramide could be produced with ease from picryl chloride. The aromatic nitro group is probably the best activating



Scheme 25: A simple view of nucleophilic aromatic substitution.



Equation 10: Hydrolysis of chlorobenzene via a benzyne mechanism.

functionality for nucleophilic aromatic substitution, but others include sulphonates, cyanides and heterocyclic nitrogens. The extent of activation is dependant upon the number of activating functionalities present as well as their position in the aromatic ring. Also, the nature of the leaving group Z and nucleophile Y can influence the reaction.

The most productive research on the mechanisms involved in nucleophilic aromatic substitution reactions has been achieved since circa 1950. In 1951, Bunnett and Zahler[34] carried out a comprehensive review of the field, and this is considered one of the foremost pieces of work on this topic, but there are a number of other reviews which have been published.[35-38]

3.1.1 Activating Substituents

Nucleophilic substitution in an aromatic system proceeds via a transition state, where (depending on the nucleophile, leaving group, and substrate) the bonds to nucleophile and leaving group are either fully or partially formed. Such transition states, because of the addition of a negative charge to the ring, are susceptible to large substituent effects. Any substituent that can stabilise the presence of an extra negative charge, stabilises the transition state and therefore is said to be activating. These substituents are electron withdrawing functionalities. Initial attack on the π - electron system is also enhanced by the polarising effect of these substituents. Any substituent which activates an aromatic ring to nucleophilic aromatic substitution, deactivates that aromatic ring to electrophilic substitution. Many theoretical treatments of aromatic substitution have been published [39(a-d)] and all agree that activation occurs via inductive activation through the σ-bond framework and through resonance effects causing polarisation of the delocalised π-electron system.

Electron withdrawing groups activate an aromatic ring to nucleophilic aromatic substitution, especially when such substituents are located ortho and/or para to the reaction centre.

This is because stabilisation of the transition state requires that the pair of electrons from the nucleophile be accommodated within the molecule by resonance movement of charge to a more electronegative ring atom, or indeed out on to the activating substituent itself. Scheme 26 shows nitro group stabilisation, and it can be seen that the charge can be accommodated on the nitro group by resonance movement of charge only when the nitro group is positioned ortho or para to the reaction centre.

3.1.2 The effect of leaving group and nucleophile.

The effect of the leaving group on nucleophilic aromatic substitution is quite substantial, but it is basically dependent upon the nucleophile used. For example, when alkoxide and amine nucleophiles are reacted with an activated halogeno substrate, fluorine is up to 10^3 times more mobile than other halogens; but when the nucleophile used is thiocyanate, fluorine is up to 10^3 times less mobile than other halogens.[40]

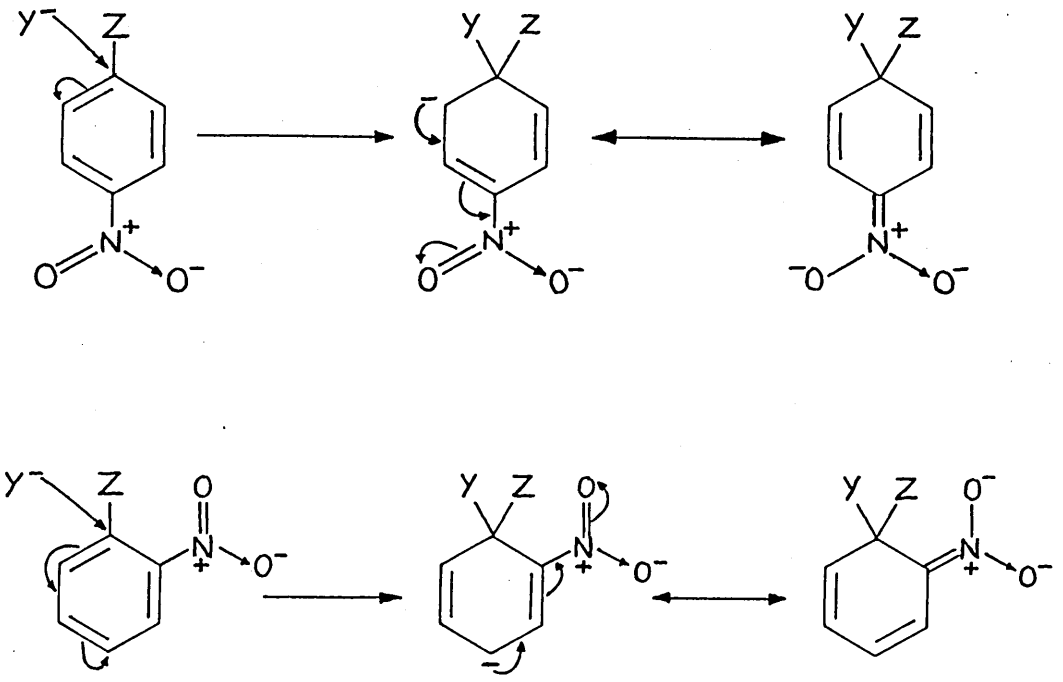
The kinetic and theromodynamic aspects of the effect of leaving group and nucleophile can seem quite complex, given the wide variety of reactions which occur, but individual examples are fairly easily understood.[40]

The effect of altering the leaving group in aliphatic systems has well known patterns, although the research on this is not substantial. Aromatic systems, however, have been investigated in considerable detail. For activated aromatic S_N2 substitution reactions (addition - elimination), Bunnett and Zahler[34] have published the following order of leaving group ability:

$$F > NO_2 > Cl, Br, I > N_3 > OSO_2R > \overset{+}{N}R_3 > OAr > OR$$

$$> SR, SAr > SO_2R > NR_2 ;$$

but they noted that the order can vary with the nucleophile and the substrate.



Scheme 26: Nitro group stabilisation of nucleophilic aromatic substitution intermediates.

It was considered initially that high electronegativity enhanced mobility, in as much that high electronegativity of the leaving group lowers the activation energy of bond formation by a nucleophile. This is true, but it is now considered that a low bond dissociation energy also enhances mobility, though only when electronegativity is unimportant,[34] i.e., when bond breaking is the rate determining step, a factor which is controlled entirely by the type of nucleophile used.

Consider the halogens; the order of mobility with first row nucleophiles is F>> Cl> Br> I. With other heavier nucleophiles, this order is reversed. There are some nucleophiles however, which exhibit borderline characteristics, e.g. thiomethoxide and thiophenoxide. The order F>> Cl> Br>I with first row nucleophiles is due to the formation of the intermediate complex (and not the bond breaking process) being the rate limiting step. The effect then of increasing electronegativity of the leaving group would be to increase the rate at which the complex is formed, so it is solely dependant upon electronegativity; hence F>> Cl> Br> I which is the order of electronegativity in the halogens. In reactions involving heavy nucleophiles, it is bond breakage which is rate limiting, which indicates that increasing the bond dissociation energy of the leaving group would give a decrease in reaction rate, hence I > Br> Cl> F in mobility.

It can be seen from the above arguments that the intermediate complex formed is a σ-adduct type complex, so therefore factors affecting the stability of σ-adducts can also be applied to nucleophilic aromatic substitution intermediates. Studies of the stability and mechanisms of formation of σ-adducts have been extensive. This wealth of information has been the subject of some very good reviews,[8(a-d)] and from these it seems clear that the nature of the aromatic nucleus, the number of nitro groups and/or other electron withdrawing substituents; the substituted or unsubstituted character of the site of nucleophilic attack; the steric effects adjacent to this position and the nature of the entering nucleophile, are all important factors affecting the thermodynamic stabilities of σ-complexes.

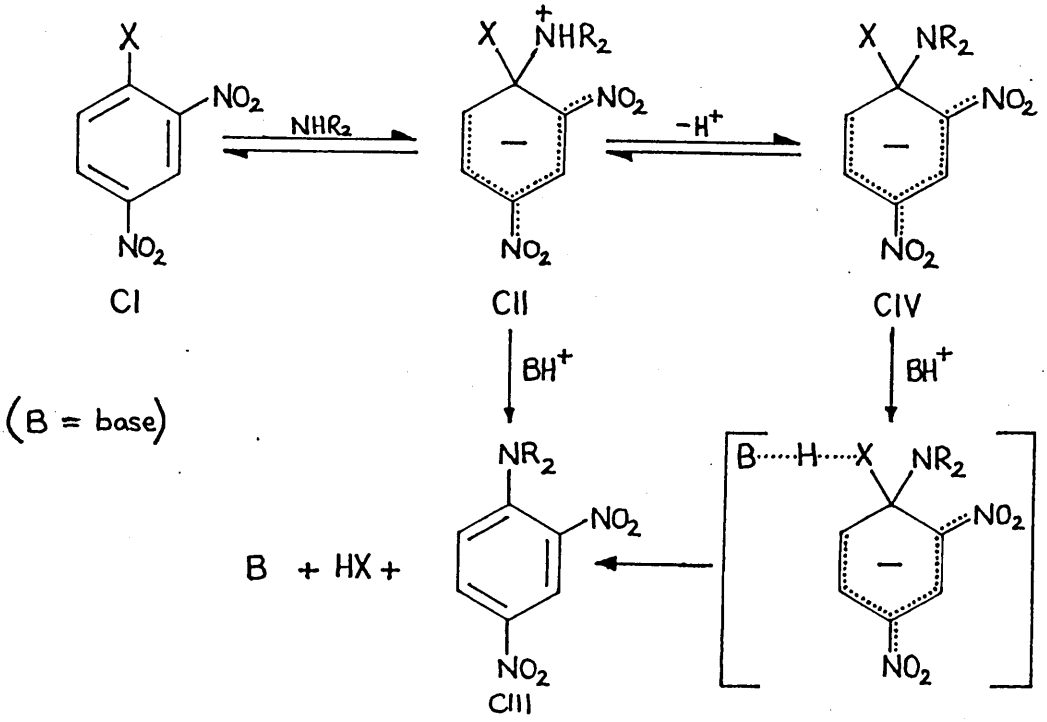
In 1973, Bernasconi and co-workers investigated secondary amines as nucleophiles in reactions with 2,4-dinitro-1-X-benzene (CI)[7a] where X is a leaving group, typically halogen (equation 11). The step CII to CIII has two kinetically accepted routes. The first, a rapid pre-equilibrium between the zwitterion and its conjugate base followed by rate limiting expulsion of the leaving group, with general acid catalysis by BH^{+}[41] The second, direct conversion of zwitterion into products, is generally referred to as the "solvent assisted" mechanism which, until the work of Bernasconi, had received very little attention.[7a]

Bernasconi carried out a kinetic study on a spiromeisenheimer complex of N - (2'-hydroxyethyl) -N- methyl - 2,4-dinitroaniline (CV, equation 12), where an intermediate similar to CIV is formed, but it is stable enough to be observed and monitored. The rate coefficient k_{-1} (equation 12) can serve as an estimate for the lower limit of the rate of decomposition of CIV to CIII (equation 11). There has been quite a substantial amount of work by Bernasconi [42(a-f)7b] and Crampton [43,7d] on spiromeisenheimer complexes and factors affecting their stability, because of their relation to intermediates in nucleophilic aromatic substitution.

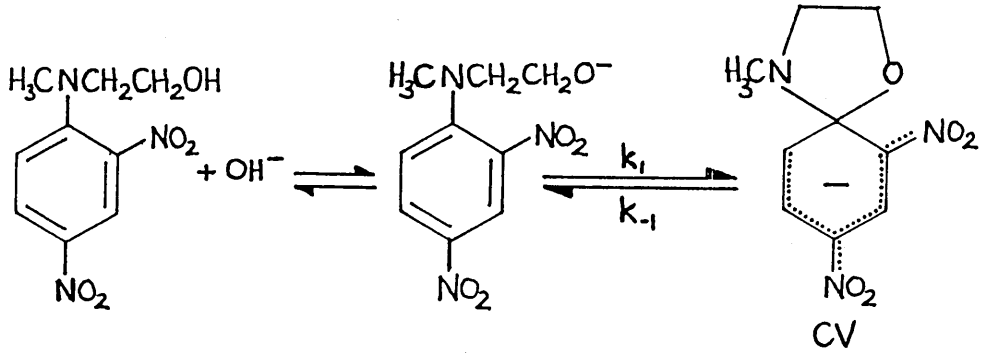
3.1.3 SUBSTRATES FOR NUCLEOPHILIC AROMATIC SUBSTITUTION.

Nucleophilic substitution of hydrogen from a trinitroaromatic compound is extremely difficult to achieve, and indeed the hydrogen must be removed by oxidation from the Meisenheimer complex formed. This oxidation does not occur cleanly and a complex mixture of products is produced. The reaction of sodium hydroxide with m-dinitrobenzene in the presence of potassium ferricyanide [34] only results in approximately 10% conversion (equation 13).

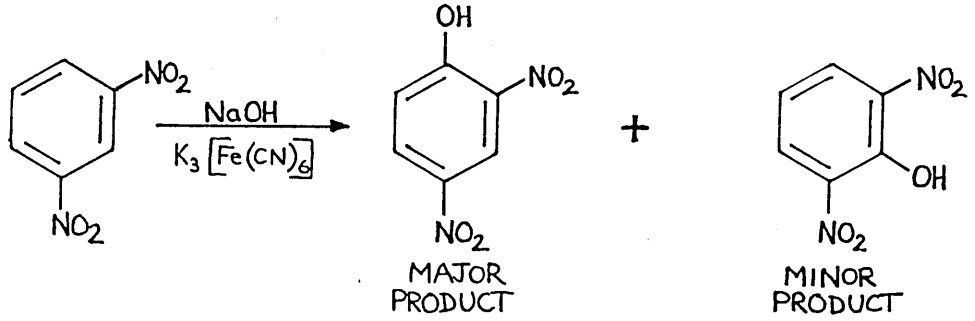
Recently, a vicarious type of nucleophilic aromatic substitution of hydrogen has been reported, [44(a-c)] which has tremendous synthetic possibilities. It involves a special type of nucleophile, for illustration, $^{-}CRYX$, where X is a leaving group, Y is an electron withdrawing group (carbanion stabilising group) and R is an alkyl function (scheme 27, equation 14).



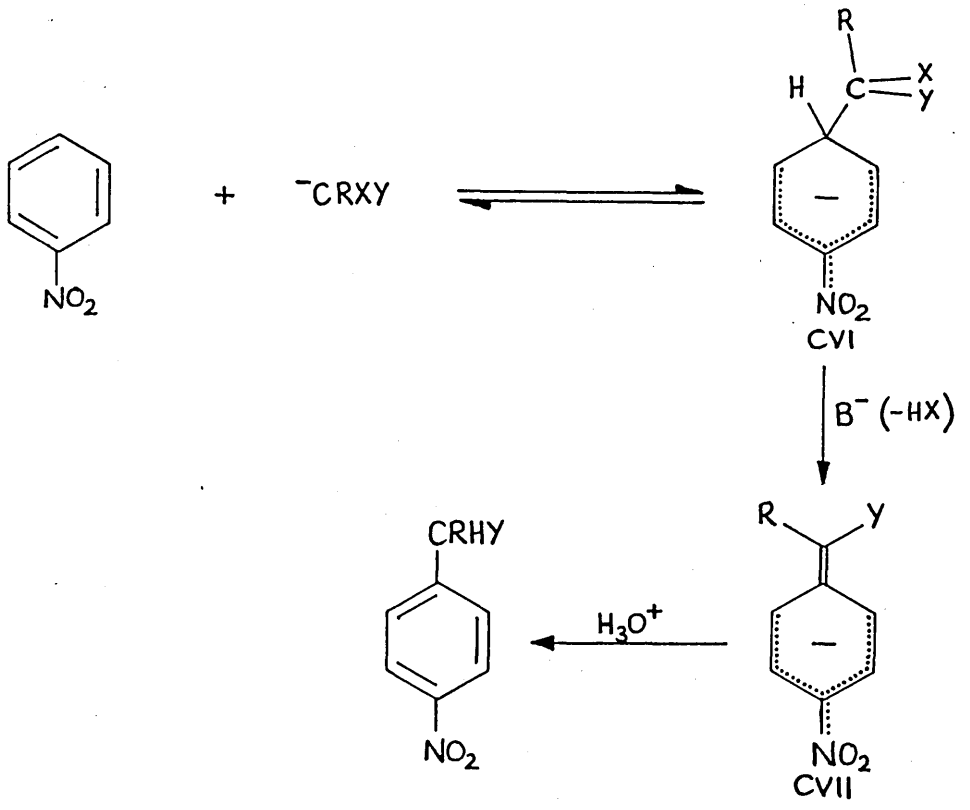
Equation 11: Reaction of secondary amines with 2,4-dinitro-1-X-benzene.



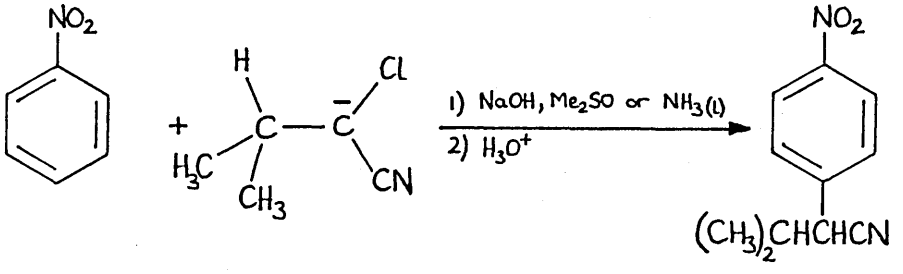
Equation 12: The formation of spiromeisenheimer complex CV.



Equation 13: Nucleophilic aromatic substitution of hydrogen.



Scheme 27:
A vicarious nucleophilic aromatic substitution of hydrogen.



Equation 14: An example of scheme 27 where X = Cl, Y = CN and R = isopropyl.

The mechanism proceeds via σ-complex formation para to the nitro group (CVI), followed by base induced dehydrohalogenation of the complex and acidification to give the required product. It appears that provided the σ-complex (CVI) is able to form, then the reaction should proceed. This method of pseudo-nucleophilic substitution has caused a great deal of excitement within synthetic organic chemistry.

The halogens are the most common leaving groups. For example, picryl chloride has been the substrate most widely used in the study of nucleophilic aromatic substitution reactions. A better substrate (for first row nucleophiles) is the more reactive picryl fluoride,[45] but unfortunately its synthesis is much more difficult. Picryl chloride can be prepared in very good yields, from picric acid and a suitable chlorinating agent, e.g., phosphoryl chloride or thionyl chloride. Also it is conveniently recrystallised from ethanol. Picryl fluoride on the other hand, has best been prepared by the oleum nitration of 1-fluoro-2,4-dinitrobenzene,[45] which only gives up to 50% yield.

Surprisingly, nitro groups are very good leaving groups, when in an activated position in an aromatic ring.[46(a-c)] In 1,2,4-trinitrobenzene, the nitro group in the 1-position has a mobility 200 times greater than that of chlorine in 1-chloro-2,4-dinitrobenzene.[46d]

3.1.4 The Scope of this Study

For the preparation of category C compounds by the route proposed earlier (scheme 17), a convenient method of preparing the starting materials (3-alkylpicryl halides) is required. Two possible routes have been considered. The first, involved the use of TNT as starting material (scheme 19). The advantages of this scheme are that the starting material is readily available, and the route does not involve any nitration steps. The second scheme considered involved nitration of a 3-alkylphenol followed by substitution of the hydroxyl moiety by halogen (scheme 20).

3.2. TNT AS STARTING MATERIAL

The proposed synthesis, from TNT, of the appropriate substrates for nucleophilic aromatic substitution reactions involves 3 steps: reduction of aromatic nitro group(s), halogenation of the ring, and re-oxidation of amino group(s).

3.2.1 Reduction of TNT

The products of the partial reduction of TNT are all known (Table 1), though recent work on the topic is quite rare and newer reduction techniques have not been applied.

Many methods of reduction of nitro groups to amino groups are known and a number were investigated in this study, but very few actually succeeded well enough to permit isolation of products and indeed only one reaction gave good yields of the desired products.

Sulphurated sodium borohydride ($NaBH_2S_3$) in THF, as described by Lalancette,[52] did not yield any reaction product even when used in four fold excess. Iron in acetic acid[53] produced very small quantities of aminonitrotoluenes which were extracted and isolated using a short silica column. Sodium polysulphide[54] also gave very small amounts of aminonitrotoluenes among many other reaction products.

The most popular method for the reduction of nitro groups is that using hydrogen sulphide in the presence of ammonium hydroxide.[47,49,51,55] Ammonium sulphide is normally credited as being the reducing species in this reaction. A similar method uses piperidine in pyridine as the base,[50] where presumably piperidinium sulphide is the reducing species. These reactions can be adapted to produce either mono-or di-reduced TNT as the major reaction product. It was found that if TNT was present in solution on addition of aqueous ammonia and hydrogen sulphide gas, the major product was 4-amino-2,6-dinitrotoluene (CVIII), which could be produced in

40% yield in this work, by this procedure. However, closer examination by nmr, ir and mass spectroscopy showed that the 4-amino-2,6-dinitrotoluene produced was contaminated with 4-hydroxylamino-2,6-dinitrotoluene (CXII), sometimes to the extent of 50% impurity.

The R_f values of these two products on a silca column are very similar and thus were very difficult to separate. Recrystallisation normally produced mixtures, but repeated recrystallisation enabled a small amount of 4-amino-2,6-dinitrotoluene (CVIII) to be obtained pure for characterisation purposes.

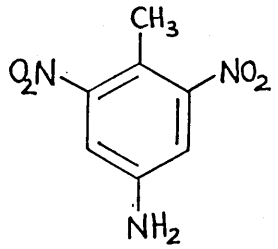
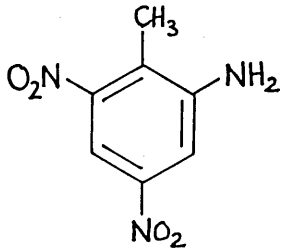
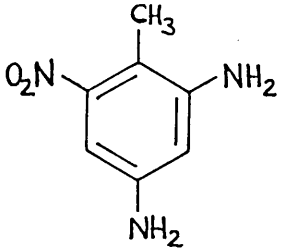
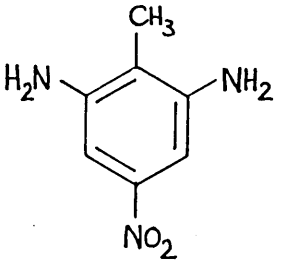
If TNT is slowly added to a solution of alcoholic ammonia, saturated with hydrogen sulphide, 2,4-diamino-6-nitrotoluene (CX) is produced in good and reproducible yields.

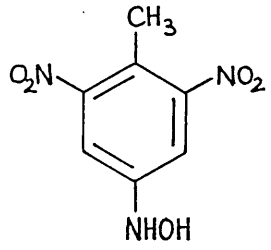
3.2.2 Bromination of Aminonitrotoluenes

The objective of this work was to produce the monobrominated derivative of 2,4-diamino-6-nitrotoluene (CX) (which was the more readily available amine derivative) or 4-amino-2,6-dinitrotoluene (CVIII) (Scheme 28).

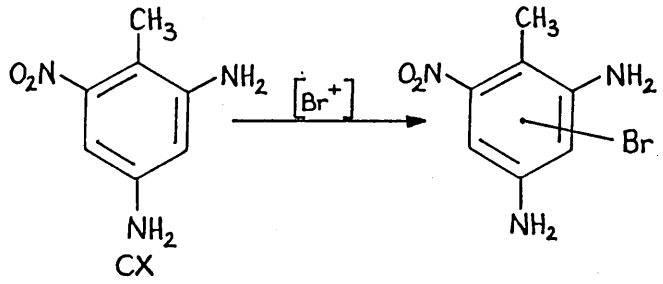
Initially reactions of 2,4-diamino-6-nitrotoluene were carried out in aqueous methanol to which bromine was added. When an excess of bromine was added, the deep orange solution lost its colour and deposited a pale yellow precipitate. Isolation and analysis of this compound showed that it did not contain any aromatic protons in its structure. Mass spectroscopy showed the characteristic pattern of a dibromo compound; thus it appeared that dibromination had produced 2,4-diamino-3,5-dibromo-6-nitrotoluene (CXIII). This would be expected to some extent, with excess bromine; even though the 5-position might be considered to be a weaker electrophile attracting site, because of its proximity to the 6-position nitro group.

Table 1: The products of the partial reduction of TNT.

NAME AND STRUCTURE	DESCRIPTION (RECRYSTALLISATION SOLVENT)	MELTING POINT.	REF.
 CVIII 4-AMINO-2,6- DINITROTOLUENE.	YELLOW NEEDLES (H_2O)	171°C	47
 CIX 2-AMINO-4,6-DINITROTOLUENE.	YELLOW CRYSTALS (H_2O)	176°C	48
 CX 2,4-DIAMINO-6-NITROTOLUENE.	ORANGE CRYSTALS (BENZENE/LIGHT PETROLEUM SPIRIT)	135°C	47,49.
 CXI 2,6-DIAMINO-4-NITROTOLUENE.	RED CRYSTALS (BENZENE/LIGHT PETROLEUM SPIRIT)	214-6°C	49,50, 51.

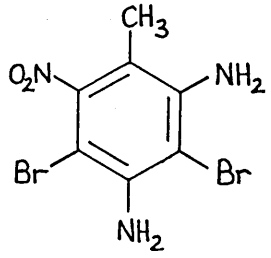


CXII



CX

Scheme 28: The bromination of 2,4-diamino-6-nitrotoluene.



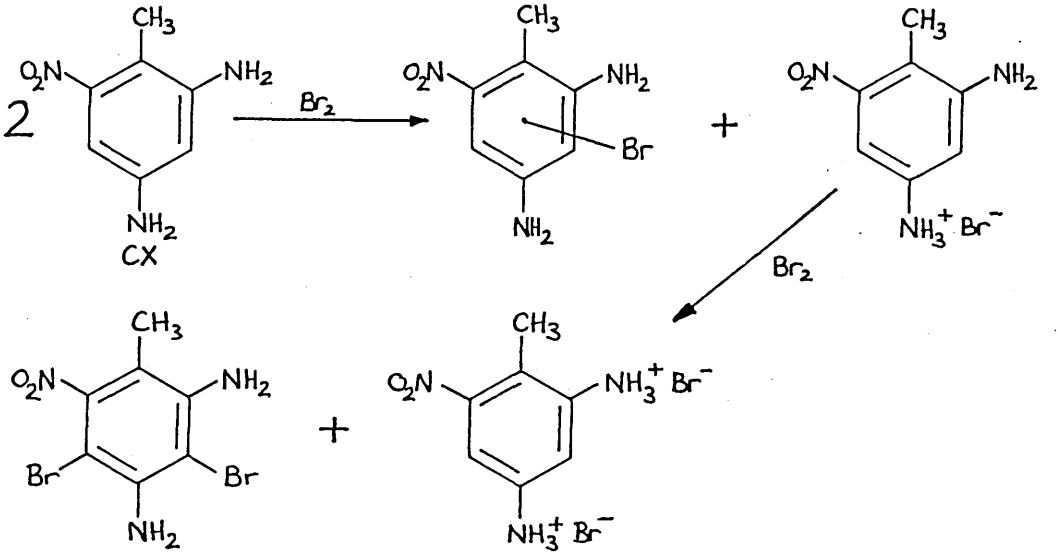
CXIII

In the equimolar reaction of 2,4-diamino-6-nitrotoluene with bromine in chloroform solution, a 50% yield of 2,4-diamino-3,5-dibromo-6-nitrotoluene was obtained together with recovered starting material (CX). Thin layer chromatography of the reaction mixture throughout the reaction, showed only the presence of the dibromo compound (CXIII) and the starting material.

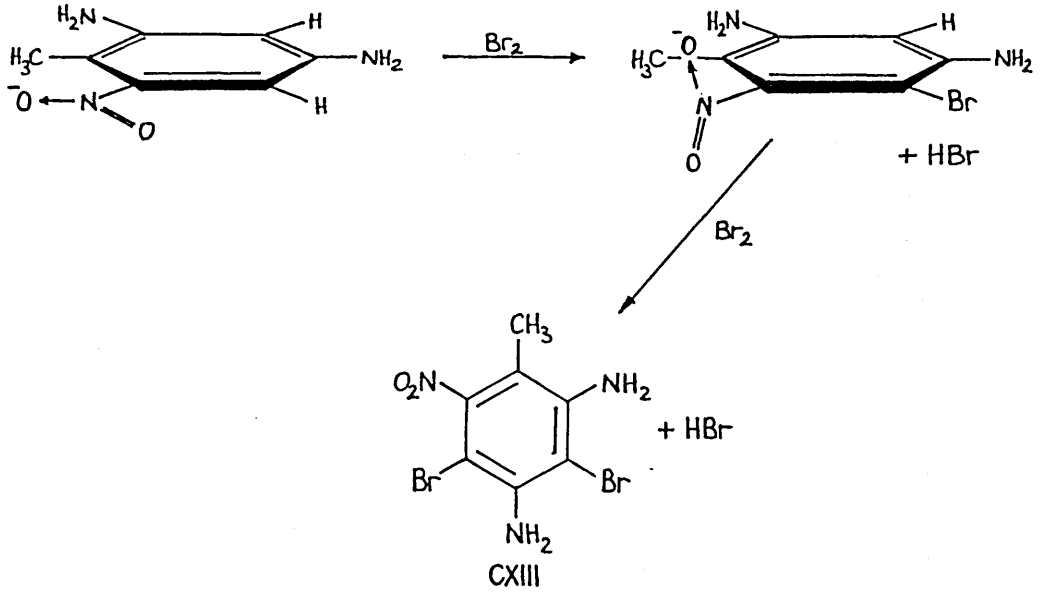
A number of other observations were made during a series of repetitions of this reaction. The addition of further bromine beyond the equimolar amount made no impression upon the reaction i.e. no more dibromo compound was obtained. Also the reaction mixture evolved fuming hydrogen bromide under reflux conditions. Further, a silvery grey solid precipitated during the reaction at room temperature which turned yellow after filtration and drying. This yellow compound was shown to be 2,4-diamino-6-nitrotoluene by thin layer chromatography with ethyl acetate and light petroleum ether eluent. Infrared spectroscopy of the silvery grey compound indicated a strong absorption between 3200 - 2500 cm^{-1}; a characteristic of an ammonium compound. Evolution of hydrogen bromide could therefore be due to decomposition of such an ammonium salt under reflux conditions.

There are two possible explanations for these facts. Either production of the monobromo compound is deactivating the starting material, or the monbromo compound itself is very much more reactive towards bromine than the starting material.

In the first instance, we must assume that bromination occurs, producing a monobromo compound and hydrogen bromide. The acid produced will neutralise the strongest base present, presumably the starting material, which will become a mono-hydrogen bromide salt. The effect of this will be to reduce the electron releasing ability of one of the amino groups, thus making the benzene ring less susceptible to electrophilic attack. It may be that this means the monobromo compound is the species most susceptible to electrophilic attack, in which case, dibromination will occur (equation 15).



Equation 15: A possible mechanism for dibromination of CX.



Equation 16: A possible mechanism for dibromination of CX.

If this were the case, then addition of a strong base to the reaction mixture could remove the hydrogen bromide as a salt. This was attempted by adding triethylamine to the reaction mixture, but again only dibromo compound and starting material were obtained. Monobromated products were not observed at all throughout the reaction.

Alternatively, if the initial point of attack by bromine is at the 5-position, then some steric strain could be introduced, causing the nitro group to twist out of the plane of the benzene ring. This would prevent resonance deactivation of the ring by the nitro group, in which case the 3-position of the ring could become more active towards electrophilic attack than the starting material (equation 16). A nitro group renders positions ortho and para to it susceptible to nucleophilic attack, and amine groups make positions ortho and para susceptible to electrophilic attack. The 3-position is para to the nitro group in the ring and ortho to the two amino groups. If the nitro group is twisted out of the plane of the ring, by addition of a bromine at position 5, then position 3 of the monobromo compound could become more susceptible to electrophilic attack than either positions 3 or 5 of 2,4-diamino-6-nitrotoluene. If this mechanism operated, there would be no reason why the reaction could not go to completion in the presence of excess bromine; but this did not occur.

It would appear from the evidence obtained that possibly both mechanisms contribute and the monobrominated compound does become more susceptible to reaction than the starting material, which becomes incapable of further reaction.

Similar results were obtained with other brominating agents; pyridinium bromide perbromide[56] and N-bromosuccinimide in dimethylformamide.[57]

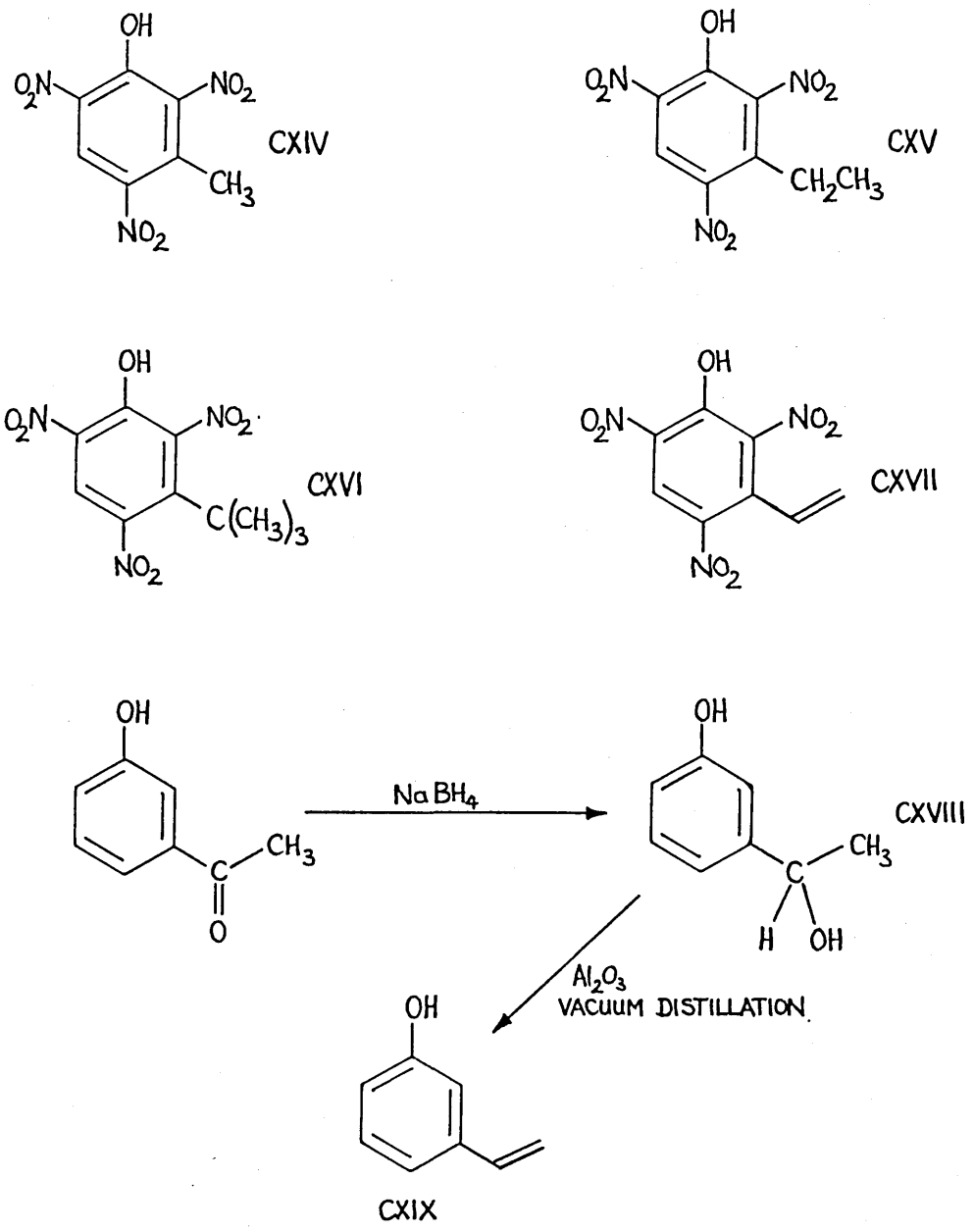
Clearly, this approach to the production of substrates for nucleophilic aromatic substitution reactions was not proving straightforward. It does not appear possible to produce the desired 3-bromo-2,4,6-trinitrotoluene by this route. Even if the synthesis of 3,5-dibromo-2,4,6-trinitrotoluene could be achieved, substitution of the bromine atoms would lead to compounds with such symmetry in the substitution pattern of the aromatic ring, that low melting points could not be predicted.

3.3 SYNTHESIS OF 3-ALKYLPICRYL CHLORIDES

As stated earlier, this method requires trinitration of a 3-alkylphenol, followed by substitution of hydroxyl by halogen.

3.3.1 Nitration of phenols

The nitration of phenols is a relatively facile procedure and in many cases trinitration is readily achieved using concentrated acids, i.e. oleum is not required. This is due to the considerable activating effect of the hydroxyl group on electrophilic aromatic substitution. Four phenols having various 3-alkyl substituents, were subjected to nitration, with the aim of producing their trinitro derivatives (CXIV - CXVII). The three picric acid derivatives having saturated side chains (CXIV,CXV,CXVI) were readily obtained in good yields (Table 2). However, the nitration of 3-vinylphenol gave problems. 3-Vinylphenol (CXIX) was synthesised from 3-hydroxyacetophenone (equation 17), but in poor yield. The major reason for the poor yield being, that the vacuum distillation of 3-vinylphenol from the intimate mixture of the carbinol (CXVIII) and activated alumina is not efficient. The carbinol has a tendency to distill over and solidify in the condenser ahead of 3-vinylphenol, which then dissolves the unchanged carbinol. The result is a poor yield of a low quality product. The purity of the product was improved by refluxing the mixture under



Equation 17: The preparation of 3-vinylphenol.

vacuum for 6 hours prior to the final vacuum distillation. Attempts to nitrate 3-vinylphenol with mixed sulphuric and nitric acids, acetyl nitrate[58] or fuming nitric acid[56] were unsuccessful and produced charred gums. Polymerisation of styrene — like molecules can occur readily and indeed probably explains why these reactions were unsuccessful.

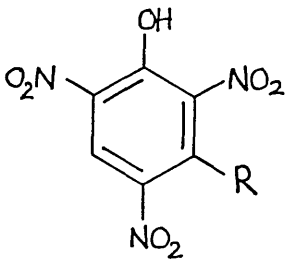
3.3.2 Chlorination reactions

Chlorination (as opposed to substitution reactions involving other halogens) was chosen because picryl chlorides are reasonably reactive compounds, but are relatively stable and do not require specialised storage arrangements.

Two reagents are popularly used for chlorination; phosphoryl chloride and thionyl chloride. 3-Methylpicric acid was treated with phosphoryl chloride in the presence of N,N-diethylaniline or N,N-dimethylformamide[56] (which both form chlorinating complexes with phosphoryl chloride). However, the yields were poor and a considerable amount of starting material was recovered from the reaction. In an alternative method, phosphoryl chloride was reacted with pyridinium 3-methylpicrate in toluene[56] to produce reasonable yields of the picryl chloride, although the crude products required treatment with a short silica column or numerous recrystallisations to produce a product of acceptable quality.

The most suitable method of chlorination of 3-alkylpicric acids was to add thionyl chloride dropwise, to a solution of the acid in DMF.[56] Yields of product were very good and only one recrystallisation was necessary to produce a high quality picryl chloride (Table 3). Thus, three 3-alkylpicryl chlorides have been synthesised in good yield and high purity as substrates for the synthesis of category C target compounds.

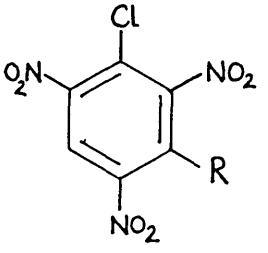
Table 2: Data obtained from the preparation of 3-alkylpicric acids.



R	YIELD*	MELTING POINT	LITERATURE MELTING POINT	REF
METHYL	78%	107-8°C	106°C 109-110°C	59 60
ETHYL	66%	84-6°C	87·5°C	59
T-BUTYL	73%	174-6°C		

* AFTER RECRYSTALLISATION.

Table 3: Data obtained from the preparation of 3-alkylpicryl chlorides.



R	YIELD*	MELTING POINT	COMPOUND NUMBER
METHYL	95%	147-9°C	CXX
ETHYL	80%	88-89·5°C	CXXI
T-BUTYL	92%	92-3°C	CXXII

* AFTER RECRYSTALLISATION.

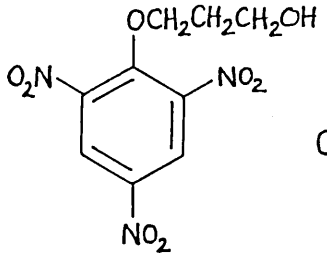
CHAPTER 4

NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS

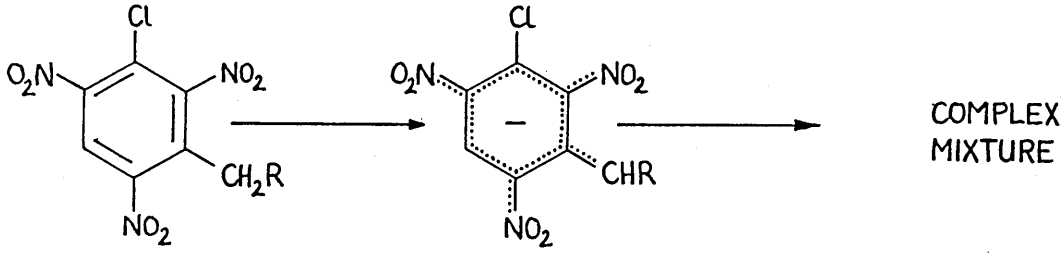
As described in Chapter 3, three 3-alkylpicryl chlorides (Table 3) have been successfully prepared from the appropriate phenol. These compounds comprised the substrates for a series of reactions with various nucleophiles in an attempt to produce compounds with structures of categories C and D, or similar, for which low melting points are anticipated to occur.

4.1. REACTIONS WITH OXYGEN NUCLEOPHILES

Of the various types of nucleophile used during this study, the most experimental difficulties were found with reactions involving oxygen nucleophiles. The most common method of preparation of picryl ethers [7(b)] is to dissolve picryl chloride in the relevant alcohol and to introduce an equimolar quantity of sodium metal. After the sodium has completely reacted, the reaction mixture is then allowed to stand for an appropriate time before precipitation of the product by addition of dilute acid. The crude picryl ether can then be filtered, or extracted with an appropriate solvent, and purified by recrystallisation or column chromatography. For example 3'-(2,4,6-trinitrophenoxy) propanol (CXXIII), m.pt. 50-52°C, can be prepared in this manner.[7(b)] In many other cases this method is also successful, but with the reactions attempted in this study is was unreliable and often led to a large number of reaction products. Reactions involving 3-methylpicryl chloride (CXX) or 3-ethylpicryl chloride (CXXI) gave products that were black and contained a complex mixture of compounds. It was realised that in addition to displacement of chloride, the attacking anion could possibly abstract a proton from the alkyl group (equation 18). This would give a TNT type anion, which could lead to a wide range of compounds as discussed earlier. Clearly, if this were the key to the



CXXIII



R = H (CXX)

R = CH_3 (CXXI)

Equation 18: The abstraction of protons from 3-alkylpicryl chlorides.

problem it should not arise with a 3-alkylpicryl chloride which does not contain α-hydrogen atoms, e.g. 3-t-butylpicryl chloride (CXXII) or 3-vinylpicryl chloride (this compound does not contain abstractable hydrogen atoms).

Alternatively, if the attacking moiety's nucleophilic character is made stronger, which could be achieved either by changing the reaction medium to an aprotic solvent, or by using less basic, more nucleophilic groups, the problem could well be reduced.

The above changes in the reaction conditions were introduced and more successful nucleophilic aromatic substitution reactions occurred and thus, the desired products were obtained. Experiments with 3-t-butylpicryl chloride with alkoxide, in the presence of the corresponding alcohol were quite successful, although the solubility of 3-t-butylpicryl chloride in some alcohols was low and a somewhat complex mixture was obtained, but the desired products could be isolated. As discussed earlier, 3-vinylpicryl chloride could not be prepared because of the difficulties at the nitration stage.

Reactions carried out in aprotic solvents were extremely successful, and this approach was preferred to that using alcohols as the reaction medium. Dipolar aprotic solvents tend to leave anions relatively unrestricted (i.e. without a solvent sphere), thus maximising their nucleophilic character. In similar reactions, Sinnott and Whiting[45] used tetrahydrofuran (THF) as their reaction medium. This is a weakly dipolar aprotic solvent, which can be readily purified, is of low boiling point and miscible with water. The use of THF led to the successful preparation of 3-t-butylpicryl ethers and 3-ethylpicryl ethers, but only one 3-methylpicryl ether. Yields were generally reasonable, although there was often a very small amount of the parent picric acid produced, probably formed during the quenching step. This was easily removed by column chromatography.

Table 4 shows the structures and melting points of the picryl ethers produced by this method.

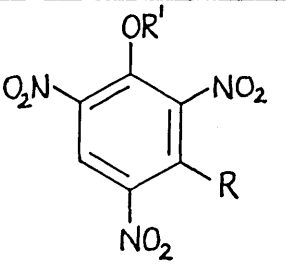
4.1.1. Reactions of 3-methylpicryl chloride

Reactions of 3-methylpicryl chloride with oxygen nucleophiles were generally not very clean. On many occasions the reactions produced no discernable major product and generally gave a large proportion of material which remained at the baseline of a TLC plate. Addition of 3-methylpicryl chloride to the alkoxide solution in THF gave a black solution (as found with reactions in alcohol), which on dilution proved to be a very concentrated green colouration. The only successful reaction was that involving 2-hydroxyethoxide ($HOCH_2CH_2O^-$) as nucleophile, in which a yield of 39% was obtained after purification. A high degree of purification was found to be required, because a dark blue smear was observed on silica whenever the reaction product was diluted.

The compound that caused this blue smear was isolated with great difficulty and in very small quantities. It was a yellow oil which displayed quite remarkable characteristics. When on a TLC plate or column, wet with eluent, its presence was easily identified as a dark blue streak. When the TLC plate or column was allowed to dry, the blue colour disappeared to be replaced by a slight buff discolouration, which was virtually undetectable. This behaviour was also displayed when a solution of this yellow oil in many different organic solvents had a small amount of silica (or alumina) added to it. If the organic solvent was evaporated to leave only the silica, then the dark blue colouration would disappear, only to be regenerated on further addition of solvent.

Infrared and nmr spectra of the yellow oil are shown in Figures 15a and 15b respectively. From these spectra it can be seen that the compound is nitroaromatic, though

Table 4: Picryl ethers produced from the reaction of 3-alkylpicryl chlorides and alkoxides.



R'	R=ME	R=ET	R=T-BU
$-CH_2CH_2OH$	70-72°C	35·5-38°C	79-83°C
$-CH_2CH_2CH_2OH$		LIQUID	68-71°C
$-CH_2CH_2OCH_3$		LIQUID	63-64°C
$-CH_2CH_2OCH_2CH_3$		LIQUID	55-57°C[a]
$-CH_2CH_2OCH_2CH_2OH$		LIQUID	83-86°C
$-CH_2CH_3$		LIQUID	
$-CH_2CH=CH_2$		LIQUID	

a) THIS PRODUCT WAS NOT COMPLETELY PURE

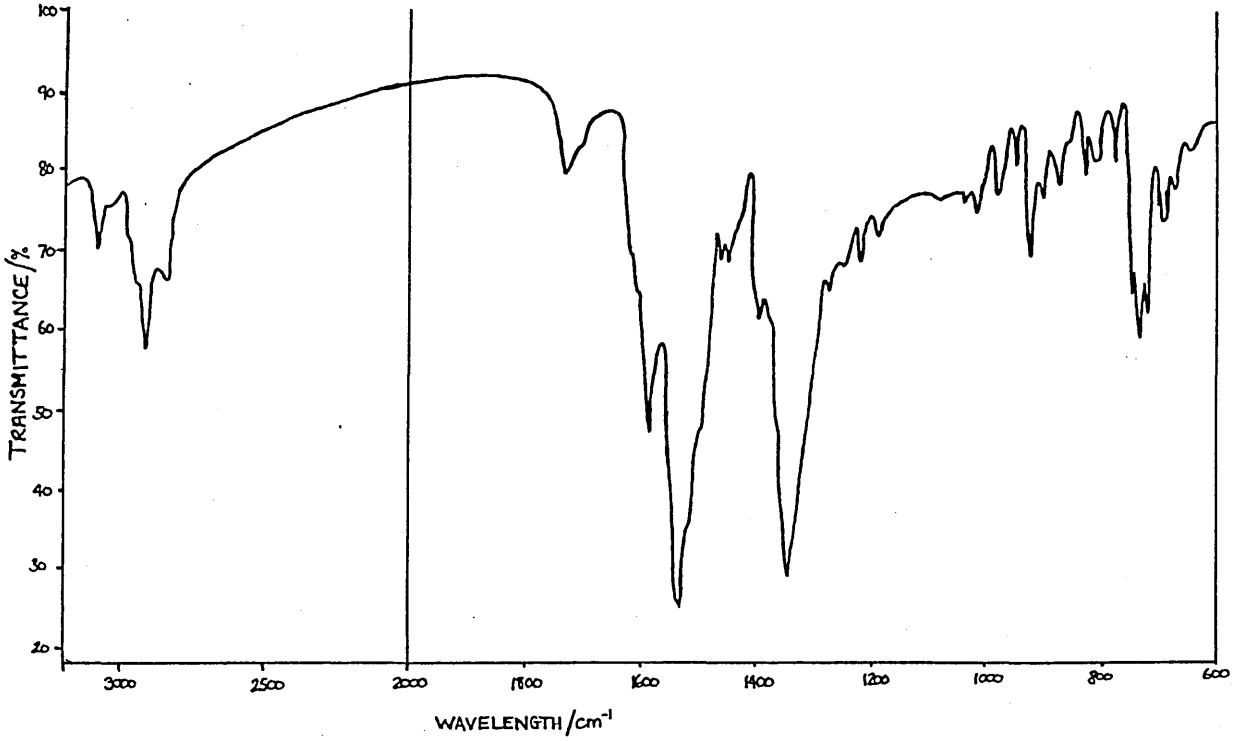


Figure 15a: The infrared spectrum of the yellow oil responsible for blue TLC streaks.

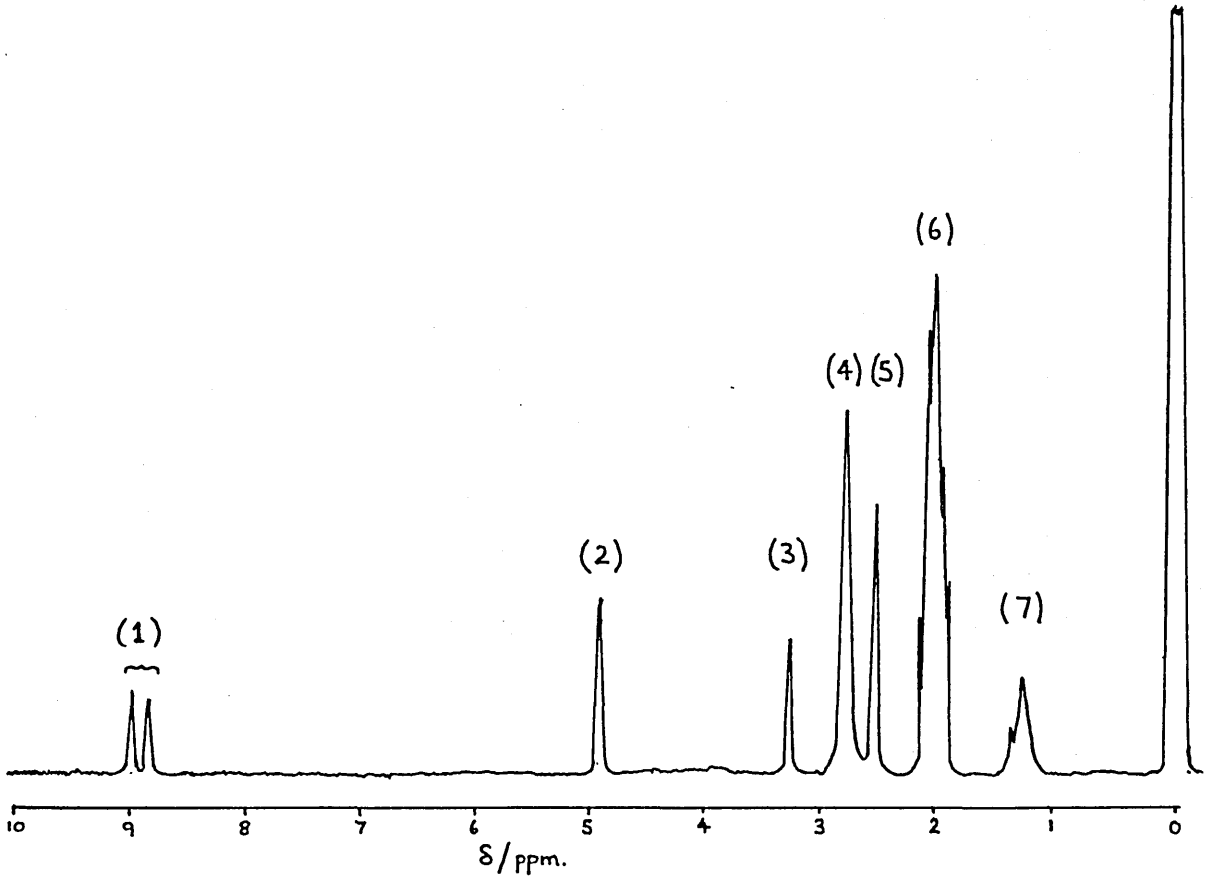


Figure 15b: The nmr spectrum of the yellow oil responsible for blue TLC streaks.

the nmr indicates that there are two aromatic protons, implying the presence of two rings in its molecular structure or a 1:1 mixture of two compounds. These aromatic protons both appear in a position downfield of that in 3-methylpicryl chloride: the starting material (the aromatic proton in 3-methylpicryl chloride is at δ= 8.65 ppm; in Figure 15b peaks (1) are at δ= 9.05 ppm and 8.9 ppm). It appears that there are not any carbon chains (e.g. 2-hydroxyethoxy groups) because there is an absence of any splitting patterns in Figure 15b. The peaks labelled (1) are due to two aromatic protons; peak (5) is almost certainly due to an aromatic methyl group; Peaks (2) and (3) integrate indicating two protons each; peak (6) is due to protonated acetone and peak (4) is due to water in the nmr solvent.

Unfortunately it was not possible to study this compound in anymore detail and a full structure could not be elucidated.

Any type of charge transfer complexes or σ-type adducts would have been destroyed in the acidic work up. However, it is possible that a nucleophilic substitution with a carbon nucleophile (produced by α-proton abstractions) has taken place as a minor side reaction, though it is unlikely to have a simple S_NAr mechanism. Alternatively, it may be that this yellow oil is a mixture of two compounds which are inseparable by TLC and column chromatography.

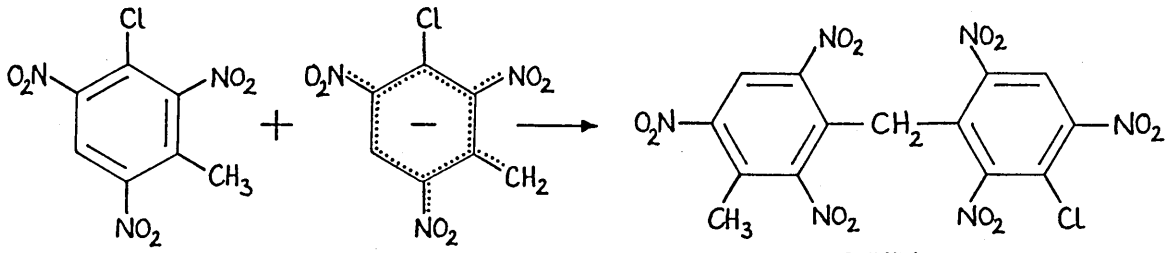
Photochemical and thermal degradation of TNT is thought to proceed via the TNT anion.[21,61,62] As in the case of TNT, proton abstraction to produce an anion is a possible mechanism of the reaction of 3-methylpicryl chloride with base, therefore it is susceptible to similar types of degradation as the TNT anion. This situation though, is complicated by the presence of the halide leaving group in an activated position.

The most likely competing reaction during the treatment of 3-methylpicryl chloride with 2-hydroxyethoxide is the substitution of chlorine by a 3-methylpicryl chloride anion (produced by proton abstraction). The expected product would then be 3-chloro-3'-methyl-2,2',4,4',6,6' -hexanitrodiphenylmethane (CXXIV) as seen in equation 19. This compound would contain two aromatic protons (Figure 15b; peak (1)), an aromatic methyl group (Figure 15b; peak (5)); and a methylene group attached to two aromatic rings (Figure 15 (b); peak (2)).[3]

In 1972 Shipp, Kaplan and Sitzmann[3] demonstrated nucleophilic displacement of chlorine in picryl chloride and 1-chloro-2,4-dinitrobenzene by the TNT anion (equation 6). The results from this work have been discussed fully in Chapter 2 and, as this study has shown, simple ionic nucleophilic aromatic substitution is almost certainly not the mechanism by which these reactions occur: the same can be said for equation 19. However, the mechanisms of equation 6 and equation 19 are likely to be very similar, with similar intermediates. Indeed, Shipp, Kaplan and Sitzmann observed a dark blue colouration on the mixing of TNT anion and picryl chloride solutions. They also studied the structure of the anions of polynitrodiphenylmethanes by n.m.r. spectroscopy which they noted were intensely coloured species. (No U.V. spectroscopic data were given for these compounds).

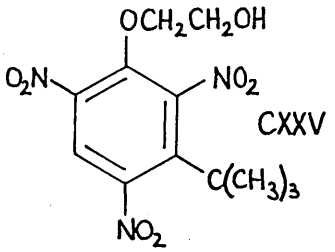
If the anions of these hexanitrodiphenylmethanes are the dark blue colourations observed, then in the reactions of 3-methylpicryl chloride with 2-hydroxyethoxide ions, the dark blue colour would appear in competition with the red colour of the nucleophilic aromatic substitution intermediate Meisenheimer complex, affording a dark green reaction mixture: exactly what was observed in this study.

If the yellow oil isolated from these reactions does have the structure CXXIV, then the blue colouration observed

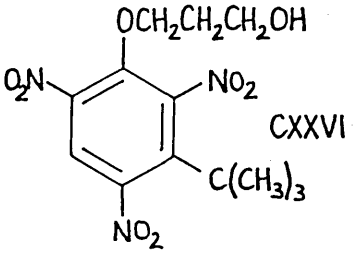


CXXIV

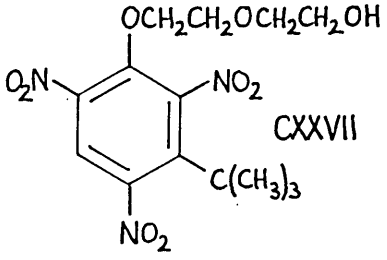
Equation 19: A possible reaction of 3-methylpicryl chloride with base.



CXXV



CXXVI



CXXVII

when absorbed on silica must be due to proton abstraction from the hexanitrodiphenylmethane by the silica, though why this is apparent only on solvation would need further study.

There is obviously a need for more studies in this interesting area and indeed a U.V. spectroscopic study of the reaction of 3-methylpicryl chloride with a 2-hydroxyethoxide is required. Also a positive identification/characterisation of the yellow oil is essential (nmr, ir, ms, elemental analysis), followed by a study of its reaction with various solvent/base systems. From these results it would be possible to ascertain whether the dark blue colouration in the reaction mixture is due to the action of base on the yellow oil, or some other reaction intermediate. Unfortunately, it was not possible to extend these ideas, nor to perfect a technique to synthesise 3-methylpicryl ethers from nucleophilic attack by alkoxides on 3-methylpicryl chloride.

4.1.2. Reactions of 3-ethylpicryl chloride

The ethers obtained from 3-ethylpicryl chloride were by far the most interesting compounds produced, with respect to the overall aims of the project. Reactions of 3-ethylpicryl chloride with alkoxides occurred cleanly, giving reasonable yields of products, which in most cases were viscous liquids at room temperature (Table 4). As previously mentioned, the reactions of 3-ethylpicryl chloride in RO^-/ROH gave a black/dark green reaction mixture, somewhat similar to that produced by 3-methylpicryl chloride. In RO^-/THF, the above problem did not occur and the yields of desired products ranged from 39% to 87% after column purification. Column chromatography was the most suitable method of purifying these compounds: i.e. for removing the small quantities of parent 3-ethylpicric acid and other impurities in the crude product. The products thus treated were shown to be pure by n.m.r. spectroscopy, although

thin layer chromatography often showed trace amounts of the parent picric acid.

The 3-ethylpicryl ethers were all viscous liquids at room temperature with the exception of 2'-(3-ethyl-2,4,6-trinitrophenoxy)ethanol, which was a low melting solid (mpt 35.5-38°C). These liquids were all extremely light sensitive and, when left in sunlight, turned from pale yellow to dark brown in less than 2 hours. Repurification could be achieved by column chromatography, which showed that the amount of light induced decomposition was small, although it was enough to completely discolour the material. Decomposition products included 3-ethylpicric acid, together with other highly coloured materials.

4.1.3. Reactions of 3-t-butylpicryl chloride

The reaction of 3-t-butylpicryl chloride with sodium 2-hydroxyethoxide in ethylene glycol solvent, was a relatively clean reaction, giving a reasonable yield (57%) of 2'(3-t-butyl-2,4,6-trinitrophenoxy)ethanol (CXXV). The reaction was also successful in THF, though there was no great improvement in yield (62%). 3-t-Butylpicryl chloride reacted successfully with sodium 3-hydroxypropoxide in propane-1,3-diol,to produce a 60% yield of 3'-(3-t-butyl-2,4,6-trinitrophenoxy)propanol (CXXVI). Also, 2"(2'-(3-t-butyl-2,4,6-trinitrophenoxy)ethoxy)ethanol (CXXVII) was produced in 53% yield by the action of sodium 2-(2'-hydroxyethoxy)ethoxide on 3-t-butylpicryl chloride in THF solvent.

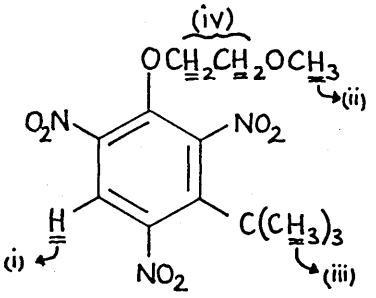
The above three reactions were the only instances observed where 3-t-butylpicryl chloride and an alkoxide reacted to give one major product. In all other reactions, more than one product was observed, although the picryl ether was the major product, and some extremely interesting chemistry emerged.

The reaction of 3-t-butypicryl chloride with 2-methoxyethoxide anions afforded a mixture of three compounds as the reaction product (A, B and C). The ^{1}H nmr spectra of these materials were substantially different, though they were obviously very similar compounds, and this data is summarised in Table 5. The major product of the three was compound A, which was the desired ether, as evidence presented later shows. For clarity in Table 5, the chemical shifts for various protons in A are identified as (i)-(iv) and the observed differences in B and C in each region are noted.

From Table 5 it can be seen that there is a vast difference in aromatic proton resonances, which show a chemical shift difference of > 1 ppm between compound A and compounds B and C. Also, compound C appears to contain one aromatic nucleus and two methoxyethoxy side chains. This evidence is confirmed by the ^{13}C nmr spectra of these compounds (Table 6). Again, for clarity in Table 6, the carbon resonances for A are identified as (i)-(v), and the differences found in B and C in each region are then given. It can be seen that the carbon attached to the aromatic proton shows a vast chemical shift difference between A and compounds B and C. Compound C shows four carbon atoms at around 70 ppm, where A and B only show two, and at approximately 58 ppm, C shows two carbon atoms and A and B only one. At this stage, the general conclusion can be made that there are two sites for nucleophilic attack in 3-t-butylpicryl chloride, producing A and B from one nucleophile attacking at different sites, with C arising from the nucleophile attacking both sites.

Further experimentation showed that the production of compound C was temperature dependant, because it was not observed at all in the reaction products unless the reaction mixture had been refluxed. Reaction of four fold excess of nucleophile with 3-t-butylpicryl chloride showed that A and B where produced at room temperature, whereas

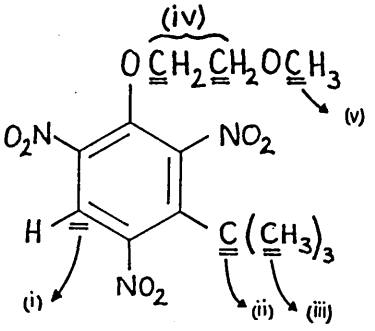
Table 5: The ^{1}H-nmr spectra of compounds A,B & C.



COMPOUND A

H	COMPOUND A	COMPOUND B	COMPOUND C
(i)	δ=8·08 ppm, s, 1H.	δ=7·05 ppm, s, 1H.	δ=7·02 ppm, s, 1H.
(ii)	δ=3·35 ppm, s, 3H.	δ=3·43 ppm, s, 3H.	δ=3·39 ppm, s, 6H.
(iii)	δ=1·50 ppm, s, 9H.	δ=1·42 ppm, s, 9H.	δ=1·42 ppm, s, 9H.
(iv)	δ=3·65 ppm, t, } 4H δ=4·28 ppm, t, }	δ=3·78 ppm, t, } 4H δ=4·25 ppm, t, }	δ=3·71 ppm, m, } 8H δ=4·25 ppm, m, }

Table 6: The ^{13}C nmr spectra of compounds A,B & C.



COMPOUND A

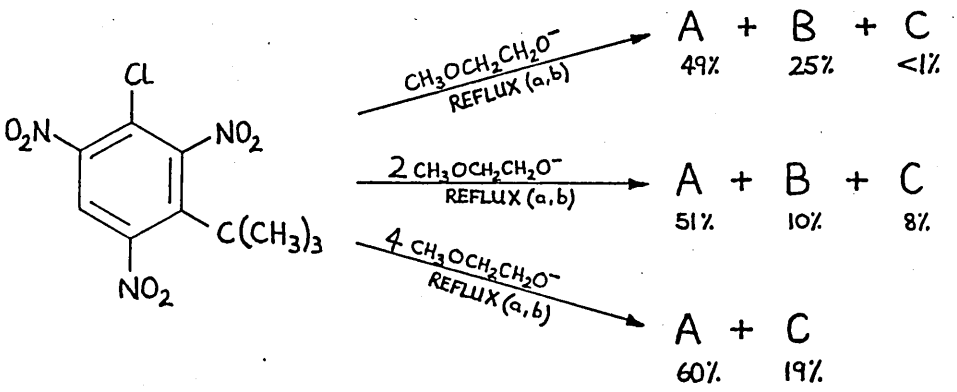
H	COMPOUND A	COMPOUND B	COMPOUND C
(i)	δ = 122·5 ppm	δ = 110·2 ppm	δ = 111·0 ppm
(ii)	δ = 38·2 ppm	δ = 36·9 ppm	δ = 36·3 ppm
(iii)	δ = 29·7 ppm	δ = 30·2 ppm	δ = 29·8 ppm
(iv)	δ = 70·9 ppm	δ = 70·2 ppm	δ = 69·2 ppm
	δ = 77·2 ppm	δ = 70·6 ppm	δ = 70·3 ppm
			δ = 71·0 ppm
			δ = 73·7 ppm
(v)	δ = 58·9 ppm	δ = 59·4 ppm	δ = 58·5 ppm
			δ = 58·7 ppm

A and C were produced at reflux temperatures. Furthermore, the amount of A produced was found to be virtually independant of the nucleophile concentration, though its yield did slightly improve the greater the excess of nucleophile. Compound A was found to be unaffected after refluxing with 2-methoxyethoxide, whereas B was totally converted to C with good yield (72%) by similar treatment. This data is summarised in equations 20 and 21. It would appear then, that there are two active sites for substitution on 3-t-butylpicryl chloride, of which the second is deactivated by substitution at the first; the first being unaffected by substitution at the second.

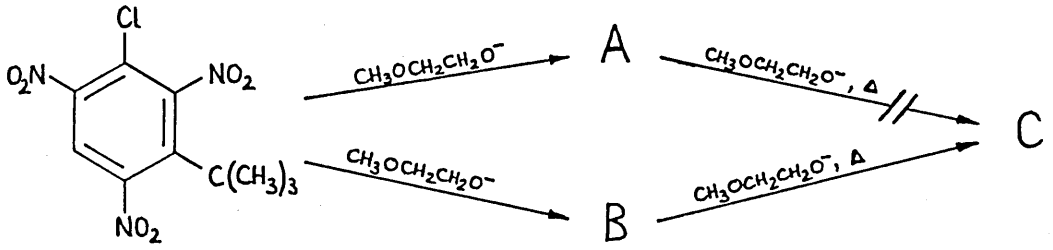
In 3-t-butylpicryl chloride, the normal site for nucleophilic attack is the carbon to which the chlorine atom is attached. The second site for substitution could be one of the aromatic nitro groups. Though substitution of one of the nitro groups would seem unlikely, because of their symmetric substitution pattern. Elemental microanalysis though, confirmed this to be the case (Table 7) , and also allowed structures to be proposed for A (CXXVIII), B(CXXIX, CXXX) and C (CXXXI, CXXXII).

The presence of the chlorine atom in compound B was confirmed by the characteristic peak splitting seen in its mass spectrum (Figure 16). The splitting pattern can be seen in the parent ion peak M, at m/e = 332 (Relative molecular mass of B), where a peak of 33% of the relative intensity of M appears at M+2 (m/e = 334). This is indicative of molecules containing ^{37}Cl (24.5% natural abundance) and ^{35}Cl (75.5% natural abundance). This splitting pattern also shows in many other peaks besides the parent ion peak.

t-Butylpicryl chloride then has potential sites for substitution at the chlorine atom and at a nitro group, and when reacted with an equimolar amount of nucleophile it gives A and B. From further evidence, it appears that



Equation 20: The effect of varying 2-methoxyethoxide concentration on the products of reaction with 3-t-butylpicryl chloride,
a, Temperature of refluxing THF (65°C)
b, Reaction time, 30 mins.

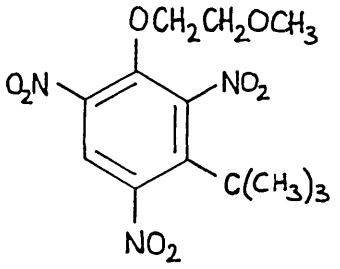


Equation 21: The reaction of 2-methoxyethoxide with 3-t-butylpicryl chloride, leading to compounds A,B & C.

Table 7: Elemental microanalysis data for compounds A,B & C.

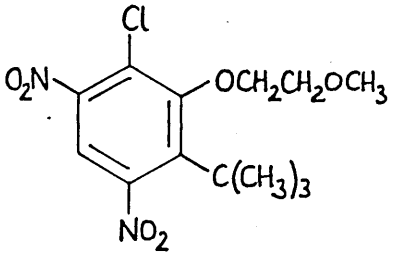
COMPOUND	% CARBON	% HYDROGEN	% NITROGEN
A THEORETICAL (CXXVIII)	45·48	4·99	12·24
A EXPERIMENTAL	45·65	5·06	12·23
B THEORETICAL (CXXXIX)	46·93	5·15	8·43
B EXPERIMENTAL	47·07	5·25	8·45
C THEORETICAL (CXXXI)	51·61	6·50	7·52
C EXPERIMENTAL	51·89	6·65	7·50

COMPOUND A

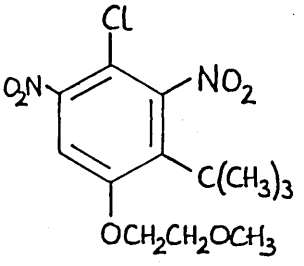


CXXVIII

COMPOUND B

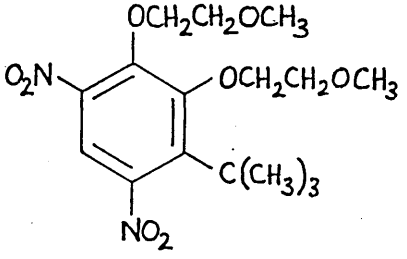


CXXIX

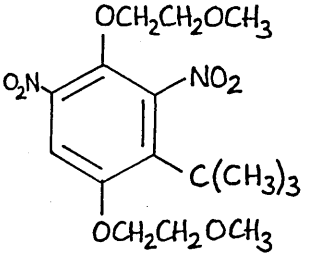


CXXX

COMPOUND C

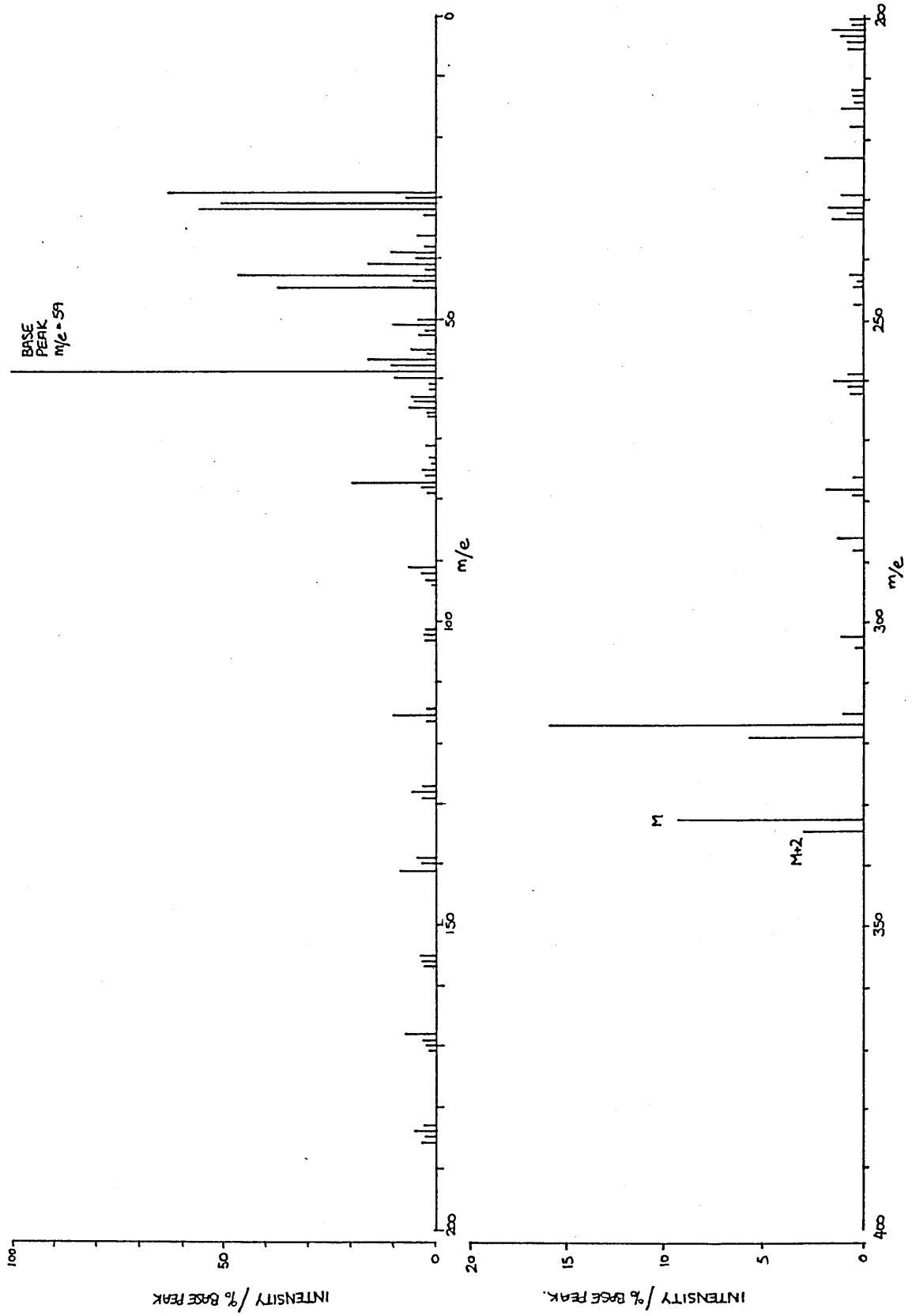


CXXXI



CXXXII

Figure 16: The mass spectrum of compound B.



the chlorine atom remaining in B is still capable of being displaced, hence, with excess nucleophile C is produced. However, in substituting the chlorine in 3-t-butylpicryl chloride to form A, the nitro groups become incapable of being displaced, hence A will not react further with excess nucleophile to form C.

Nitro group substitution in these reactions may proceed for the following reason. In 3-t-butylpicryl chloride, the favoured "in-plane" conformation for the nitro groups either side of the bulky t-butyl group is likely to be severely hindered, and they will probably both be twisted out of the plane of the ring to relieve the steric strain. This is illustrated by Figure 17. If this is so, then the resonance interaction between the nitro groups and the aromatic ring will be markedly reduced, which would weaken the carbon to nitrogen bonds. An inductive electron withdrawing effect would, however, still occur and polarise the carbon to nitrogen bond, such that the carbon atom would become susceptible to nucleophilic attack. The nitro group, without resonance stabilisation, would thus be a good leaving group, as in aliphatic systems. Nucleophilic substitution of either of the nitro groups ortho to the t-butyl group thus becomes possible. From the relative yields of A and B, it can be seen that nitro group substitution is the less preferred reaction, but is nevertheless quite significant.

The question as to which nitro group is substituted (2 or 4 position) is more difficult to answer. Consideration of the nmr data seems to indicate that such a large shift in an aromatic proton (Table 5), could only be caused by substitution in a position ortho to it, i.e. 4-nitro group displacement (a large shift is also seen in the ^{13}C nmr for the carbon attached to the aromatic proton (Table 6)). Also, substitution at the 4-position is likely to be less hindered than at the 2-position due to the smaller steric repulsion of a neighbouring hydrogen as opposed to a

chlorine. Confirmation of the position of substitution could be obtained by X-ray crystallography. X-ray crystallography analysis of B has been initiated, but it is not a simple problem and work is still in progress. Appendix A summarises the crystallographic data obtained to date. It appears that B has a statistically centrosymmetric crystal structure due to inherent disorder, though the molecule itself is non-symmetrical and was initially thought likely to have a non-centrosymmetric crystal structure. Although not yet confirmed by X-ray analysis the nmr evidence suggests that 4-nitro groups substitution is preferred.

The substitution of one of the nitro groups in 3-t-butylpicryl chloride by 2-methoxyethoxide (producing B) would tend to deactivate the ring (particularly ortho and para to the substituent) to nucleophilic attack, due to the replacement of an electron donating group. However, there is still sufficient activation of the chlorine atom because B reacts with 2-methoxyethoxide, producing C by chlorine substitution, although this requires higher temperatures to be effective. This implies that there is deactivation to a greater extent than is found in 1-chloro-2,4-dinitrobenzene, which reacts readily with alkoxides at room temperature.[40]

The picryl ether A is not susceptible to loss of a nitro group because of the effect of changing from a chlorine atom to an ether oxygen at the 1 position of the ring. This oxygen causes the carbon atoms at the 2 and 4 positions of the ring to be less attractive to nucleophiles and nitro group substitution is therefore much more difficult.

These three product types were found with various alkoxide nucleophiles, RO^-, where R was $-CH_2CH_2OCH_3$; $-CH_2CH_2OCH_2CH_3$; $-CH_2CH_3$; and $-CH_2CH=CH_2$. It was not observed where R was $-CH_2CH_2OH$;$-CH_2CH_2CH_2OH$; $-CH_2CH_2OCH_2CH_2OH$. In these cases only the expected picryl ethers were obtained.

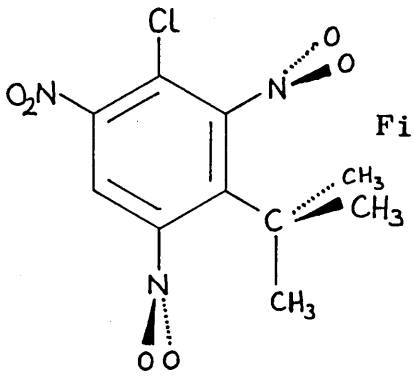
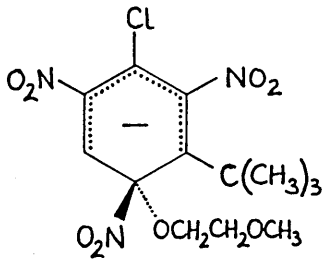
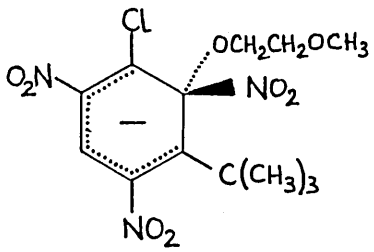


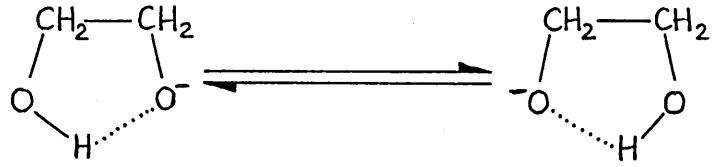
Figure 17: A view of the steric twisting of the nitro groups in 3-t-butylpicryl chloride (CXXII).



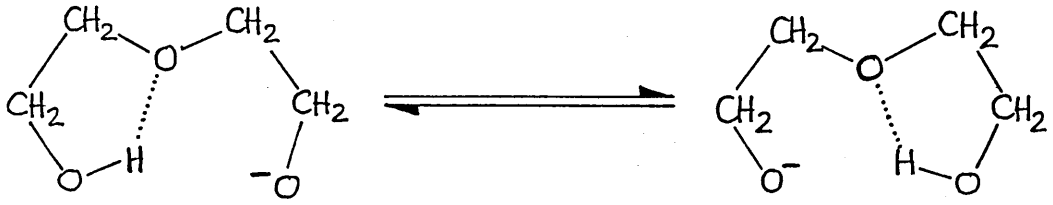
CXXXIII



CXXXIV



Equation 22: Stabilisation of 2-hydroxyethoxide ions by intramolecular hydrogen bonding.



Equation 23: Stabilisation of 2-(2'-hydroxyethoxy) ethoxide by intramolecular hydrogen bonding.

It would appear that when the alkoxide chain has a terminal hydroxy function, nitro group substitution is unfavourable.

Substitution of chlorine in 3-t-butylpicryl chloride is relatively facile because the nitro groups activate the ring system to nucleophilic substitution. As discussed earlier, the nitro group can act as a good leaving group in the right circumstances. However, in symmetrically trinitrated compounds, nucleophilic substitution of one of the nitro groups is most unusual.

Gold and Rochester[63] photo-induced nitro group substitution in a sym-trinitrated system, and some hexasubstituted benzenes have been shown to display nitro group substitution[64]. But, with the compounds described here, in which a pentasubstituted system is involved, nitro group substitution (which is <u>not</u> photo-induced) is indeed a novel observation.

During nitro group substitution the reaction mechanism would generate an intermediate of structure CXXXIII or CXXXIV. The only stabilisation for these σ-complex type intermediates would be the inductive electron withdrawing power afforded by the two nitro groups meta to the reaction centre. Meta nitro groups are very much weaker in supporting nucleophilic aromatic substitution than are nitro groups situated ortho or para to the reaction centre. Thus, the main driving force for this reaction to take place, is relief of steric strain in the starting material. With reactive nucleophiles it is likely that both types of substitution could occur, with displacement of chlorine more favoured. If the attacking nucleophile has greater stability, then its reactivity would be reduced and selectivity would be increased. It is possible that alkoxides with terminal hydroxy functions are stabilized to some extent by intramolecular hydrogen bonding, as shown in equations 22 and 23, and under these circumstances, only the more preferred substitution of chlorine can take place.

As has been previously stated, this type of nitro group substitution has not been reported in the literature. On the evidence presented here, it may be possible to induce this type of nitro group substitution in a dinitro system, e.g. 3-t-butyl-1-chloro-2,4,-dinitrobenzene (CXXXV). Indeed, a study of the nucleophilic substitution characteristics of CXXXV, CXXXVI and CXXXVII could supply some clues as to the orientation of substitution in the trinitro system.

A dinitro system would have slightly reduced activity towards nucleophilic aromatic substitution of chlorine compared to the trinitro system. Compound CXXXV should therefore give a greater ratio of nitro group substitution to chlorine substitution. This is because the steric activation of the susceptible nitro group should not reduce in the absence of the 6-position nitro group. Compounds CXXXVI and CXXXVII may be less active to nitro group substitution as, when compared to t-butylpicryl chloride, the absent nitro groups would lie adjacent to the t-butyl group, therefore conformational compensation for this may slightly reduce the steric strain in the system as a whole. If the steric features of these three compounds are not significantly altered by the absence of one of the three nitro groups, then the site of nitro group substitution may be observed, purely by monitoring the reaction products from their nucleophilic substitution reactions. This can then be considered analogous to the trinitro system and the observed results applied.

Selective syntheses of CXXXV, CXXXVI and CXXXVII would be somewhat difficult, though direct nitration may be employed for the production of CXXXVI, for steric reasons. The synthesis of CXXXV and CXXXVII may be more haphazard by these methods.

It may be possible to use the Von Richter reaction[65,66], with a subsequent decarboxylation step, to produce CXXXV

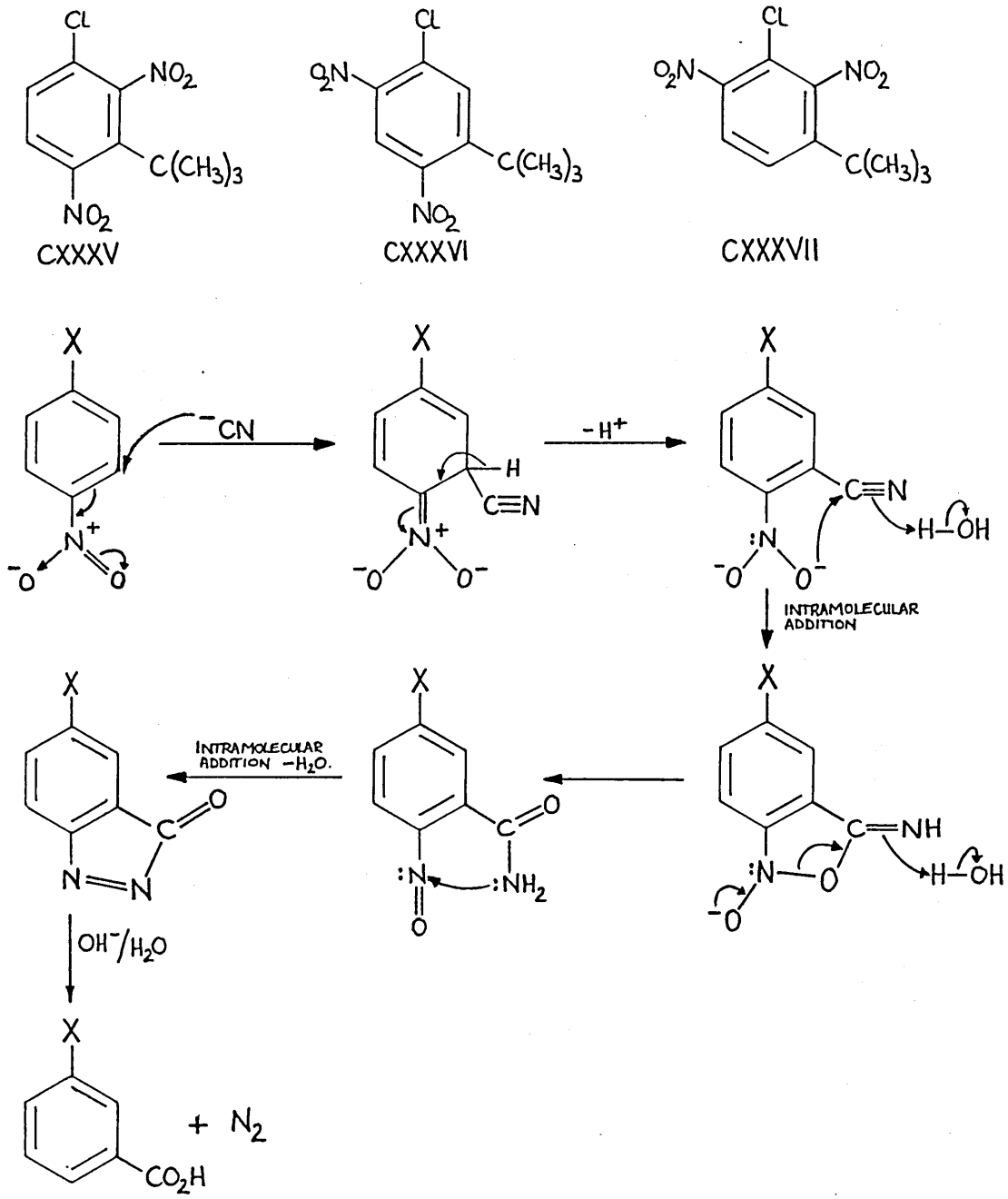
and CXXXVII using 3-t-butylpicryl chloride as a starting material. The Von Richter reaction uses the cyanide ion as an attacking nucleophile, whereby the initial σ-adducts formed, appear to undergo an elimination resulting in the loss of a nitro group. The cyanide is transformed to a carboxylic acid group. The mechanism for this reaction is shown in equation 24 with para-X-nitrobenzene[67] where X is a leaving group. The reaction with t-butylpicryl chloride would be more complicated than the mechanism shown in equation 24, because of the high activity of the ring and also the substituents in the 1 and 3 ring positions. The mechanism shown in equation 24 requires the presence of a protic solvent. However, reaction does occur in DMSO[68], but it is much more complicated.

The synthetic utility of the Von Richter reaction applied to 3-t-butylpicryl chloride would need a detailed study before realisation of its full potential.

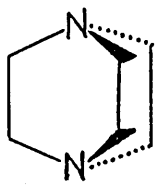
4.2. REACTIONS WITH SULPHUR NUCLEOPHILES

The reactions carried out using sulphur nucleophiles were originally initiated in order to utilise a less basic nucleophile, in as attempt to reduce proton abstraction from 3-methyl and 3-ethylpicryl chlorides, which had produced complex mixtures of products with oxygen nucleophiles. If the pK_a values of alcohols and thiols are compared, it can be seen that the basicity differs by approximately five orders of magnitude (e.g. pK_a (EtOH) = 15.5; pK_a (EtSH) = 10.5)[69]. It was also recognised that sulphur analogues of Category C compounds could reveal some potentially useful compounds with low melting points.

The preparation of picryl thioethers from the nucleophilic action of mercaptides on picryl chloride, has been reported in the literature[45] as a very facile procedure, as was found in this study. The reactions were very rapid and gave good yields (50-85%) of crystalline



Equation 24: The mechanism of the Von Richter reaction.



CXXXVIII

pale yellow solids, which were however light sensitive and generally of higher melting point than their oxygen analogues, as shown in Table 8.

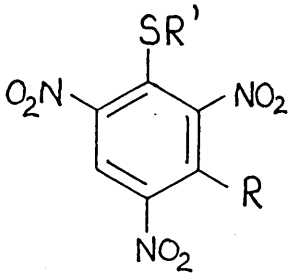
Three mercaptides were used as nucleophiles; ethyl mercaptide ($CH_3CH_2S^-$), 2-hydroxyethyl mercaptide ($HOCH_2CH_2S^-$) and methoxycarbonylmethyl mercaptide ($CH_3OC(O)CH_2S^-$). Reactions were carried out in dichloromethane and 1,4-diaza[2:2:2]bicycloöctane (DABCO, CXXXVIII) used as the base to generate the mercaptide from the appropriate thiol.

In the case of the t-butylpicryl derivatives, there was no indication of nitro group substitution, as was observed with some oxygen nucleophiles. Evidently, the lesser basicity of the mercaptides does not allow nitro group substitution as a route to products. Table 8 shows the thioethers obtained and their melting points.

All of the three 3-alkylpicryl chlorides gave very little reaction with methoxycarbonylmethyl mercaptide, and most of the picryl chlorides could be recovered from the reaction mixtures, along with some degradation products. It would appear that the presence of the carbonyl group reduced the nucleophilicity of the mercaptide, such that reaction was not possible.

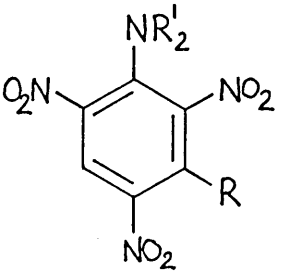
Previous references to these compounds, were not found in the literature and, as expected, they had fairly low melting points, though higher in comparison to their oxygen analogues. The yields of these compounds were much better than their oxygen analogues, and increasing either the 3-alkyl chain length, or the mercaptide chain length, or both could, as hypothesised in Chapter 1, lead to liquid products. Unfortunately though, the longer chain lengths which would be required to reduce the thioether melting points would have a detrimental effect on their explosive character. The inclusion of sulphur in these compounds

Table 8: The melting points of the 3-alkylpicryl thioethers prepared.

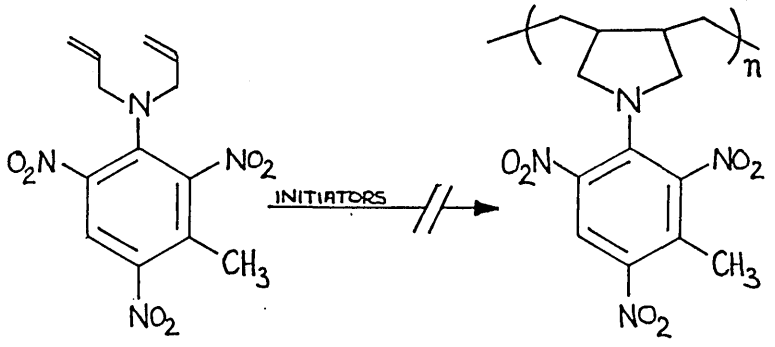


R'	R=Me	R=Et	R=t-Bu
$-CH_2CH_3$	90-94°C	52-53·5°C	90-93°C
$-CH_2CH_2OH$	87-88°C	51-53°C	95-96·5°C

Table 9: The melting points of the 3-alkylpicramides prepared.



R'	R=Me	R=Et	R=t-Bu
$-CH_2CH_3$	80-81·5°C	101-102°C	137-139°C
$-CH_2CH_2CH_3$	80-86·5°C	93-95°C	125-127°C
$-CH_2CH_2CH_2CH_3$	90-92°C	38-39°C	67-70°C
$-CH_2CH=CH_2$	63-64·5°C	48-49·5°C	IMPURE



Equation 25: The cyclopolymerisation of N,N-diallyl-3-methylpicramide.

would also have a detrimental effect on the explosive character of these types of compound. The reason for this is that the effect of replacing the oxygen of an ether with a sulphur, is to reduce the internal oxygen content and replace it with something which requires oxygen for efficient burning. Therefore, not only does sulphur reduce the internal oxygen content (oxygen balance, see Appendix B), it also increases the internal oxygen requirement. Also the increase in chain length increases the internal oxygen requirement, therefore, to be effective, increases in chain length and addition of sulphur, should be accompanied by addition of oxygen bearing functional groups, the best being the nitro group. Aliphatic nitro groups were indicated in the study in Chapter 1 as having a melting point increasing effect, also their thermal and chemical stability is somewhat less than would be expected of a compound to satisfy the aims of this project.

Whilst being easier and more productive to manufacture, and indicating that liquids would be obtainable, 3-alkylpicryl thioethers are unlikely to be the most effective compounds, considering the criteria governing this study.

4.3. REACTIONS WITH NITROGEN NUCLEOPHILES

The reactions of 3-alkylpicryl chlorides with secondary amines were very successful. As with the reactions with sulphur nucleophiles, the secondary amines were chosen because of their less basic, more nucleophilic character compared to alkoxides, thus reducing the possibility of proton abstraction from the substrate. Four dialkylamines were used in these reactions and the compounds produced are shown in Table 9. Such 3-substituted picramides have not before been reported in the literature.

Although N,N-di-n-propyl-3-methylpicramide appeared to be pure by TLC and spectroscopic methods, it exhibited

a rather broad melting range. Melting commenced at 80°C but did not appear to develop significantly within the sample until 85°C was reached, when it proceeded rapidly and was completed at 86.5°C.

The reaction of diallylamine with 3-t-butylpicryl chloride, to produce N,N-diallyl-3-t-butylpicramide, was carried out under a variety of conditions, but in all cases, the product was contaminated with significant amounts of starting material, from which it could not be readily separated.

The melting point criteria stated in Chapter 1 are not so obviously displayed in these compounds. For any one nucleophile successfully reacted with all three picryl chlorides, the expected order of product melting points is related to the 3-alkyl substituent, such that methyl$\simeq$ t-butyl>ethyl. For sulphur and oxygen nucleophiles, this pattern is observed in the products, but for the nitrogen nucleophiles outlined in Table 9, it can be seen that only two out of the four nucleophiles used give products which follow this pattern.

As with mercaptides, the secondary amines did not show any nitro group substitutions when reacted with 3-t-butylpicryl chloride. This reinforces the hypothesis that nitro group substitution only occurs with the more reactive, less selective nucleophiles.

Attempts to cyclopolymerise N,N-diallyl-3-methylpicramide using radical or cationic initiators were unsuccessful, probably due to the inhibiting effect of the nitroaromatic system. Cyclopolymerisation occurs readily with many N,N-diallyl compounds (equation 25)[70].

CHAPTER 5

SUMMARY AND CONCLUDING REMARKS

In considering the results of any scientific study, the major points of discussion are the fundamental value of what has been discovered, its potential for future use, and the novelty and applications of the research. The purpose of this chapter is to present the highlights of this study and to discuss the value, potential and novelty of the results. Also included are some thoughts for future experimentation in each of the particular areas previously discussed, either to gain further information, or as a way of improving the experimental techniques which have been used.

5.1 THE LITERATURE SEARCH

The literature search produced a vast amount of data which, where possible, was collated into schemes that could relate the melting point of compounds to their molecular features. Inspection of these schemes (Schemes 1-14) showed that there were four features which appeared to consistently affect the melting points of these polynitroaromatic compounds. These were:

(i) the nature of the functional groups in the molecule;

(ii) the length of any aliphatic side chains;

(iii) the degree of asymmetry of the molecule; particularly the pattern of benzene ring substitutions;

(iv) the number of nitro groups.

These features were used to propose some compound classes (Figure 3) which would be likely to show low melting characteristics : the targets of the synthetic programme. Throughout the many searches of the past literature, a detailed study of melting point to structure relationships

for organic compounds was not found. Also, this approach of carrying out a literature search, then identifying melting point/structure criteria which lead to target compounds, seems a novel approach to an applied synthetic programme. As can be seen in Appendix B, these criteria were quite successful in their predictive ability : six polynitroaromatic compounds (targetted compounds) were prepared which were liquids at room temperature.

Though this method proved successful in this instance, the structural criteria identified as influencing melting point may not be generally applicable as this study was limited to a small group of polynitroaromatic compounds. However, this work seems to have identified a very basic gap in organic chemistry. Though melting point predictions may only be approximate, one feels that it is an area in which further study is required, and from which benefits would accrue.

5.2 THE TNT ANION IN SYNTHESIS

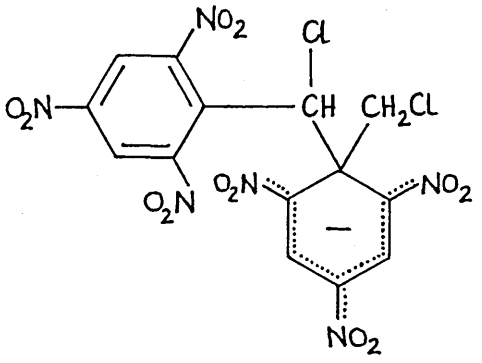
The use of the TNT anion as a nucleophile in synthetic chemistry proved to be much more difficult than anticipated. As described in chapter 2, the TNT anion was a very poor nucleophile, and reaction with normally good substrates for aliphatic nucleophilic substitution, failed to produce any of the desired compounds. The exception to this rule was p-nitrobenzyl bromide (PNBBr). Spectroscopic studies showed very fast σ-adduct formation in the PNBBr reaction, which was absent in other reactions. Also radical formation was seen to be minimal, whereas in other reactions radicals were observed to cause rapid decay of the nmr spectra, probably due to radical decomposition of the TNT anion. It appeared from the evidence that σ-adduct formation allowed ionic nucleophilic substitution to take place, but when σ-adduct formation was not favoured, the TNT anion's weak nucleophilic character was not enough to drive the reaction. It may be that σ-adduct formation partially

localises the negative charge to enable the substitution intermediate to form, thus the energy barrier of formation is lowered (equation 9). This work casts doubt upon the proposal by Shipp et.al. that the TNT anion is an effective nucleophile and that TNBB (XCIV) is formed by a simple ionic mechanism. However, the radical mechanism of schemes 22 and 23 do not seem appropriate since there is little evidence of radical species in the system. The mechanism proposed in equation 9 provides a more satisfactory explanation for the formation of TNBB than so far offered.

The mechanism of the PNBBr reaction may be clarified by further work at low temperatures, which should be enough to slow the reaction down without changing its course, thus allowing more detailed observation of the intermediates. The reaction of TNT with base is temperature sensitive and indeed TNT anion formation can be stopped altogether if the reaction temperature is too low[74]. If the potassium salt of the TNT anion[19] was to be used as a starting material instead of TNT, then these problems may be overcome. Alternatively, it may be advantageous to employ flow nmr techniques to observe the course of the reaction through its early stages[19]. This would be a more appropriate technique as it would eliminate the need for any alteration in reaction conditions.

The ionic-type mechanism of equation 9 may be the key also to the coupling reaction of TNT in aqueous alkaline sodium hypochlorite: a reaction which is industrially important in the preparation of HNS and HNBB[23,24]. This process relies on nucleophilic substitution of chlorine in 2,4,6-trinitrobenzyl chloride by the 2,4,6-trinitrobenzyl chloride anion. In experiments completed in this study, the TNBCl anion was shown also to be a very poor nucleophile with normally good substrates for aliphatic nucleophilic substitution. So it would appear that this reaction may also be a σ-adduct enhanced reaction; the intermediate σ-adduct being CXXXIX. It is clear that in reports of

the work previously carried out on the Shipp reaction, no reference has ever been made to such a mechanism.



CXXXIX

In conclusion, concerning the industrial aim of this study, no significant synthetic steps to liquid or low melting polynitroaromatic compounds were made by utilising the TNT anion, which is clearly not generally applicable as a nucleophile as suggested by Shipp and co-workers.

5.3 SUBSTRATES FOR NUCLEOPHILIC AROMATIC SUBSTITUTION

Scheme 19 in chapter 3 was the approach used for the preparation of 3-alkylpicryl halides directly from TNT. Though the suitability of this method was superceded by a superior preparation, starting from the parent phenol (scheme 20), the chemistry in this area proved to be very interesting.

The reduction of TNT to 2,4-diamino-6-nitrotoluene was quite successful, once the procedure had been optimised. However, reduction of TNT to 4-amino-2,6-dinitrotoluene was not quite so successful, i.e. yields were lower and the product was substantially contaminated with 4-hydroxylamino-2,6-dinitrotoluene, and purification proved very difficult.

The subsequent bromination of 2,4-diamino-6-nitrotoluene turned out to be an uncontrollable reaction. The required 3-bromo-2,4-diamino-6-nitrotoluene was never found in any reaction mixture, not even transiently. However, 2,4-diamino-3,5-dibromo-6-nitrotoluene was always produced.

Even when equimolar quantities were used, the resulting product contained 50% starting material and 50% of the dibromo derivative. In chapter 3, two possible explanations for this phenomenon are discussed (Equations 15 and 16). Firstly, the acid/base mechanism, which deactivates the starting material; and secondly the steric mechanism where the monobromo derivative is very much more reactive that the starting material. The second mechanism is fundamental to the molecule and therefore if this is the explanation, it would be difficult to influence the course of the reaction. However, the first mechanism implies that the physico-chemical parameters of the reaction are reaction controlling, and could be influenced by solution conditions. A number of attempts to alter the course of the reaction were unsuccessful.

The evidence suggests that both possibilities contribute to formation of product and that the monobrominated compound does become more susceptible to reaction than the starting material, which becomes incapable of further reaction.

This line of study was discontinued because of the success of the second method of preparation of 3-alkylpicryl halides (Scheme 20), however, the bromo derivatives of 2,4-diamino-6-nitrotoluene have never been reported in the literature and this is the first observation of this novel reaction.

Further study into this system would be necessary to increase understanding of the mechanism. It would be interesting to observe the action of chlorine on 2,4-diamino-6-nitrotoluene to see if the same type of reaction occurs. Also, partial deactivation of the amine groups may facilitate monobromination: probably most easily achieved via the Schotten-Baumann benzoylation reaction[54]. It would be very helpful to obtain X-ray crystal structures of both 2,4-diamino-6-nitrotoluene and 2,4-diamino-3,5-dibromo-6-nitrotoluene, which may give support for the second mechanism suggested, i.e. to indicate whether addition of a 5- position bromine twists the 6- position nitro group out of the plane of the ring.

Before attempting to optimise the bromination steps in this route, it would be prudent to attempt re-oxidation of the amino groups using the dibromo derivative, which has been produced. This would provide an assessment of the feasibility of the final step in the reaction, and the usefulness of sodium borate[75] as an amine oxidising agent in such highly substituted systems.

The method which proved more successful for the production of 3-alkylpicryl chlorides (Scheme 20) involved the complete nitration of various 3-alkylphenols and subsequent treatment with thionyl chloride/DMF to affect the chlorination. This produced the required compounds in very good yields (up to 75% over the two steps).

5.4 NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS

The preparation of category C compounds required some changes to the standard method of picryl ether production. When 3-methylpicryl chloride and 3-ethylpicryl chloride were treated with alkoxides in alcohols, little of the desired product was formed. This was because of the high basicity of the oxygen nucleophiles, which meant that proton abstraction from the side chain α-carbon atom became the dominant reaction. The resultant anions and σ-adducts were susceptible to radical decomposition, similar to the way in which the TNT anion decomposes. Three approaches to overcome this unwanted decay were investigated.

(i) Use of a nucleophile with less basic character and greater nucleophilic activity, to increase the probability of nucleophilic aromatic substitution. As can be seen in Chapter 4, this approach led to the synthesis of some interesting low melting picryl thio-ethers and N,N-dialkylpicramides. The melting points of these compounds are summarised in Appendix B.

(ii) 3-t-Butylpicryl chloride was chosen as a substrate because of its lack of abstractable protons on the side chain α-carbon atom. Reaction with alkoxides gave the desired picryl ethers in good yield. However, the use of 3-t-Butylpicryl chloride introduced a competing nitro group substitution reaction with oxygen nucleophiles. A detailed study of this interesting reaction can be found in Chapter 4. The introduction of the bulky t-butyl group must physically twist the nitro groups positioned either side of it, out of the plane of the benzene ring, facilitating the substitution of one of these moieties. Some evidence suggests that the nitro group in position 4 is substituted, though confirmation is required. Nitro group substitution products only account for one third of the total reaction product, the major product being the picryl ether. When 3-t-butylpicryl chloride is reacted with nucleophiles having a terminal hydroxy function, e.g. $^{-}OCH_2CH_2OH$ or $^{-}OCH_2CH_2CH_2OH$, nitro group substitution was not observed; nor was it observed in reactions with nitrogen and sulphur nucleophiles. This suggested that the hydroxy group gave the nucleophile some selectivity, possibly by an intramolecular stabilisation mechanism (equations 22 and 23, Chapter 4).

These nitro group substitutions are novel observations and have never been seen before in symmetrical trinitro systems outside hexa-substituted systems[64], and such a system is worthy of further study. It should be possible to produce dominant nitro group substitution by use of a less mobile halogen atom (e.g. 3-t-butylpicryl bromide) or completely eliminate it, by use of a more mobile halogen atom (e.g. 3-t-butylpicryl fluoride).

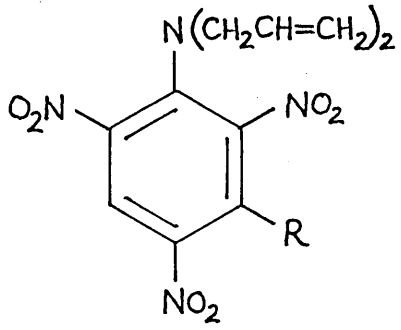
(iii) α-Proton abstraction was also reduced with oxygen nucleophiles, by enhancing their nucleophilic character. This was achieved by changing from a protic solvent to a dipolar aprotic solvent. Such solvents are known to leave anions relatively unhindered[27]. With a

solvent sphere, oxygen nucleophiles are more likely to show basic character as their nucleophilic character would be smothered. This obviously happens with alkoxides in alcohols. However, in THF, up to 60% yields were obtained with 3-ethylpicryl chloride as the substrate. But, 3-methylpicryl chloride still produced very complex reaction mixtures, although one ether was isolated. The melting points of the compounds prepared are shown in Appendix B and Chapter 4.

It was originally proposed that category D compounds would be synthesised by nucleophilic attack by cyanide ions on 3-alkylpicryl chlorides followed by hydrolysis and esterification. However, the literature suggested that complications could arise in this type of situation, whereby aromatic substitution by cyanide can remove nitro groups ortho to the site of substitution (the Von Richter reaction)[67]. Because of these possible complications, this approach was not followed.

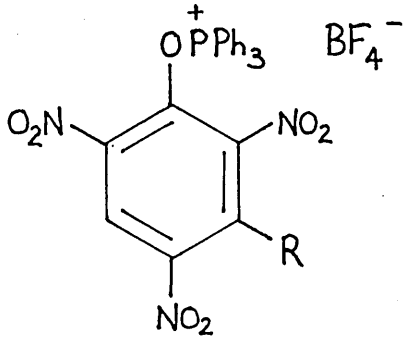
However, this part of the programme was the most successful and several nitro aromatic liquids or low melting solids were produced. Although, as synthesised, these compounds will be too low in oxygen balance to be satisfactory for the industrial aims of this study. It would be possible to increase the oxygen balance of these compounds by adding nitro groups to their side chains, although this would have two adverse effects; a) to increase the melting point of the compounds, and b) to decrease their air/water/thermal stability (see Appendix B).

Addition of aliphatic nitro groups to the side chains of compound CXL should be relatively facile[76], although the stability and melting point of the final product(s) would be of concern. A limited number of reactions of 3-alkylpicryl halides with nitroalkoxides were attempted, but no products were isolated.



CXL

The chemistry in this part of the programme has opened up many avenues for possible further study. An interesting development to this branch of chemistry would be a better preparation of picryl fluorides. If a suitable fluorinating agent could be found, then it would be possible to use a method similar to that used in this study to prepare picryl chlorides from their parent phenols. Also, literature has shown that chloride can be replaced by fluoride in an aromatic system[77,78], and fluoride Meisenheimer complexes have been observed[79]. Therefore, it may be possible to effect a replacement reaction at the end of the picryl chloride preparation to produce appropriate picryl fluorides. A further compound with potential as a substrate in nucleophilic aromatic substitution reaction is (3-alkyl-2,4,6-trinitrophenoxy)triphenylphosphonium tetrafluoroborate (CXLI). Compounds of this type have previously been used to prepare alkyl aryl ethers[80], but never under such extreme electron withdrawing conditions.



CXLI

5.5 CONCLUDING REMARKS

Finally, it must be noted that the likelihood of any of the specific polynitroaromatic liquids or low melting solids that have been produced, being used as plasticisers for explosives is remote, mainly because of their questionable thermal/light stability and low oxygen balance (see Appendix B). But, importantly, what this study has produced is a new approach to the synthesis of such polynitroaromatic compounds, which, with further work, is likely to yield some suitable compounds. It has also provided some fundamental contributions to a better understanding of TNT chemistry and of nucleophilic aromatic substitution reactions.

CHAPTER 6

EXPERIMENTAL

6.1 GENERAL

6.1.1 Explosives

The explosive materials necessary for this work, be they experimental products or substances supplied by P.E.R.M.E., were all kept in a yellow metal cupboard, which was bolted to the bench in the laboratory and locked at all times. This yellow cupboard was a licenced mode B explosives store, registered with South Yorkshire Police and Fire Services, in compliance with 1875 Explosives Act. The store was also the subject of regular inspections by these two services (Appendix C shows licence details).

P.E.R.M.E. provided up to 200 g of TNT under water at any one time and the net explosive content of the explosive store was never above this figure. The TNT was stored in plastic containers, each holding 50 g under water. These containers were kept in an H84 ammunition box, appropriately labelled with the contents, which in turn was kept inside the above mentioned cupboard. Any removal from, or addition to the TNT stock was noted in a dedicated log book.

Any residues from experimental work or recrystallisations were poured into a three gallon plastic bucket, lined with a polythene bin liner. With time, the more volatile organic solvents evaporated away leaving the explosive waste dispersed under water. Arrangements were made with P.E.R.M.E. for the waste to be collected when necessary and disposed of by burning.

The amount of TNT, or any other explosive substance, used in experiments never exceeded 0.5 g. Sufficient TNT was removed from the store, logged, filtered to remove any water and recrystallised from methanol. The pure TNT was then dried under vacuum. Mpt. 81-2°C (Lit. 82°C)[71].

All of the washings from the purifications were poured into the waste bucket. To keep friction and contact with metals to a minimum, plastic or bone spatulas were used in all experimental work involving explosives, and plastic sinters covered with filter paper were used in place of glass sinters for filtration. Neither starting materials nor products were heat dried: drying was achieved by vacuum only and naked flames were never used in the vicinity of experimental work.

Because of the carcinogenic nature of polynitroarmatic compounds, caution must be exercised in their handling. Heavy duty rubber gloves were worn at all times during experimental work involving these materials. An insight into the handling of explosive substances in a chemistry laboratory was provided by a two week period spent at P.E.R.M.E. in Waltham Abbey under the supervision of Dr. P. Golding.

6.1.2 Chromatography

Column chromatography and thin layer chromatography were used extensively throughout the work.

Purification column chromatography took place on a short column with a valved bellows to decrease elution times. The silica used was Kieselgel 60F 254 large mesh size, and the eluent either ethyl acetate/petroleum spirit (40º60°) or diethyl ether/petroleum spirit (40°-60°). These eluents for purification columns contained up to 50% (V/V) of the more polar solvent.

Separation columns were prepared in a similar way, but with TLC grade silica (Kieselgel 60F 254), i.e. a much finer grade as the stationary phase. The eluents for separation columns used in the same components as for purification, but contained less of the polar component, though exact proportions were determined for each individual column by thin layer chromatography. Because separation columns take a much longer time, the eluent was acidified

with one drop of glacial acetic acid per 500 cm^3 prior to the adsorption of the sample. The silica, being slightly basic in nature, tends to have a degrading effect on polynitroaromatic compounds, especially when long elution times are encountered. The acetic acid therefore, was added to counteract this.

For thin layer chromatography (TLC), ready prepared Kieselgel 60F 254 silica chromatoplates were used, with incorporated fluorescent indicator to facilitate product identification. The eluent used consisted of ethyl acetate and diethyl ether as the polar additive and petroleum spirit (40°-60°) as the nonpolar remainder. The proportion of polar constituent was less than 50%, such that product separation was achieved. TLC was used to evaluate reaction times; in preparation for separation and purification columns; and in assessment of column performance.

6.1.3. Reagents

The solvents used throughout this project were always dried prior to use and some were further purified by distillation. Molecular sieve type 4A was used to dry dimethylsulphoxide, dioxane, alcohols, pyridine and acetic acid. Diethyl ether and toluene were dried by storing over sodium wire. All other solvents used were distilled prior to use and stored over molecular sieve type 4A, with the exception of tetrahydrofuran, ethyl acetate and petroleum spirit (40°-60°) which were always used freshly distilled.

Hydrogen sulphide was generated from a Kipps apparatus, charged with ferrous sulphide and 5 M hydrochloric acid.

TNT and 2,4,6-trinitrobenzyl chloride (TNBCl) were obtained from P.E.R.M.E. whose supplier was Kodak. All other chemicals were obtained from Aldrich Chemical Company or BDH Chemicals Limited. The purity of the chemicals obtained were known and if deemed necessary, further purifications were carried out.

6.1.4. Instrumentation

Infrared spectroscopy was carried out on a Pye Unicam SP3-100 spectrophotometer, using the potassium bromide disc method for solids and sodium chloride plates for liquids.

Ultraviolet spectroscopy used a Pye Unicam SP800 spectrophotometer for the U.V. study (Chapter 2) and scanning spectra; and a Pye Unicam SP200 spectrophotometer for single wavelength observations.

NMR spectroscopy used the Bruker 80 MHz spectrometer at Sheffield City Polytechnic, though the nmr study of Chapter 2 was carried out on the Perkin Elmer 60 MHz instrument at Humberside College of Higher Education. Also the Faculty of Technology at Humberside College of Higher Education offered a Mass Spectrometry service which was gratefully used.

Samples for elemental microanalysis were sent to EMA Limited, Beaworthy, Devon.

Melting points were determined on a Beckmann melting points apparatus and are uncorrected.

6.2 TNT ANION IN SYNTHESIS

6.2.1 Phase Transfer Catalysis Experiments (General procedure)[27]

TNT (0.5 g, 2.2×10^{-3} mol) was dissolved in dry dichloromethane (10 cm^3) and to this was added an equimolar amount of the desired substrate. The aqueous layer added to this consisted of sodium hydroxide (0.092 g, 2.3×10^{-3} mol) and a catalytic amount (2-3 mole%) of tetra-n-butylammonium hydroxide in water (10 cm^3). Vigorous stirring was applied on addition and throughout the total reaction time. After the desired time, the reaction mixture was placed into a separating funnel and the lower organic layer drawn off. Analysis by thin layer chromatography

was generally enough to show the success or failure of the reaction. Successful reactions were evaporated to dryness and applied to a separation column.

The one reaction in this section which did show that some substitution had taken place was when the substrate was p-nitrobenzyl bromide, where a crude yield of 40% was obtained of 2,4,4',6 -tetranitrobibenzyl. This low yield is probably due to the unsuitability of the bromine in PNBBr as a phase transfer catalysis leaving group. Other substrates used were ethyl chloroacetate, 1-chlorobutane, allyl chloride and allyl bromide. These substrates gave only very complex mixtures, most likely TNT decomposition products.

6.2.2. The Preparation of 2,4,4',6-Tetranitrobibenzyl

Equivalent amounts of TNT (0.5 g 2.2 x 10^{-3}mol) and p-nitrobenzyl bromide (0.48 g, 2.2 x 10^{-3}mol) were dissolved in tetrahydrofuran (20 cm^3) and methanol (10 cm^3). The base, aqueous sodium hydroxide (0.1 g, 2.5 x 10^{-3}mol in 25 cm^3 water), was then added. The reaction was stirred for 30 minutes after the addition of base, during which time a precipitate formed. The precipitate was collected, washed thoroughly with methanol and recrystallised from ethanol. The yield was 0.57 g, 71% of yellow platelets. Mpt. 181-2°C (not reported by Shipp et. al.[3]). NMR and ir spectroscopy confirmed the purity of this compound. The nmr spectrum of this compound can be seen in Figure 14 (4). This spectrum clearly showed no residual TNT or PNBBr (c/f Figure 14 (1) and 14 (2)).

The main infrared peaks for TNBB are ((s) indicates the strong peaks and (w) weak peaks):

3100, 2940 (w), 2880 (w), 1608 (s), 1552 (s), 1526 (s), 1478, 1420, 1352 (s), 1115, 1085, 942, 930, 915, 880, 861, 840, 795, 740, 720 cm^{-1}.

6.2.3 Solvent/Base Survey. A Typical Procedure

TNT (0.5 g, 2.2 x 10^{-3}mol) and p-nitrobenzyl bromide (0.48 g, 2.2 x 10^{-3}mol) were dissolved in dimethylformamide (15 cm^3). Methanolic potassium hydroxide (0.13 g, 2.3 x 10^{-3}mol in 6 cm^3 methanol) was added and the reaction carried out under a nitrogen atmosphere, with stirring. After a reaction time of 1 hour, the mixture was quenched in dilute hydrochloric acid (300 cm^3 of 0.5 M) and allowed to stand for a further hour to enable precipitation to reach completion.

The precipitate was then filtered off and dried under vacuum over silica gel. The resultant solids were analysed by thin layer chromatography and infrared spectroscopy in an effort to discern the major constituent(s) of the product.

For the purposes of this survey, as many features were kept constant as practicably possibly, when solid bases were used a further 6 cm^3 of solvent were added. Other than that, the procedure stayed the same.

6.2.4. The U.V. Study

This study was carried out on a Pye Unicam SP800 ultraviolet spectrometer. The procedure was to start a reaction of the type shown in 6.2.3 (time= 0), then at two minute intervals (15 second intervals for the initial two minutes) a small aliquot of the reaction mixture was removed, and added to a glass cuvette containing the reaction solvent. A U.V. spectrum was then recorded against a reference of the same reaction solvent. The results obtained were then analysed by measuring the absorbences recorded at 506 nm and 441 nm and calculating the absorbance ratio A_{506}/A_{441}. This series of ratios was then drawn graphically against time, thus displaying an ultraviolet reaction profile.

6.2.5. The NMR Study

The spectrometer used for this study was the Perkin Elmer 60 MHz instrument of the Faculty of Technology, Humberside College of Higher Education. This study consisted of three parts: reaction of the TNT anion with p-nitrobenzyl bromide; reaction of the TNT anion with p-cyanobenzyl bromide; and observation of TNT anion decay.

The procedure used was to dissolve TNT (62.5 mg, 2.75 x 10^{-4}mol) and a substrate (PNBBr [59.4 mg, 2.75 x 10^{-4}mol]; PCNBBr [53.9 mg, 2.75 x 10^{-4}mol]; noting for TNT anion observation) in deuterated dimethylsulphoxide ($(CD_3)_2SO$: 0.5 cm^3) and to add a small quantity of tetramethylsilane as the internal nmr reference (though in this case the TMS was already incorporated into the d^6-DMSO). This mixture was placed in a clean, dry nmr tube, to which a solution of AR potassium hydroxide (15.4 mg, 2.75 x 10^{-4}mol) in deuterated methanol (CD_3OD : 0.125 cm^3) was added by syringe. The nmr tube was shaken and placed into the spectrometer. Spectra were then taken as often as possible for 20 minutes (approximately every 90 seconds) and at five minute intervals for the next 40 minutes. After the required period of time, the reaction mixture was analysed to see that a typical reaction had taken place.

6.3 SUBSTRATES FOR NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS

6.3.1 Reduction of TNT by sulphurated sodium borohydride.[52]

Sulphurated sodium borohydride was prepared by the addition of 3 equivalents of sulphur (0.22 g, 6.9 x 10^{-3} mol) to sodium borohydride (0.087 g, 2.3 x 10^{-3}mol), in THF (30 cm^3) with stirring and without cooling (equation 26). Once prepared in a THF suspension, the $NaBH_2S_3$ was used in situ.

$$NaBH_4 + 3S \xrightarrow[25°]{THF} NaBH_2S_3 + H_2$$

Equation 26 : The preparation of sulphurated sodium borohydride.

TNT (0.5 g, 2.2 x 10^{-3}mol) dissolved in THF (10 cm^3) was added to a suspension of $NaBH_2S_3$ (0.304 g, 2.3 x 10^{-3}mol) in THF (30 cm^3), and the mixture stirred for 5 hours at room temperature. After this time the THF was distilled off and the residue hydrolysed with dilute hydrochloric acid (0.5 M, 100 cm^3). The sulphur produced was filtered off and the resultant solution neutralised and extracted with ethyl acetate. The extracts were dried over anhydrous magnesium sulphate and the ethyl acetate evaporated under reduced pressure. The solid obtained contained many components, as shown by TLC, but mainly unchanged TNT.

6.3.2 The Reduction of TNT using Iron in Acetic Acid

TNT (0.5 g, 2.2 x 10^{-3}mol) was added to glacial acetic acid (10 cm^3) in a 50 cm^3 round bottomed flask. Iron filings (1 g, 0.018 mol) were then added slowly with vigorous stirring and the resultant mixture heated on a boiling water bath for one hour. After this time, dilute acetic acid (50 cm^3) was added, followed by filtration and extraction with ethyl acetate. The extracts were dried with anhydrous magnesium sulphate and the ethyl acetate removed under reduced pressure. Thin layer chromatography (with 50% ethyl acetate/petroleum spirit (40° - 60°) eluent) detected six products and considerable baseline material. The two major products were isolated by column chromatography, though the yields of both were very low. Infrared spectroscopy showed amine group NH stretching and nitro group NO stretching for both products, though clearly the yields were unsatisfactory.

Product 1 : yellow solid, yield 5 mg;

$\bar{\nu}_{as}$ (NH) = 3520 cm^{-1}, $\bar{\nu}_{s}$ (NH) = 3430 cm^{-1}

$\bar{\nu}_{as}$ (NO) = 1541 cm^{-1}, $\bar{\nu}_{s}$ (NO) = 1355 cm^{-1}

Product 2 : red solid, yield 7 mg;

$\bar{\nu}_{as}$ (NH) = 3460 cm^{-1}, $\bar{\nu}_{s}$ (NH) = 3390 cm^{-1}

$\bar{\nu}_{as}$ (NO) = 1520 cm^{-1}, $\bar{\nu}_{s}$ (NO) = 1355 cm^{-1}

6.3.3 Reduction of TNT using sodium polysulphide

Equation 27 shows the reaction of sodium polysulphide with nitro groups.[54] A solution of sodium polysulphide was prepared by adding sulphur (0.15 g, 4.7 x 10^{-3}mol) to an aqueous solution containing sodium sulphide nonahydrate (0.6 g, 2.5 x 10^{-3}mol in 20 cm^3 water) and warming until clear.

$$RNO_2 + Na_2S_2 + H_2O \longrightarrow RNH_2 + Na_2S_2O_3$$

Equation 27 : the reduction of nitro groups with sodium polysulphide.

TNT (0.5 g, 2.2 x 10^{-3}mol) was warmed in water (15 cm^3) until molten. The sodium polysulphide solution was then added over 15 - 30 minutes with vigorous stirring. The resultant dark brown mixture was boiled for 20 minutes and cooled. After cooling, water (50 cm^3) was added and the mixture extracted with ethyl acetate. Thin layer chromatography showed a large amount of baseline material and a very small amount of the yellow solid observed in 6.3.2. The yield being so poor, column separation was deemed to be unnecessary.

6.3.4 Reduction of TNT using Hydrogen Sulphide Gas

a) The preparation of 2,4-diamino-6-nitrotoluene (CX).

Method (i)[50]: Gaseous hydrogen sulphide was passed through a hot mixture of pyridine (25 cm^3) and piperidine (2 cm^3). After half an hour, TNT (0.5 g, 2.2 x 10^{-3}mol) in pyridine (10 cm^3) was added dropwise over a period of half an hour. Heating was continued for a further hour with hydrogen sulphide still being passed through the mixture. The solvent was then removed under reduced pressure and the resultant solid extracted with hydrochloric acid (5 M, 100 cm^3) and filtered to remove the sulphur. Neutralisation of the filtrate and further extraction with diethyl ether afforded an orange red solid, which was recrystallised from toluene/petroleum spirit (40° - 60°), giving red needle like crystals (Mpt. 132-133°C). Yield 0.23 g (62%).

Method (ii)[51]:(a) A mixture of ethanol (30 cm^3) and ammonia solution (0.88 sp.gr., 6 drops) was cooled to 0°C and saturated with hydrogen sulphide. TNT (0.5 g, 2.2 x 10^{-3}mol) in hot ethanol (30 cm^3) was slowly added with vigorous stirring. The mixture, which became dark red after the addition of the TNT, was refluxed for one hour with continuous hydrogen sulphide addition. Water (100 cm^3) was added and the resultant mixture boiled on a water bath to remove the alcohol. Sulphur was filtered off and the resultant aqueous solution was cooled and extracted with diethyl ether. The extracts were dried with anhydrous magnesium sulphate and the ether removed under reduced pressure. Recrystallisation was carried out as in Method (i). Yield. 0.25 g (68%).

Infrared spectrum:- 3450(s), 3370(s), 3270, 1645(s), 1627, 1580(w), 1530(s), 1503, 1465(w), 1390(w), 1355(s), 1340(s), 1255, 1195, 1170, 1041, 910, 860, 827, 780 cm^{-1}.

^{1}H-nmr spectrum:- δ= 2.06 ppm, 3H , singlet;
δ= 3.63 ppm, Broad singlet, 11.5 Hz half height width;
δ= 6.17 ppm, doublet, 1H, J = 2.7 Hz;
δ= 6.53 ppm, doublet, 1H, J = 2.7 Hz.

(b) The preparation of 4-amino-2,6-dinitrotoluene (CVIII)[47,49]. TNT (0.5 g, 2.2 x 10^{-3}mol) was dissolved in 1,4-dioxane (25 cm^3) and ammonia solution (0.88 sp.gr., 0.5cm^3) was added. Hydrogen sulphide was then passed through, the temperature being maintained below 40°C, until no further exothermic reaction was observed. Sulphur was removed by filtration and the solvents removed under reduced pressure. The solid obtained was recrystallised from water, yield 0.16 g (37%). This product, however always contained up to 50% of 4-hydroxylamino-2,6-dinitrotoluene (CXII) as is shown by ir, nmr and ms data. It was however very difficult to separate out this impurity, though repeated recrystallisation was able to separate enough of the amino derivative to enable characterisation (Mpt 168-171°C).

Infrared spectrum of hydroxylamine (CXII):- 3600-3300 (broad peak(s)), 3400, 3350, 3100(w), 2920(w), 2850(w), 1620, 1540(s), 1485, 1460(w), 1440(w), 1415(w), 1390, 1350(s), 1300, 1255(w), 1195(w), 1030, 1015, 990, 902(s), 850, 800(s), 765, 755, 740, 720 cm^{-1}.

Infrared spectrum of amine (CVIII):- 3540(s), 3430(s), 3300(w), 3130(w), 2950(w), 1645(s), 1540(s), 1505, 1440, 1400(w), 1370(s), 1355 (s), 1320, 1205(w), 1095(w), 1030(w), 905, 890, 810, 775(w), 745(w), 730 cm^{-1}.

^{1}H-nmr Spectrum of reaction product (mixture of CXII and CVIII):-

δ= 2.41 ppm, singlet, } Integration ratio $\frac{1.29}{1}$
δ= 2.49 ppm, singlet; }

δ= 4.13 ppm, singlet, Very broad 20 Hz half height width;

δ= 7.24 ppm, singlet;

δ= 7.60 ppm, singlet.

Note: This spectrum was very weak. The integrations were meaningless as the peak at δ=7.24 ppm coincided with the $CHCl_3$ peak and the peaks at δ=2.41 and 2.49 ppm were very close and surrounded by severe noise.

^{1}H-nmr spectrum of amine (CVIII):

= 2.41 ppm, singlet, 3H;

= 4.14 ppm, broad singlet, 2H, 23 Hz half height width;

= 7.26 ppm, singlet, (V. close to $CHCl_3$ peak);

Mass spectrum of the product mixture gave the following results:

Molecular ion (M) at 197 $\Longrightarrow$ CVII

M + 1 at 198 $\longrightarrow$ 8.33% M (Theoretical 8.64%)

M + 2 at 199 $\longrightarrow$ 0.95% M (Theoretical 1.08%)

Molecular ion (M) at 213 $\Longrightarrow$ CXII

M + 1 at 214 $\longrightarrow$ 10.7% M (Theoretical 8.64%)

M + 2 at 215 $\longrightarrow$ 1.78% M (Theoretical 1.29%)

6.3.5. Bromination of Reduced TNT Species

(i) A solution of bromine in chloroform was prepared to a known concentration. A solution of 2,4-diamino-6-nitrotoluene (CX) in chloroform was treated with the appropriate amount of the bromine solution, and the reaction mixture refluxed for half an hour. The insoluble products could be obtained by filtration of the reaction mixture, and the brominated product by removal of the chloroform under reduced pressure. Purification of the products could be obtained by column chromatography. In these reactions, there were three products obtained: 2,4-diamino-3,5-dibromo-6-nitrotoluene (CXIII), recovered starting material (CX), and a hydrogen bromide salt of the starting material, though the latter tended to be very easily decomposed to CX and hydrogen bromide.

The spectral data for 2,4 - diamino - 3,5-dibromo - 6-nitrotoluene is as follows:

Infrared spectrum: 3520, 3440(s), 2950(w), 1625(s), 1540(s), 1475, 1390, 1350(w), 1315, 1195(w), 1150(w), 1080(w), 1025(w), 950, 795, 725(w) cm^{-1}.

(Note the absence of aromatic CH stretching between 3000 - 3100 cm^{-1}).

^1H-nmr spectrum:

δ = 2.03 ppm, singlet, 3H;

δ = 4.32 ppm, broad singlet, (19Hz half height width)

δ = 4.65 ppm, broad singlet, (13.6Hz half height width)

} 4H;

(Note the absence of aromatic Protons (6-9 ppm)).

Mass spectrum.

The characteristic fragment patterns for a dibromo compound are evident in this spectrum.

Molecular ion, M, at 323

M + 2 at 325 = 219% M (Theoretical 196%)

M + 4 at 327 = 109% M (Theoretical 96%)

Fragment ion at 277 = M - NO_2

279 = 185% of peak at 277 (Theoretical 196%)

281 = 95% of peak at 277 (Theoretical 96%)

Fragment ion at 197 = M - NO_2-Br

199 = 95% of peak at 197 (Theoretical 97.7%)

Infrared spectrum of the hydrogen bromide salt of the starting material: 3090, 2850(s) (very broad; 2500 - 3300 cm^{-1}), 2570(s), 1610(w), 1540(s), 1490(s), 1450(w), 1420(w), 1385(w), 1355(s), 1305(w), 1245(w), 1195(w), 1110, 1045(w), 905, 880, 805, 730(w), 720 cm^{-1}.

(ii) Pyridinium bromide perbromide (0.24 g of 80% purity, 6 x 10^{-4}mol) was added to a solution of CX (0.1 g, 5.9 x 10^{-4}mol) in pyridine (10 cm^3). The reaction mixture was stirred at room temperature for 5 hours. Reaction

progress was monitored by TLC every half hour. The reaction mixture was quenched in water (100 cm^3) and extracted with diethyl ether. The extracts were dried with anhydrous magnesium sulphate and the ether removed under reduced pressure. The resulting solid was passed down a short column and this gave 0.75 g (38%) of CXIII and 0.045 g (45%) of CX.

(iii) The use of N-bromosuccinimide was achieved in a similar way to pyridinium bromide perbromide except dimethylformide was the reaction solvent and the reaction time was three days. In this time very little reaction had taken place.

The reaction of 2,4-diamino-6-nitrotoluene (CX) in water required the use of methanol, to bring the reagents into solution. A known molarity solution of bromine in methanol was added to water (20 cm^3). This was then added to a solution of CX dissolved in the minimum amount of methanol. Reaction was instantaneous and the 2,4-diamino-3,5-dibromo-6-nitrotoluene could be filtered off and thoroughly washed with water.

6.4 THE NITRATION AND CHLORINATION OF PHENOLS.

6.4.1 The Nitration of m-Cresol[54]

m-Cresol (10.8 g, 0.1 mol) was placed in a dry, one litre round bottomed flask, and concentrated sulphuric acid (98%, 23 g, 12.5 cm^3) was added with shaking. This mixture was heated on a boiling water bath for half hour, then cooled in an ice/water bath until very viscous. Concentrated nitric acid (70%, 38 cm^3) was added with gentle shaking, then placed on a cork stand in a closed fume cupboard. Approximately one minute after the addition of the nitric acid, a very vigorous reaction took place in which copious red fumes were evolved. When this reaction had subsided, the vessel was heated on a boiling water bath for two hours with occasional shaking. After this

time, cold water (100 cm^3) was added and the vessel chilled in ice/water. The solid formed was filtered off and recrystallised from aqueous ethanol. Yield of 3-methylpicric acid 19.9 g (78%), mpt. 107-8°C (lit. 106°C)[60].

This method was also used to prepare 3-ethylpicric acid (yield 65%, mpt 84-6°C) and 3-t-butylpicric acid (yield 73%, mpt 174-6°C).

The spectral data for these three compounds is summarised below.

(i) 3-Methylpicric acid:

Infrared spectrum: 3450(s,broad), 3250(w), 3150(w), 2950(w), 1815(w), 1635(s), 1600(s), 1550(s), 1465, 1430, 1380, 1350(s), 1320, 1290, 1270, 1220, 1165(s), 1060, 920, 910, 890, 765, 740, 720, 680, 660 cm^{-1}.

^{1}H-nmr spectrum: δ= 2.60 ppm, singlet, 3H;
δ= 8.98 ppm, singlet, 1H;
δ= 11.11 ppm, broad singlet (16 Hz at half height width), 1H.

(ii) 3-Ethylpicric acid:

Infrared spectrum: 3500(s,broad), 3250, 3150, 3050(w), 2950(w), 1845(w), 1635, 1600(s), 1560(s), 1540(s), 1450(s), 1380, 1350(s), 1280, 1205, 1165(s), 1095, 1060, 1035, 955, 925, 890, 830(w), 800, 780, 750, 735, 700, 675 cm^1.

^{1}H-nmr spectrum: δ= 1.30 ppm, triplet, 3H, J=7.4 Hz;
δ= 2.96 ppm, quartet, 2H, J=7.4 Hz;
δ= 8.97 ppm, singlet, 1H.
(Broad hydroxy hydrogen not observed).

(iii) 3-t-Butylpicric acid:

Infrared spectrum: 3200(broad), 3080, 3030, 2980(w), 2960(w), 2910(w), 1810(w), 1615, 1580, 1540(s), 1525, 1465, 1435, 1420, 1400(w), 1365(s), 1325(s), 1250, 1230, 1205, 1180, 1160, 1140(s), 990, 915(s), 885(w), 820(w), 810(w), 795(w), 775, 760(w), 745, 720, 675 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.50 ppm, singlet, 9H;
δ= 8.27 ppm, singlet, 1H.
(Broad hydroxy hydrogen not observed).

6.4.2 The Preparation of 3-Vinylphenol

A reaction scheme for this is shown in equation 17 (Chapter 3).

6.4.2.1 The reduction of m-Hydroxyacetophenone.

m-Hydroxyacetophenone (13.6 g, 0.1 mol) was dissolved in methanol (100 cm^3) and a solution of sodium borohydride (7.65 g, 0.2 mol in 2 M sodium hydroxide (5 cm^3) and water (45 cm^3) was added dropwise with vigorous stirring. The reaction was kept at or below room temperature throughout the addition with an ice bath. When all of the borohydride had been added, the reaction mixture was left stirring for half hour, after which the methanol was removed under reduced pressure. The resultant mixture was diluted with water (100 cm^3) and carefully acidified to destroy the excess borohydride. The mixture was then extracted with diethyl ether. The extracts were dried over anhydrous magnesium sulphate and the ether removed under reduced pressure.

Crude yield 11.77 g (85% of 1-(m-hydroxyphenyl)ethanol).

Infrared spectrum of m-Hydroxyacetophenone: 3170 broad, 2950(w), 2810(w), 2695(w), 2600(w), 1955(w), 1870(w), 1790(w), 1725(w), 1660(s), 1575(s), 1485, 1425, 1360(s), 1300(s), 1260(s), 1215(s), 1165(w), 1080(w), 1015, 995, 980(w), 960, 910, 865, 795(s), 720, 705, 680(s), 605 cm^{-1}.

Infrared spectrum of crude 1-(m-hydroxyphenyl)ethanol: 3380(s), 3050 broad, 2970, 2920(w), 2850(w), 2800(w), 2720(w), 2610(w), 2560(w), 1970(w), 1840(w), 1725(w), 1660(w), 1610, 1585(s), 1480, 1450, 1405, 1365(s), 1325(w), 1290(w), 1275(s), 1165, 1155, 1086, 1070(s), 1020(w), 1005, 995, 960(w), 935, 865(s), 780(s), 730, 695(s), 620 cm^{-1}.

6.4.2.2 The dehydration of 1-(m-hydroxyphenyl)ethanol.

The crude 1-(m-hydroxyphenyl)ethanol (11.77 g) from 6.4.2.1 was intimately mixed with twice its weight of activated alumina (activated by 3 days at 120°C and 1-5 mm Hg). The mixture was ground with a pestle and mortar before being placed in a vacuum reflux apparatus and refluxed for 6 hours. The mixture was then vacuumed distilled and 3-vinylphenol was collected at 84-86°C at 0.04 mm Hg (Lit 105°C, 5 mm Hg)[72]. The product was a colourless, fairly viscous liquid with the characteristic phenolic smell. Yield, 4.12 g (40% from crude 1-(m-hydroxyphenyl)ethanol, 34% from m-Hydroxyacetophenone).

One problem encountered was that the distilled product was contaminated with unreacted 1-(m-hydroxyphenyl)ethanol which seemed to sublime from the alumina mixture. This problem was minimised by collecting only very narrow fractions of distillate.

Infrared spectrum: 3400(s,broad), 3140(w), 3050(w), 1950(w), 1850(w), 1620, 1600, 1590(s), 1510, 1465(s), 1430, 1340, 1305(w), 1280(s), 1260, 1245, 1160(s), 1080, 1030(w), 1000, 930(s), 875, 795, 730(w), 720, 700(w), 670 cm^{-1}.

^{1}H-nmr spectrum: This shows a typical ABX spectrum[73] (See fig 18 for ABX labelling), but the two peaks for the X proton at higher chemical shift are not visible because of the benzene ring multiplet. There is also an impurity of 1(m - hydroxyphenyl) ethanol visible and from

comparison of the integration it was calculated as 14.5 mol% impurity.

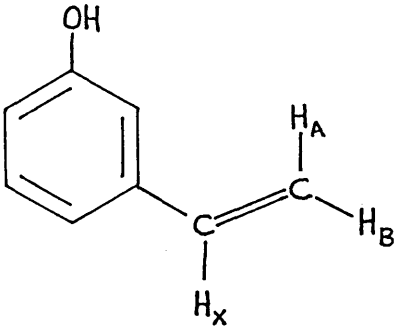


Figure 18 : The ABX labelling in 3-vinylphenol

δ= 1.39 ppm, doublet, J=5.6 Hz;
δ= 4.75 ppm, quartet, J=5.6 Hz;
} 1-(m-hydroxyphenyl)ethanol

δ= 5.15 ppm, doublet, H_B, J_{BX} = 10.4 Hz, J_{AB} = 0 Hz;

δ= 5.61 ppm, doublet, H_A, J_{AX} = 17.6 Hz, J_{AB} = 0 Hz;

δ= 6.47 ppm, doublet, H_X, J_{BX} = 10.4 Hz. (visible as a doublet but should be a quartet centred on = 6.58 ppm split primarily by J_{AX} and secondly by J_{BX}).

δ= 6.87 ppm, benzene ring multiplet consisting of 7 visible peaks.

6.4.3 The nitration of 3-vinylphenol

Three nitration procedures were attempted on this compound.

6.4.3.1 Nitration using mixed acids.

The nitration procedure adopted in section 6.4.1 was repeated using 3-vinylphenol instead of m-cresol. On addition of the concentrated sulphuric acid to the phenol, a brown tar was obtained and on completion of the nitration, only a very highly degraded mixture was obtained.

6.4.3.2 Nitration using acetyl nitrate[58].

This procedure had previously been used for the nitration of alkenes. It was used in this instance in a five fold excess over 3-vinylphenol.

Nitric acid (96%, 3.5 g, 0.053 mol) was added dropwise to a solution of acetic anhydride (4.25 g, 0.042 mol) in glacial acetic acid (10 cm^3) with strong cooling in a dry ice/acetone bath, to keep the reaction temperature at 25°C. 3-vinylphenol (1 g, 8.3 x 10^{-3}mol) in glacial acetic acid (5 cm^3) was added in one portion, once again with strong cooling in an attempt to keep the reaction temperature below 10°C. The resultant mixture was quenched in iced water (400 cm^3) and extracted with ethyl acetate. Addition of the 3-vinylphenol caused a very violent reaction to occur, even with this strong cooling the temperature was uncontrollable. The reaction products seen by thin layer chromatography were many, which implied that phenol decomposition had taken place.

6.4.3.3 Nitration using 96% Nitric acid[56]

3-Vinylphenol (1 g, 8.3 x 10^{-3}mol) was placed into a round bottomed flask and cooled in a dry ice/acetone bath. Nitric acid (96%, 3.5 g, 0.053 mol) was added dropwise. Once again a very violent reaction occurred and components inside the flask began to burn. The reaction was immediately quenched with water and the reaction aborted.

6.4.4 The Chlorination of 3-Methylpicric acid[56]

3-Methylpicric acid (4 g, 0.016 mol) was dissolved in dry N,N-dimethylformamide (20 cm^3). Thionyl chloride (redistilled, 2 g, 1.2 cm^3, 0.0168 mol) was added dropwise with vigorous stirring. The mixture was left to stir for 30 minutes with gentle heating and subsequently poured into an ice/water mixture. 3-methylpicryl chloride was

filtered off with suction and recrystallised from ethanol. Yield 4.1 g, (95%), mpt.148-9°C.

This method was also used to prepare 3-ethylpicryl chloride (Yield 79%: mpt 88-89.5°C) and 3-t-butylpicryl chloride (Yield 92%: mpt 91-3°C).

Chlorination of 3-methylpicric acid was also attempted by using phosphoryl chloride with N,N-diethylaniline; phosphoryl chloride with N,N-dimethylformamide; and phosphoryl chloride reacted with pyridinium 3-methylpicrate, though these methods were not as successful as that described above.

(i) 3-Methylpicryl chloride:

Infrared spectrum: 3085, 2910(w), 2870(w), 1795(w), 1600, 1580, 1540(s), 1435, 1380, 1335(s), 1280(w), 1210, 1175, 1035(w), 1020(w), 970, 910, 900, 850(w), 770, 760(w), 745, 730(s), 720, 665, 640 cm^{-1}.

^{1}H-nmr: δ= 2.60 ppm, singlet, 3H;
δ= 8.65 ppm, singlet, 1H.

(ii) 3-Ethylpicryl chloride:

Infrared spectrum: 3080, 3020(w), 2970(w), 2930(w), 2870(w), 1860(w), 1625(w), 1580(s), 1560(s), 1530(s), 1470, 1440(w), 1385, 1340(s), 1255(w), 1245(w), 1200(w), 1180(w), 1165(w), 1060, 1040(w), 975, 945, 935, 915, 835, 820, 795, 775, 760, 745, 720(s), 680, 630 cm^{-1}

^{1}H-nmr: δ= 1.42 ppm, triplet, 3H, J = 7.4 Hz;
δ= 2.97 ppm, quartet, 2H, J = 7.4 Hz;
δ= 8.65 ppm, singlet, 1H.

(iii) 3-t-Butylpicryl chloride.

Infrared spectrum: 3080, 3020(w), 2990(w), 2980(w), 2920(w), 2860(w), 1810(w), 1570, 1540(s), 1525, 1465, 1430(w), 1400(w), 1365(s), 1340(s), 1325(s), 1230, 1195(w), 1105, 1050, 1015, 1005(w), 845(w), 820, 800(w), 770, 740, 720(s), 670, 625 cm^{-1}

^1H-nmr: δ= 1.51 ppm, singlet, 9H;
δ= 8.04 ppm, singlet, 1H.

6.5 NUCLEOPHILIC AROMATIC SUBSTITUTION REACTIONS

6.5.1 Reactions with Oxygen nucleophiles

6.5.1.1 Alkoxides in Alcohols (General Method)

3-Alkylpicryl chloride (0.5 g) was dissolved in the required alcohol (15 cm^3). Sodium (1.5 mol equivalents w.r.t. 3-alkylpicryl chloride) was added to another portion of the required alcohol (10 cm^3) and allowed to react completely. The sodium alkoxide in alcohol solution was then rapidly added, with stirring, to the 3-alkylpicryl chloride solution. The reaction mixture was then left at room temperature for one hour, after which it was quenched in acidic iced water (250 cm^3 containing 20 cm^3 2 M hydrochloric acid). The resultant mixture was extracted with diethyl ether, the extracts dried over anhydrous magnesium sulphate and the ether evaporated under reduced pressure. The resultant material was analysed by thin layer chromatography and if any dominant products appeared, then they were purified/separated by column chromatography.

6.5.1.2 Alkoxides in Tetrahydrofuran (General Method).

THF (20 cm^3) was distilled into the reaction vessel and the required alcohol added (1 cm^3). Sodium (2 mole equivalents w.r.t. 3-alkylpicryl chloride) was added to this solution and allowed to react completely. 3-alkylpicryl chloride (0.5 g) was dissolved in freshly distilled THF (10 cm^3) and quickly added to the alkoxide/THF solution

with stirring. The mixture was gently refluxed for half an hour (the condenser being fitted with a drying tube), after which it was quenched in acidic iced water (250 cm^3, containing 20 cm^3 2 M hydrochloric acid). Precipitation was allowed half an hour for completion, after which the products were extracted with diethyl ether. The extracts were dried over anhydrous magnesium sulphate and the ether evaporated under reduced pressure. The resultant material was analysed by thin layer chromatography and any major products were isolated by a purification/separation column.

Compounds produced by these methods are listed below with relevant yields and spectral data (melting points are recorded in Chapter 4).

2' - (3-Methyl-2,4,6-trinitrophenoxy)ethanol (Yield 39%).

Infrared spectrum: 3580, 3110, 3070(w), 3000(w), 2940, 2920, 2870(w), 1810(w), 1610, 1585, 1525(s), 1465, 1435(w), 1405(w), 1340(s), 1305, 1275(w), 1215(w), 1175(w), 1080, 1060, 1030, 985, 925(w), 905, 885, 830, 820(w), 790, 765(w), 740, 735, 690, 670 cm^{-1}.

^{1}H-nmr spectrum: δ= 2.21 ppm, singlet, 1H, half height width = 5.8 Hz;
δ= 2.59 ppm, singlet, 3H;
δ= 3.91 ppm, triplet, 2H, J = 3.5 Hz;
δ= 4.33 ppm, triplet, 2H, J = 3.5 Hz;
δ= 8.73 ppm, singlet, 1H.

^{13}C nmr spectrum: δ= 15.1 ppm,
δ= 61.6 ppm,
δ= 79.7 ppm,
δ= 123.8 ppm,
δ= 133.1 ppm, weak peak.
other aryl peaks were lost in spectral noise.

2'-(3-Ethyl-2,4,6-trinitrophenoxy)ethanol (Yield 44%).

Infrared spectrum: 3590(w), 3100(w), 2980(w), 2955(w), 2930(w), 2875(w), 1840(w), 1735(w), 1610, 1590(s), 1530(s), 1470, 1450, 1415, 1375(w), 1345(s), 1315(w), 1280, 1245(w), 1215, 1175(w), 1085, 1070(w), 1045(s), 1005, 960, 900(w), 880, 835, 825, 790, 740, 700, 670 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.33 ppm, triplet, 3H, J = 7.6 Hz;
δ= 2.36 ppm, singlet, 1H, half height width = 3.25 Hz;
δ= 2.91 ppm, quartet, 2H, J = 7.6 Hz;
δ= 3.91 ppm, triplet, 2H, J = 4.4 Hz;
δ= 4.31 ppm, triplet, 2H, J = 4.4 Hz;
δ= 8.72 ppm, singlet, 1H.

^{13}C-nmr spectrum: δ= 14.5 ppm,
δ= 22.6 ppm,
δ= 61.6 ppm,
δ= 79.7 ppm,
δ= 124.2 ppm,
δ= 138.3 ppm, weak peak,
δ= 140.1 ppm, very weak peak,
δ= 143.6 ppm, weak peak,
δ= 148.5 ppm, weak peak.
other aryl peaks were lost in spectral noise

2'-(3-t-Butyl-2,4,6-trinitrophenoxy)ethanol (Yield 62%).

Infrared spectrum: 3620(w), 3120, 3060(w), 3000(w), 2960, 2550(w), 1830(w), 1610, 1590, 1565(s), 1540(s), 1490, 1455, 1400, 1380, 1365(s), 1345(s), 1280(w), 1255, 1240, 1200(w), 1175(w), 1160, 1080, 1045, 1015(s), 970(w), 930, 915, 890, 850, 830(w), 815, 780, 760(w), 750, 725, 690cm^{-1}

^{1}H-nmr spectrum: δ= 1.48 ppm, singlet, 9H;
δ= 2.43 ppm, singlet, 1H, half height width = 5.8 Hz;

δ= 3.90 ppm, triplet, 2H, J = 4.4 Hz;
δ= 4.26 ppm, triplet, 2H, J = 4.4 Hz;
δ= 8.12 ppm, singlet, 1H.

^{13}C-nmr spectrum: δ= 29.8 ppm,
δ= 38.2 ppm, weak peak,
δ= 61.4 ppm,
δ= 79.9 ppm,
δ= 122.8 ppm,
δ= 140.1 ppm, weak peak,
δ= 140.7 ppm, weak peak,
δ= 146.7 ppm, weak peak,
δ= 147.1 ppm, weak peak,
δ= 148.2 ppm, weak peak,

3'-(3-ethyl-2,4,6-trinitrophenoxy)propan-1'-ol (Yield 87%).

Infrared spectrum: 3560(w), 3080(w), 2950, 2910, 2865, 1685(w), 1595, 1575, 1525(s), 1460, 1445, 1405(w), 1365, 1335(s), 1265, 1235(w), 1180(w), 1165(w), 1085(w), 1030(s), 950, 905, 850(w), 815(w), 770(w), 725, 680(w) cm^{-1}.

^{1}H-nmr spectrum: δ= 1.33 ppm, triplet, 3H, J = 7.7 Hz;
δ= 2.04 ppm, quintet, 2H, J = 6.1 Hz;
δ= 2.38 ppm, singlet, 1H, half height width = 10.2 Hz;
δ= 2.91 ppm, quartet, 2H, J = 7.7 Hz;
δ= 3.78 ppm, triplet, 2H, J = 6.1 Hz;
δ= 4.34 ppm, triplet, 2H, J = 6.1 Hz;
δ= 8.72 ppm, singlet, 1H.

3'-(3-t-Butyl-2,4,6-trinitrophenoxy)propan-1-ol. (Yield 60%).

Infrared spectrum: 3530, 3070, 3025(w), 2970, 2920, 2890, 1820(w), 1595, 1575, 1535(s), 1465, 1440, 1415(w), 1365(w), 1350(s), 1335(s), 1265(w), 1250, 1225, 1150, 1080(w), 1065(w), 1045(s), 1040(s), 1000(s), 950, 925, 910, 870, 815(w), 790(w), 765, 755, 740, 720, 690, 660(w) cm^{-1}.

^{1}H-nmr spectrum: δ= 1.50 ppm, singlet, 9H;
δ= 2.00 ppm, quintet, 2H, J = 6.1 Hz;
δ= 2.24 ppm, singlet, 1H, half height width = 4.06 Hz;
δ= 3.77 ppm, triplet, 2H, J = 6.1 Hz;
δ= 4.26 ppm, triplet, 2H, J = 6.1 Hz;
δ= 8.09 ppm, singlet, 1H.

^{13}C-nmr spectrum: δ= 29.7 ppm,
δ= 32.5 ppm,
δ= 38.1 ppm, weak peak,
δ= 58.6 ppm,
δ= 76.2 ppm,
δ= 122.7 ppm,
δ= 140.4 ppm, weak peak,
δ= 140.8 ppm, weak peak,
δ= 146.9 ppm, weak peak,
δ= 147.6 ppm, weak peak,
δ= 148.8 ppm, weak peak.

2'-Methoxy-1'-(3-ethyl-2,4.6-trinitrophenoxy)ethane (Yield 43%).

Infrared spectrum: 3100, 2980, 2940, 2880, 2820, 1610, 1585(s), 1540(s), 1470, 1410, 1345(s), 1305(w), 1275, 1240(w), 1200, 1175(w), 1130, 1100, 1065, 1045(s), 1025(w), 980 (w), 955 (w), 920, 850, 835, 825, 810 (w), 785, 735 cm^{1}.

^{1}H-nmr spectrum: δ= 1.33 ppm, triplet, 3H, J = 7.4 Hz;
δ= 2.89 ppm, quartet, 2H, J = 7.4 Hz;
δ= 3.29 ppm, singlet, 3H;
δ= 3.65 ppm, triplet, 2H, J = 4.4 Hz;
δ= 4.31 ppm, triplet, 2H, J = 4.4 Hz;
δ= 8.69 ppm, singlet, 1H.

^{13}C-nmr spectrum: δ= 14.5 ppm,
δ= 22.6 ppm,
δ= 58.9 ppm,

δ = 71.1 ppm,
δ = 77.1 ppm,
δ = 124.0 ppm,
δ = 138.1 ppm, weak peak;
δ = 140.6 ppm, weak peak,
δ = 143.5 ppm, weak peak,
δ = 148.7 ppm, weak peak,
other aryl peaks were lost in spectral noise

2'-Methoxy-1'-(3-t-butyl-2,4,6-trinitrophenoxy)ethane (CXXVIII) (Yields and nmr spectra are displayed in Chapter 4).

Infrared spectrum: 3100, 3040, 2930, 2900(w), 2860(w), 2810(w), 1790(w), 1605, 1580, 1545(s), 1530, 1470, 1445, 1390, 1370, 1355(s), 1340, 1290, 1250, 1235, 1195, 1160, 1130, 1095, 1035(s), 1000, 930, 900, 850, 825, 805, 780, 760, 745, 725, 695, 675 cm^{-1}.

Nitro substituted competitor (Compound B, CXXIX or CXXX)

Infrared spectrum: 3080, 3020(w), 2980, 2950, 2920, 2890, 2840(w), 2810, 2720(w), 1825(w), 1600(s), 1540(s), 1495(w), 1460(s), 1400(w), 1380, 1370, 1350(s), 1340, 1290(s), 1255, 1240, 1210(w), 1200, 1170(w), 1130(s), 1105, 1080, 1065, 990, 955, 915(s), 860, 835, 810, 795, 755(w), 720, 690, 675 cm^{-1}.

Disubstituted competitor (Compound C, CXXXI or CXXXII).

Infrared spectrum: 3100(w), 3060(w), 3015(w), 2980, 2960(w), 2920, 2890(w), 2820(w), 1720(w), 1600, 1525(s), 1490, 1470, 1445, 1360(s), 1350(s), 1305, 1280(w), 1265, 1245, 1220, 1190, 1160, 1125(s), 1090, 1060(s), 1035(s), 985, 975, 955, 905, 880, 870, 845, 835, 810, 790(w), 770, 725, 705(s), 655 cm^{-1}.

2'-Ethoxy-1'-(3-ethyl-2,4,6-trinitrophenoxy)ethane
(Yield 52%)

Infrared spectrum: 3080(w), 2960, 2930, 2875, 1600, 1580(s), 1545(s), 1530, 1460, 1410, 1370(w), 1345(s), 1300(w), 1280, 1260, 1240(w), 1190(w), 1175(w), 1130, 1105, 1095, 1065(w), 1045(s), 1005(w), 955(w), 940(w), 925, 905(w), 845, 835, 825, 790, 740 cm^{-1}.

^1H-nmr spectrum: δ= 1.11 ppm, triplet, 3H, J = 7.0 Hz;
δ= 1.33 ppm, triplet, 3H, J = 7.3 Hz;
δ= 2.90 ppm, quartet, 2H, J = 7.3 Hz;
δ= 3.46 ppm, quartet, 2H, J = 7.0 Hz;
δ= 3.68 ppm, triplet, 2H, J = 4.4 Hz;
δ= 4.36 ppm, triplet, 2H, J = 4.4 Hz;
δ= 8.68 ppm, singlet, 1H.

2'-Ethoxy-1'-(3-t-butyl-2,4,6-trinitrophenoxy)ethane.

This was not produced pure, because it was inseparable from its nitro substituted competitor.

^1H-nmr - selected peaks:
t-butyl protons: δ= 1.42 ppm, singlet, nitro group substituted product;
δ= 1.51 ppm, singlet, desired ether.
Aromatic protons: δ= 7.13 ppm, singlet, nitro group substituted product;
δ= 8.07 ppm, singlet, desired ether.

Integrations imply 27% nitro group substitution, 73% chlorine substitution.

2'-(2"-Hydroxyethoxy)-1'-(3-ethyl-2,4,6-trinitrophenoxy)ethane. (Yield 49%).

Infrared spectrum: 3560, 3095, 2940, 2920, 2880, 1605, 1585(s), 1535(s), 1465, 1410, 1345(s), 1310(w), 1275, 1245(w), 1190(w), 1175(w), 1130, 1095(w), 1065, 1045(s), 1005, 955, 920, 885(w), 840, 825, 785, 690, 670 cm^{-1}.

^{1}H-nmr spectrum: δ = 1.38 ppm, triplet, 3H, J = 7.4 Hz;
δ = 2.02 ppm, singlet, 1H, half height width = 3.3 Hz;
δ = 2.94 ppm, quartet, 2H, J = 7.4 Hz;
δ = 3.56 ppm, singlet, 4H;
δ = 3.77 ppm, triplet, 2H, J = 4.3 Hz;
δ = 4.43 ppm, triplet, 2H, J = 4.3 Hz;
δ = 8.70 ppm, singlet, 1H.

2'-(2"-Hydroxyethoxy)-1'-(3-t-butyl-2,4,6-trinitrophenoxy)ethane (Yield 53%).

Infrared spectrum: 3590, 3080, 3030, 2920, 2870, 1810(w), 1605, 1580(s), 1550(s), 1525, 1465, 1440, 1360(s), 1340(s), 1300, 1250, 1235(w), 1170(w), 1160, 1130, 1075, 1060, 1030(s), 990, 935, 910, 885, 845, 830(w), 820(w), 800, 775(w), 755(w), 740, 720, 685 cm^{-1}.

'H-nmr spectrum: δ = 1.51 ppm, singlet, 9H;
δ = 2.52 ppm, singlet, 1H, half height width = 10.5 Hz;
δ = 3.62 ppm, singlet, 4H;
δ = 3.77 ppm, triplet, 2H, J = 4.7 Hz;
δ = 4.30 ppm, triplet, 2H, J = 4.7 Hz;
δ = 8.10 ppm, singlet, 1H.

(3-Ethyl-2,4,6-trinitrophenoxy)ethane (Yield 72%)

Infrared spectrum: 3080, 3040, 2970, 2920, 2880(w), 2860(w), 1690(w), 1600, 1580(s), 1525(s), 1465, 1445, 1405, 1335(s), 1260, 1235(w), 1180(w), 1165(w), 1140(w), 1090, 1055, 1035(s), 995, 945, 910, 830, 815(w), 775, 725, 680, 660(w) cm ^{1}.

^{1}H-nmr spectrum: δ = 1.33 ppm, triplet, 3H, J = 7.7 Hz;
δ = 1.43 ppm, triplet, 3H, J = 7.0 Hz;
δ = 2.90 ppm, quartet, 2H, J = 7.7 Hz;
δ = 4.26 ppm, quartet, 2H, J = 7.0 Hz;
δ = 8.68 ppm, singlet, 1H.

(3-t-Butyl-2,4,6-trinitrophenoxy)ethane (Yield 50%).

Infrared spectrum: 3050, 3010, 2970, 2910, 2710(w), 2510(w), 2310(w), 1800(w), 1590, 1565(s), 1540(s), 1460, 1435, 1355(s), 1345, 1325(s), 1270, 1240, 1225, 1185(w), 1145, 1100, 1010(s), 980, 915, 900, 840, 810, 795, 765, 745(w), 735, 710, 680, 665 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.41 ppm, triplet, 3H, J = 7.7 Hz;
δ= 1.49 ppm, singlet, 9H,
δ= 4.19 ppm, quartet, 2H, J = 7.7 Hz;
δ= 8.07 ppm, singlet, 1H.

Product of nitro group substitution. (Yield 17%).

^{1}H-nmr spectrum: δ= 1.42 ppm, singlet, 9H;
δ= 1.50 ppm, triplet, 3H, J = 7.0 Hz;
δ= 4.15 ppm, quartet, 2H, J = 7.0 Hz;
δ = 6.92 ppm, singlet, 1H.

3'-(3-Ethyl-2,4,6-trinitrophenoxy)propene (Yield 52%).

Infrared Spectrum: 3080, 2960, 2920, 2860(w), 1600, 1575(s), 1525(s), 1425, 1400, 1335(s), 1265, 1230(w), 1180(w), 1165(w), 1085, 1055, 1030(s), 985, 950, 930, 900, 845, 815, 800(w), 775, 730, 695 cm^{-1}.

^{1}H-nmr spectrum (consider Figure 19):

δ = 1.33 ppm, triplet, 3H, J = 7.7 Hz;
δ = 2.90 ppm, quartet, 2H, J = 7.7 Hz;
δ = 4.70 ppm, doublet, 2H, J_{CD} = 5.9 Hz (H^D);
δ = 5.29 ppm, doublet, 1H, J_{BC} = 3.2 Hz (H^B);
δ = 5.45 ppm, doublet, 1H, J_{AC} = 4.1 Hz (H^A);
δ = 5.97 ppm, four triplets, 1H, split by J_{CD}, J_{BC} and J_{AC} (H^C);
δ = 8.71 ppm, singlet, 1H.

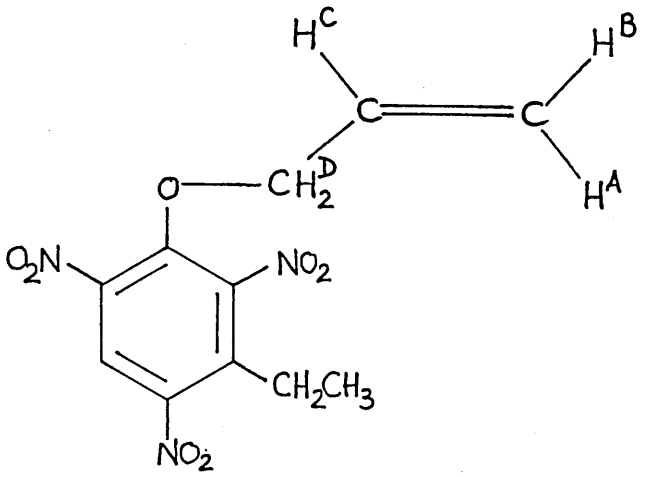


Figure 19 : Labelling of the allyl protons on 3'-(3-ethyl-2,4,6-trinitrophenoxy)propene for nmr purposes.

3'-(3-t-Butyl-2,4,6-trinitrophenoxy)propene:

It was not possible to isolate this compound from its nitro group substituted competitor.

^{1}H-nmr spectrum (selected peaks):

δ = 1.43 ppm, singlet, nitro group substituted compound;

δ = 1.49 ppm, singlet, desired ether;

δ = 6.96 ppm, singlet, nitro group substituted compound;

δ = 8.08 ppm, singlet, desired ether.

Integrations show that this mixture contained 68% desired ether, 32% nitro substituted ether.

6.5.2. Reactions With Nitrogen Nucleophiles (General procedure).

3-Alkylpicryl chloride (0.5 g) was dissolved in dry chloroform (20 cm^3) and three equivalents of the required dialkylamine added. The mixture was refluxed until thin layer chromatography showed that all of the 3-alkylpicryl

chloride had reacted. The chloroform was then distilled off and the crude product recrystallised from aqueous ethanol.

The melting points for the compounds produced by this method are recorded in Chapter 4. Yield and spectral data for each compound is listed below.

N,N-Diethyl-3-methylpicramide (Yield 62%).

Infrared spectrum: 3080(w), 3060, 2980, 2930, 2920(w), 2870, 1590(s), 1565(s), 1525(s), 1480, 1465, 1450(w), 1435, 1410, 1380, 1350(s), 1330(s), 1315, 1285, 1275(w), 1205, 1180, 1150(w), 1105, 1060, 1030, 940(w), 910, 900(w), 800, 780, 755, 740, 720, 680, 640 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.13 ppm, triplet, 6H, J = 7.4 Hz;
δ= 2.52 ppm, singlet, 3H;
δ= 3.14 ppm, quartet, 4H, J = 7.4 Hz;
δ= 8.50 ppm, singlet, 1H.

N,N-Diethyl-3-ethylpicramide (Yield 73%).

Infrared spectrum: 3080(w), 3050, 2980, 2940, 2900(w), 2870, 1580(s), 1565(s), 1530(s), 1520, 1475, 1465, 1415(w), 1385(w), 1370, 1340, 1320(s), 1285, 1275, 1194, 1180, 1170, 1145(w), 1135(w), 1125(w), 1110, 1090(w), 1070, 1055, 1040, 945(w), 930, 910, 900(w), 790, 780, 765(w), 740, 720, 700, 640 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.12 ppm, triplet, 6H, J = 7.1 Hz;
δ= 1.33 ppm, triplet, 3H, J = 7.6 Hz;
δ= 2.83 ppm, quartet, 2H, J = 7.6 Hz;
δ= 3.14 ppm, quartet, 4H, J = 7.1 Hz;
δ= 8.49 ppm, singlet, 1H.

N,N-Diethyl-3-t-butylpicramide (Yield 63%).

Infrared spectrum: 3060, 3010, 2970, 2920, 2860, 2840, 1805(w), 1585, 1540(s), 1465, 1450, 1440, 1375(s), 1365(s), 1355(s), 1345(s), 1300, 1250, 1230, 1195(w), 1170, 1155, 1125, 1115, 1080(w), 1065, 1030, 975, 915, 905, 815(w), 790(w), 760, 735, 715, 650 cm^{-1}.

^{1}H-nmr spectrum: δ = 1.02 ppm, triplet, 6H, J = 7.5 Hz;
δ = 1.47 ppm, singlet, 9H,
δ = 3.03 ppm, quartet, 4H, J = 7.5 Hz;
δ = 7.79 ppm, singlet, 1H.

N,N-Di-n-propyl-3-methylpicramide (Yield 43%).

Infrared spectrum: 3080, 2960, 2930, 1840(w), 1595(s), 1570(s), 1525(s), 1515(s), 1505, 1475, 1460, 1430, 1405, 1375, 1355, 1335, 1320(s), 1285, 1250, 1200, 1170, 1110, 1090, 1065. 1025, 945(w), 920, 905, 865, 835, 770, 755, 740, 725, 680, 650 cm^{-1}.

^{1}H-nmr spectrum: δ = 0.86 ppm, triplet, 6H, J = 7.4 Hz;
δ = 1.75 ppm, sextet, 4H, J = 7.4 Hz;
δ = 2.51 ppm, singlet, 3H;
δ = 3.03 ppm, triplet, 4H, J = 7.4 Hz;
δ = 8.50 ppm, singlet, 1H.

N,N-Di-n-propyl-3-ethylpicramide. (Yield 49%).

Infrared spectrum: 3080, 3050, 2960, 2930, 2870, 1855(w), 1590(s), 1565(s), 1525(s), 1510(s), 1475, 1465, 1455, 1430(w), 1410(w), 1390(w), 1365, 1345, 1325(s), 1290, 1260, 1245, 1195, 1170, 1110, 1090(w), 1065, 1045, 945(w), 930, 905, 865(w), 835, 810, 780, 760(w), 740, 725, 700, 665(w), 655 cm^{-1}.

^{1}H-nmr spectrum: δ = 0.86 ppm, triplet, 6H, J = 7.0 Hz;
δ = 1.33 ppm, triplet, 7H, J = 7.3 Hz;

δ = 1.56 ppm, sextet, 7H, J = 7.0 Hz;
δ = 2.84 ppm, quartet, J = 7.3 Hz;
δ = 3.01 ppm, triplet, J = 7.0 Hz; } 6H
δ = 8.51 ppm, singlet, 1H.

N,N-Di-n-propyl-3-t-butylpicramide. (Yield 59%).

Infrared spectrum: 3060, 3010, 2960(s), 2920, 2860, 1805(w), 1585, 1560, 1530(s), 1460, 1450, 1410(w), 1365(s), 1350(s), 1325, 1290(w), 1230, 1195(w), 1160, 1135, 1090, 1035, 1005, 940, 920, 905, 890, 835, 815(w), 800(w), 785, 735, 715, 665 cm^{-1}.

^{1}H-nmr spectrum: δ = 0.83 ppm, triplet, 6H, J = 7.0 Hz;
δ = 1.45 ppm, sextet, J = 7.0 Hz;
δ = 1.47 ppm, singlet, } 13H;
δ = 2.91 ppm, triplet, 4H, J = 7.0 Hz;
δ = 7.78 ppm, singlet, 1H.

N,N-Di-n-butyl-3-methylpicramide (Yield 78%)

Infrared spectrum: 3090, 2950(s), 2920, 2860, 1590(s), 1555(s), 1525(s), 1505, 1475, 1455, 1425, 1410, 1385, 1350(s), 1325(s), 1295, 1260, 1230, 1200(w), 1170, 1115(w), 1105(w), 1070, 1050(w), 1030, 1000, 960(w), 940(w), 915, 875, 850(w), 820(w), 805(w), 780(w), 745, 735, 720, 680 cm^{-1}.

^{1}H-nmr spectrum: δ = 0.89 ppm, triplet, J = 7.1 Hz
δ = 1.40 ppm, unresolvable multiplet } 14H;
δ = 2.50 ppm, singlet, 3H;
δ = 3.05 ppm, triplet, 4H, J = 7.1 Hz;
δ = 8.52 ppm, singlet, 1H.

N,N-Di-n-butyl-3-ethylpicramide (Yield 46%).

Infrared spectrum: 3080, 3060, 2950(s), 2920, 2860, 1595(s), 1565(s), 1525(s), 1515(s), 1475, 1460, 1450,

1415(w), 1390(w), 1370, 1350, 1325(s), 1290, 1265(w), 1225, 1190(w), 1165, 1120(w), 1100(w), 1065, 1050, 1010(w), 945(w), 915, 895(w), 840(w), 805, 780, 765(w), 740, 730, 720, 700, 660 cm^{-1}.

^{1}H-nmr spectrum: δ= 0.89 ppm, triplet, J = 7.6 Hz
δ= 1.33 ppm, triplet, J = 7.0 Hz
δ= 1.39 ppm, unresolvable multiplet } 17H;
δ= 2.82 ppm, quartet, J = 7.0 Hz
δ= 3.05 ppm, triplet, J = 7.6 Hz } 6H;
δ= 8.05 ppm, singlet, 1H.

N,N-Di-n-butyl-3-t-butylpicramide (Yield 73%)

Infrared spectrum: 3060, 3020, 2950(s), 2920, 2860, 1590, 1560(s), 1540(s), 1525(s), 1460, 1450, 1440, 1365(s), 1350(s), 1335, 1300(w), 1290(w), 1275(w), 1250(w), 1230, 1210, 1195(w), 1155, 1125, 1090, 1035, 1020, 1000(w), 970(w), 950(w), 940(w), 915, 905, 845(w), 815(w), 780, 740, 710, 655, 620(w) cm^{1}.

^{1}H-nmr spectrum: δ= 0.88 ppm, triplet, 6H, J = 7.0 Hz;
δ= 1.31 ppm, multiplet,
δ= 1.47 ppm, singlet, } 17H;
δ= 2.93 ppm, triplet, 4H, J = 7.0 Hz;
δ= 7.78 ppm, singlet, 1H.

N,N-Diallyl-3-methylpicramide (Yield 67%).

Infrared spectrum: 3080, 2910(w), 2850(w), 1740(w), 1635(w), 1595(s), 1570(s), 1520(s), 1480, 1445(w), 1410, 1380, 1340(s), 1325(s), 1290(w), 1255, 1245(w), 1225(w), 1200(w), 1160(w), 1150(w), 1115, 1080, 1030, 980, 930(s), 915, 840, 820(w), 785(w), 760, 750, 735, 695(w), 675, 655 cm^{-1}.

^{1}H-nmr spectrum (coupling constant notation, see Figure 19) : δ= 2.53 ppm, singlet, 3H;

δ= 3.67 ppm, doublet, 4H, J_{CD} = 6.3 Hz;

δ= 5.07 ppm, doublet, J_{BC} = 5.8 Hz; } 4H

δ= 5.25 ppm, doublet, J_{AC} = 2.6 Hz; }

δ= 5.71 ppm, Four triplets - split by J_{AC}, J_{BC}, and J_{CD}, 2H;

δ= 8.49 ppm, singlet, 1H.

N,N-diallyl-3-ethylpicramide (Yield 58%).

Infrared spectrum: 3080, 3040(w), 2980, 2940(w), 2900, 2855, 1870(w), 1840(w), 1635(w), 1595(s), 1575(s), 1525(s), 1475, 1445, 1410, 1375, 1340(s), 1275, 1245, 1225, 1200(w), 1170(w), 1150, 1120, 1100, 1070, 1055, 1000(w), 990, 955, 935(s), 920, 900, 850, 810, 785(w), 775, 740(w), 730, 710, 685, 655, 605(w) cm^{-1}.

^{1}H-nmr spectrum: (Coupling constant notation, see Figure 19). δ= 1.32 ppm, triplet, 3H, J = 7.5 Hz;

δ= 2.83 ppm, quartet, 2H, J = 7.5 Hz;

δ= 3.68 ppm, doublet, 4H, J_{CD} = 6.4 Hz;

δ= 5.07 ppm, doublet, J_{BC} = 5.4 Hz; } 4H

δ= 5.25 ppm, doublet, J_{AC} = 2.7 Hz; }

δ= 5.74 ppm, Four triplets split by J_{AC}, J_{BC}, and J_{CD}, 2H;

δ= 8.49 ppm, singlet, 1H.

N,N-diallyl-3-t-butylpicramide

- Reaction not perfected, as starting material very evident in the product. ^{1}H-nmr showed the products to be 57% starting material, 43% desired picramide.

6.5.3 Reactions with Sulphur Nucleophiles

3-Alkylpicryl chloride (0.5 g) was dissolved in dry dichloromethane (20 cm^3). One equivalent of the required

thiol was added with one equivalent of 1,4-diazabicyclooctane with stirring. The mixture was left at room temperature until the initial red colour was replaced by a clear yellow or half hour (which ever came first). The solution was then washed with water (10 cm^3), 2 M hydrochloric acid (10 cm^3), water (10 cm^3) and saturated sodium hydrogen carbonate, then dried over anhydrous magnesium sulphate. The dichloromethane was then vacuum distilled and the crude product recrystallised from dichloromethane/petroleum spirit, (40°-60°).

The melting point data for the compounds produced by this method are recorded in Chapter 4. Yield and spectral data are listed below.

2'-(3-Methyl-2,4,6-trinitrothiophenoxy)ethanol. (Yield 72%).

Infrared spectrum: 3530, 3080, 2960, 2940, 2920, 1580, 1575, 1525(s), 1460(w), 1430(w), 1380(s), 1330(s), 1275, 1210(w), 1175(w), 1140(w), 1055, 1040(w), 1020, 995, 960, 920(w), 905, 895, 840, 815(w), 770, 755(w), 745(w), 730, 720, 660, 635 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.92 ppm, singlet, 1H, half height width = 12.0 Hz;
δ= 2.55 ppm, singlet, 3H;
δ= 3.17 ppm, triplet, 2H, J = 5.7 Hz;
δ= 3.83 ppm, singlet, 2H, half height width = 13.5 Hz;
δ= 8.44 ppm, singlet, 1H.

2'-(3-Ethyl-2,4,6-trinitrothiophenoxy)ethanol (Yield 78%)

Infrared spectrum: 3510, 3095, 2980, 2910(w), 2880, 1575, 1540(s), 1525(s), 1470, 1450, 1420(s), 1390, 1370, 1345(s), 1310(w), 1285, 1240(w), 1200(w), 1175(w), 1075, 1060, 1025, 980(w), 945, 915, 900, 830, 820, 800, 770, 740(w), 730, 720, 690 cm^{-1}.

^{1}H-nmr spectrum: δ= 1.32 ppm, triplet, 3H, J = 7.6 Hz;
δ= 1.96 ppm, singlet, 1H, half height width = 8.6 Hz;
δ= 2.86 ppm, quartet, 2H, J = 7.6 Hz;
δ= 3.16 ppm, triplet, 2H, J = 5.7 Hz;
δ= 3.83 ppm, triplet, 2H, J = 5.7 Hz;
δ= 8.41 ppm, singlet, 1H.

2'-(3-t-Butyl-2,4,6-trinitrothiophenoxy) ethanol (Yield 65%)

Infrared Spectrum: 3070, 3010(w), 2970, 2930, 2910, 2860, 1540(s), 1530(s), 1465, 1450(w), 1420(w), 1400(w), 1365(s), 1320(s), 1280, 1225, 1190(w), 1165(w), 1095(w), 1060(s), 1015(w), 1005, 945, 940(w), 915, 890, 845(w), 815, 795(w), 760, 750(w), 720, 645 cm^{-1}

^{1}H-nmr spectrum:
δ = 1.35 ppm, singlet, 9H;
δ = 1.84 ppm, singlet, 1H, half height width = 8.4 Hz;
δ = 3.14 ppm, triplet, 2H, J = 5.8 Hz;
δ = 7.79 ppm, singlet, 1H.

(3-Methyl-2,4,6-trinitrothiophenoxy)ethane (Yield 64%)

Infrared Spectrum: 3100, 3010(w), 2990(w), 2970, 2920, 2860(w), 1800(w), 1595, 1575, 1540(s), 1525(s), 1445, 1375(s), 1350(s), 1330(s), 1275(w), 1260, 1230, 1215, 1180, 1145(w), 1055, 1035, 965, 910, 900, 840, 820, 770, 755(w), 745, 725(s), 660, 640 cm^{-1}.

^{1}H-nmr Spectrum:
δ = 1.27 ppm, triplet, 3H, J = 7.7 Hz;
δ= 2.54 ppm, singlet, 3H;
δ= 3.01 ppm, quartet, 2H, J = 7.7 Hz;
δ= 8.40 ppm, singlet, 1H.

(3-Ethyl-2,4,6-trinitrothiophenoxy)ethane (Yield 51%)

Infrared Spectrum: 3090, 2990, 2930, 1565, 1540(s), 1530(s), 1495(w), 1465, 1450, 1425, 1385, 1370, 1340(s), 1310(w), 1280(w), 1265, 1235, 1205(w), 1105(w), 1080(w), 1060, 1040(w), 970, 950, 920, 900, 840, 825, 805, 780, 770, 745, 735, 725, 700 cm^{-1}.

^{1}H-nmr Spectrum:

δ = 1.28 ppm, triplet, J = 7.7 Hz;
δ = 1.33 ppm, triplet, J = 7.7 Hz; } 6H

δ = 2.86 ppm, quartet, J = 7.7 Hz;
δ = 3.01 ppm, quartet, J = 7.7 Hz; } 4H

δ = 8.36 ppm, singlet, 1H.

(3-t-Butyl-2,4,6-trinitrothiophenoxy)ethane (Yield 85%)

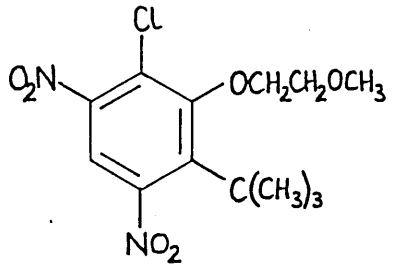
Infrared Spectrum: 3070, 2980, 2930, 2870, 1550(s), 1540(s), 1530(s), 1500, 1470, 1445, 1400(w), 1365(s), 1345(s), 1320(s), 1270(w), 1255, 1230, 1200(w), 1170(w), 1140(w), 1105, 1060, 1000(w), 975, 955, 920, 900, 870(w), 850(w), 825, 805, 790, 770, 755 cm^{-1}.

^{1}H-nmr Spectrum:

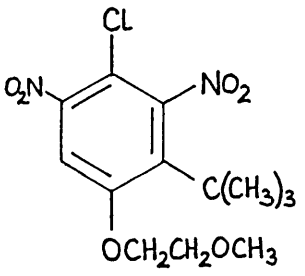
δ = 1.26 ppm, triplet, 3H, J = 7.7 Hz;
δ = 1.50 ppm, singlet, 9H;
δ = 2.98 ppm, quartet, 2H, J = 7.7 Hz;
δ = 7.76 ppm, singlet, 1H.

APPENDIX A

X-RAY CRYSTAL DATA FOR COMPOUND B



CXXVIII



CXXIX

Compound B was postulated to be either CXXVIII or CXXIX. Colourless crystals were selected for photographic examination and the following crystal data obtained:

UNIT CELL: a = 8.164(5) Å, b = 22.973(16) Å,
c = 8.338(6) Å. $\alpha = \beta = \gamma = 90^{o}$.

SPACE GROUP: Systematic absences do not distinguish between the two space groups $P_{na}2_1$ and P_{nma}. However, density measurements (ρ = 1.41 g cm^{-3} by flotation techniques) do indicate that there are four molecules in the unit cell.

For $P_{na}2_1$ - This implies no special symmetry for the molecule.

For P_{nma} - This requires the molecule to either have a centre of symmetry or a mirror plane. Since neither of these symmetry elements is present in the molecule (unless it is statistically disordered), X-ray analysis has been conducted in the space group $P_{na}2_1$.

Data Collection

A crystal, of approximate dimensions 0.20 mm X 0.25 mm X 0.30 mm, was mounted on a Stöe Stadi 2 two-circle defractometer with the a-axis coincident with the w-axis of the instrument. 666 Unique reflections were collected

using the background - w scan background technique and with monochromatic H_o - K_r radiation.

X-Ray Analysis

Direct methods techniques have been employed in the non-centrosymmetric space group $P_{na}2_1$ but, to date, the analysis has not been successfully concluded. It may be that the structure is highly disordered, in which case analysis in the centrosymmetric space group may be appropriate. Work is currently in progress in this direction.

APPENDIX B

OXYGEN BALANCE

An explosive mixture generally contains two ingredients, an oxidiser and a fuel. This substance can then burn without using atmospheric oxygen. An explosive detonation is a shock propogated burning with a very fast reaction velocity (up to 9000 ms^{-1}) producing gaseous products. Organic explosives, such as TNT and nitroglycerine, contain oxidiser and fuel within their own molecule. An indication of the degree to which the oxidiser and fuel are matched in these molecules/mixtures, is the oxygen balance. Oxygen balance is a measure of the oxygen excess (or deficiency) after the burning process has taken place. This gram oxygen excess is then expressed as a percentage of the molecular weight of the original molecule/fuel.

EXAMPLE: Nitroglycerine (NG) $C_3H_5N_3O_9$ (m.wt.227.1)

$$C_3H_5N_3O_9 \longrightarrow 3CO_2 + 2\tfrac{1}{2}H_2O + 1\tfrac{1}{2}N_2 + \tfrac{1}{4}O_2$$

Oxygen Excess = $\frac{1}{4}O_2$ = 8 g oxygen per mole of NG.

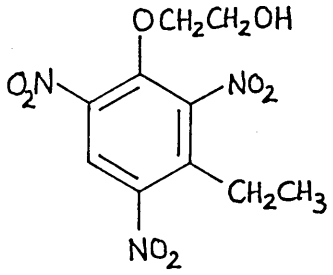
$$\text{Oxygen Balance} = \frac{8}{227.1} \times 100 = \underline{3.52\%}.$$

Generally, for $C_aH_bN_cO_dS_e$;

$$\text{Oxygen Balance} = \left(d - 2a - 2e - \frac{b}{2}\right) \times \frac{1600}{\text{m.wt.}} \%$$

Oxygen balance only gives an indication as to what extent a compound or mixture can support its own combustion to the exclusion of atmospheric oxygen. It gives no indication of sensitivity, explosive power or detonation velocity. It can therefore only be used as a guide to likely explosive compounds. Any compound with an oxygen balance of greater than -100%, could have enough internal oxygen to support its own combustion, for example, TNT = -74%; Picric acid = -45.4%; 3-Methylpicric acid (trinitro-m-cresol) = -62.5%.

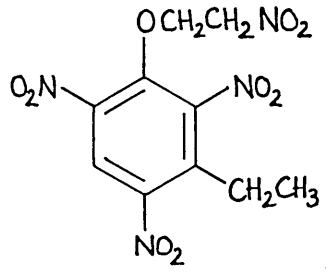
Table A shows the oxygen balances of the compounds produced in this study. It can be seen that their oxygen balances range from -80.8% to -177.6%. None of the liquids produced give oxygen balances of greater than -100%. The nearest to the requirement is 2'-(3-ethyl-2,4,6-trinitrophenoxy)ethanol (CXLII), which



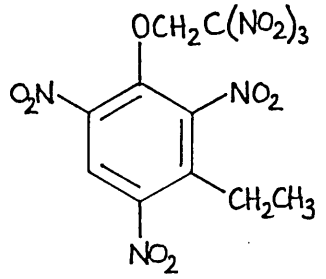
CXLII
M.PT. = 35.5–38°C
OXYGEN BALANCE = -93%

has a melting point below 40°C and an oxygen balance of greater than -100%.

Compounds such as CXLIII and CXLIV would have superior oxygen balances, and they should be synthesisable by methods found within this thesis. However, it is likely that their melting points will be too high, and their stability is likely to be lower than desired.

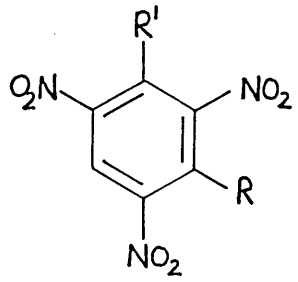


OXYGEN BALANCE = -77.5%
CXLIII



OXYGEN BALANCE = -41.9%
CXLIV

TABLE A: Oxygen Balances of the compounds produced in this study.



R	R'	M.Pt. /°C	Ox.Bal./%
Me	$-SCH_2CH_2OH$	87-88	-92.3
Et	$-SCH_2CH_2OH$	51-53	-102.1
t-Bu	$-SCH_2CH_2OH$	95-96.5	-122.8
Me	$-SCH_2CH_3$	90.5-94.5	-103.1
Et	$-SCH_2CH_3$	52-53.5	-112.7
t-Bu	$-SCH_2CH_3$	90-93	-133.6
Me	$-N(CH_2CH_3)_2$	80.5-81.5	-123.4
Et	$-N(CH_2CH_3)_2$	101-102	-133.2
t-Bu	$-N(CH_2CH_3)_2$	137-139	-150.4
Me	$-N(CH_2CH_2CH_3)_2$	80-86	-142.2
Et	$-N(CH_2CH_2CH_3)_2$	93-95	-150.4
t-Bu	$-N(CH_2CH_2CH_3)_2$	125-127	-165.0
Me	$-N(CH_2CH_2CH_2CH_3)_2$	90-92	-158.0
Et	$-N(CH_2CH_2CH_2CH_3)_2$	38-39	-165.0
t-Bu	$-N(CH_2CH_2CH_2CH_3)_2$	69-70	-177.6
Me	$-N(CH_2CH=CH_2)_2$	63.5-64.5	-134.1
Et	$-N(CH_2CH=CH_2)_2$	48-49.5	-142.7
Me	$-OCH_2CH_2OH$	70-72	-80.8
Et	$-OCH_2CH_2OH$	35.5-38	-93.0
t-Bu	$-OCH_2CH_2OH$	79-83	-114.2
Et	$-OCH_2CH_2CH_2OH$	LIQUID	-104.1
t-Bu	$-OCH_2CH_2CH_2OH$	68-71	-123.5
Et	$-OCH_2CH_2OCH_3$	LIQUID	-104.1
t-Bu	$-OCH_2CH_2OCH_3$	63-64	-123.5
Et	$-OCH_2CH_2OCH_2CH_3$	LIQUID	-114.2
Et	$-OCH_2CH_2OCH_2CH_2OH$	LIQUID	-104.3
t-Bu	$-OCH_2CH_2OCH_2CH_2OH$	83-86	-132.1
Et	$-OCH_2CH_3$	LIQUID	-103.8
Et	$-OCH_2CH=CH_2$	LIQUID	-110.4

APPENDIX C

EXPLOSIVES LICENCING.

Synthetic and mechanistic studies in polynitroaromatic chemistry were carried out at Sheffield City Polytechnic between 1977 and 1985, in collaboration with the Ministry of Defence (PERME, now RARDE), Waltham Abbey.

Before work in this field commenced, an agreement was reached with the Health and Safety Executive and PERME, concerning the practices to be adopted for the storage and use of TNT and other polynitroaromatic compounds (see H.S.E. Letter, page C2). A licence was obtained annually from South Yorkshire Police (pages C3 and C4) and the store registered with South Yorkshire Fire Service (page C5). This store was annually inspected by both of these Authorities.

Safety Executive

London W2 4TF

Telephone 01-229 3456
ext

HM INSPECTORATE OF EXPLOSIVES

Dr G C Corfield
Chemistry Department
Sheffield City Polytechnic
Pond Street
Sheffield S1 1WV

Your reference

Our reference

Date ~~October~~ November 1977

Dear Dr Corfield

RESEARCH PROJECT INVOLVING THE USE OF TNT

Following our recent phone discussion and my discussion with Mr L Cole, Establishment Safety Officer, PERME Waltham Abbey, the following points were agreed.

1 PERME would supply up to 200 grammes of TNT at a time wetted with water and packed in plastic bottles 10 grammes to the bottle, the bottles to be contained in a metal box.

2 At Sheffield Polytechnic the metal box would be kept in a locked metal cabinet and ½ gramme samples would be withdrawn as required for the experimental work being carried out.

3 Residues arising from the experimental work which would be in the form of solutions would be kept in a plastic bottle and returned to PERME for disposal.

Under the above conditions it is my opinion that the operations you will be carrying out at Sheffield are covered by the exemption to the Explosives Act 1875, Section 4 relating to the use of small quantities of explosives for chemical experiments. The quantity of explosives you will be keeping is within that allowed for keeping for private use but in order to comply with Order in Council No 12 you should apply to the Chief Officer of Police of the district in which the Polytechnic is situated for a certificate to keep explosives.

When you have commenced your experimental work at Sheffield I will visit you in order to assure myself that conditions are satisfactory.

I will let Mr Cole have a copy of this letter and hope that I have covered all the points which were discussed.

Yours faithfully

A F HEATHER
HM INSPECTOR OF EXPLOSIVES

SCOP

EXPLOSIVES ACT, 1875

CERTIFICATE

Form B

(Premises registered for Mixed Explosives)

I, the undersigned, ~~being [or~~ being authorised in writing by P.WRIGHT] Chief Officer of Police for . SOUTH YORKSHIRE , ~~[or being Clerk of the Court of~~ , ~~by direction of such Court~~], do hereby certify that* ANTHONY MURLES DAVIS , of SHEFFIELD CITY POLYTECHNIC,POND STREET is a fit person to keep, during the continuance of this Certificate, at his MODE 'B' registered premises at SHEFFIELD CITY POLYTECHNIC,CHEMISTRY DEPT the following Explosives, namely: SEE OVER to an amount not exceeding that which may be lawfully kept under an Order in Council on premises registered for the keeping of Mixed Explosives

This Certificate continues until the THIRTY FIRST day of DECEMBER next after the date hereof, or until any earlier date at which another Certificate is granted in respect of the above-mentioned premises, person or at which it is revoked by the Chief Officer of Police [*or as the case may be*].

(Signed) _____

This FIRST day of JANUARY 19 84

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*NOTE—Where the premises are occupied by persons trading under the name of a firm or by a limited company, the name of such firm or company may be inserted in the Certificate.

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South Yorkshire County Council

EXPLOSIVES ACT, 1875

Application having been made for registration in pursuance of Section 21 of the Explosives Act, 1875, in respect of the under-mentioned Premises, and a fee of £5.00 having been paid, the premises are hereby registered until the 30th September, 19 84.

Name of Occupier... Anthony Murbo Harris - Sheffield Polytechnic

Trade or Business... Education

Address of Premises... Sheffield City Polytechnic

Pond Street, Sheffield S1 1WB

Maximum Quantity of Gunpowder to be kept... —

Maximum Quantity of other Explosive to be kept... 1 lb.

Nature of other Explosive... Mixed Explosives

Method of Keeping... Mode B.

Observations... DETONATORS - ROOM 7106 - TNT - ROOM 807-8

Dated this 1st day of December 19 83.

282022.

H E Wright 24

Chief Fire Officer

25bks/774/7G714 B

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Post-Graduate Studies

Post-Graduate studies included a short lecture course on asymmetric synthesis by Dr.J.F.Stoddart of the University of Sheffield; the lectures of the M.Sc. course on Instrumental Analysis at Sheffield City Polytechnic; the B.Sc.IV lecture course on Mass Spectroscopy and NMR Spectroscopy, given by Dr.J.H.Little at Sheffield City Polytechnic; and other lectures and research colloquia at both the University and Polytechnic of Sheffield.

The annual meetings of the Chemical Society, Organic Reaction Mechanisms Group were attended in January 1983 (University College, London) and January 1984 (King's College, London). In July 1982 the 3rd International Conference on "Reaction Mechanisms in Solution" was attended at the University of Kent at Canterbury.

At the commencement of this project, a two week period was spent at PERME, Waltham Abbey, under the supervision of Dr.P.Golding, for instruction in the use of explosive compounds as chemicals.