Some kinetic mechanistic and synthetic studies of the reactions of cyanide ions with aromatic nitro-compounds

Elsegood, Simon Edward

SOME KINETIC, MECHANISTIC AND SYNTHETIC STUDIES OF THE REACTIONS OF CYANIDE IONS WITH AROMATIC NITRO-COMPOUNDS.

by Simon E. Elsegood.

A thesis submitted for the degree of Doctor of Philosophy in the Department of Chemistry, University of Durham, 1991.

ABSTRACT

The reactions of cyanide ions with some benzene derivatives activated with electron-withdrawing groups have been studied in methanol, and in DMSO, and in mixtures of these solvents. The studies have involved spectroscopic measurements of reactants, intermediates and products together with kinetic measurements and the isolation of reaction products. The techniques used include uv/visible spectrophotometry, proton N.M.R. spectroscopy, e.s.r. spectroscopy, polarography and H.P.L.C.

There is evidence from the reaction of 1,3,5-trinitrobenzene with excess cyanide in methanol that methanolysis of the cyanide ion produces a significant concentration of methoxide ions, which may also attack the substrate. A methanolysis constant of approximately $4x10^{-4}moldm^{-3}$ has been calculated, which leads to a value of 13.52 for the pK_a of hydrogen cyanide in methanol.

The reaction of a slight excess of potassium cyanide with *meta*-dinitrobenzene in methanol has been previously reported to yield 2-methoxy-6-nitrobenzonitrile. The author has confirmed that this is the major product, although isomeric methoxy-nitrobenzonitriles are also produced in small quantities. The reactions of the possible intermediates, 2,4- and 2,6-dinitrobenzonitrile, with methoxide in methanol have been studied. There is evidence for initial partitioning of the parent between reversible production of solvate, *via* attack of the methoxide at the cyano group, and irreversible substitution of a nitro group by methoxide. In a second slower stage the solvate is converted, *via* parent, to substitution products. With the same reagents in DMSO there is evidence for the reversible formation of sigma-adducts by attack at unsubstituted ring positions, followed by the irreversible substitution of nitro groups.

There is evidence for common intermediates and products in the reactions of *meta*-dinitrobenzene, 2,4-dinitrobenzonitrile and 1-fluoro-2,4-dinitrobenzene with cyanide in media rich in DMSO. Under such conditions *meta*-dinitrobenzene and 1-fluoro-2,4-dinitrobenzene undergo reaction to produce 2,4-dinitrobenzonitrile, which then reacts further with excess cyanide to produce two isomeric nitro-dicyanophenols. The natures of these reactions, which involve substitution of a ring hydrogen by a cyano group, are discussed.

With a large excess of cyanide in media rich in DMSO 1-chloro-, 1-bromo- and 1-iodo-2,4-dinitrobenzene yield a product with a uv/vis spectrum similar to 2,4-dinitrophenoxide. With small excesses of cyanide there is NMR evidence for the production of 5-cyano-2,4-dinitrophenol. Tentative suggestions are made for the possible mechanisms for the production of these species, and comparisons drawn with the reactions of 1-fluoro-2,4-dinitrobenzene under similar conditions.

A common feature of these reactions is the unusual ability of the cyanide ion to replace a ring hydrogen atom. It is suggested that initial attack of cyanide at unsubstituted ring positions yields anionic adducts which may transfer an electron to yield radicals. The presence of the electron-withdrawing cyano group makes these radicals sufficiently acidic to lose a proton, yielding aromatic radical anions containing cyano substituents. The latter species give rise to the observed products. Evidence is presented for the observation of dicyano-dinitrobenzene radical anions.

SOME KINETIC, MECHANISTIC AND SYNTHETIC STUDIES OF THE REACTIONS OF CYANIDE IONS WITH AROMATIC NITRO-COMPOUNDS.

by

Simon Edward Elsegood, B.Sc.Hons.(Dunelm).

A thesis submitted for the degree of Doctor of Philosophy in the Department of Chemistry, University of Durham, 1991.

CONTENTS

ACKNOWLEDGEMENTS

The author wishes to acknowledge the invaluable contributions made to this work by Dr.M.R.Crampton of the Chemistry Department, University of Durham, and Dr.J.H. Atherton of I.C.I. Fine Chemicals Manufacturing Organisation, Blackley, Manchester. Hanif, John, Shirlene, Alan, Jav, Tim, John, Lyn, Maureen and Colin are all thanked for their encouragement and companionship. The author is especially grateful to his parents and Jen for their support and forbearance throughout the last three years. Lastly thanks are also due to all the technical staff at the Chemistry Department in Durham, and those who have helped the author in the Process Technology and Development group at I.C.I. Blackley.

This work has been directly funded by I.C.I. Fine Chemicals Manufacturing Organisation, Blackley, Manchester.

DECLARATION

The material in this thesis is the result of research performed in the Department of Chemistry, University of Durham, between October 1988 and October 1991. It has not been submitted for any other degree, and is the author's own work except where acknowledged by reference.

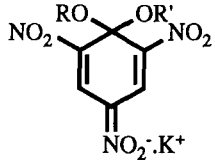
STATEMENT OF COPYRIGHT

CHAPTER 1

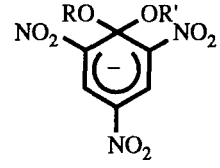
INTRODUCTION

1.1 GENERAL MEISENHEIMER COMPLEX CHEMISTRY.

Anionic sigma-complexes may form as stable or transient species from covalent addition of nucleophiles to a substituted or unsubstituted ring carbon atom of electron-deficient aromatic and heteroaromatic substrates.[1,2] Jackson's [3] proposed structure (1.1) for the red coloured species resulting from the reaction of picryl ethers with potassium alkoxides was confirmed by the experimental evidence of Meisenheimer.[4] More recent studies using nuclear magnetic resonance (NMR) and crystallography [5] show that the structure is better represented by (1.2), indicating delocalisation of the negative charge.



(1.1)



(1.2)

The possible different types of activated aromatic substrates and nucleophiles are many and varied, and reviewed well in the literature.[1,2,5-7] In the section below (section.1.1.1) brief examples are given which illustrate the range of this field of chemistry.

1.1.1 Scope

There is considerable NMR [8,9] and spectroscopic [10] evidence that in both methanol and dimethylsulphoxide (DMSO) 1,3,5-trinitrobenzene (TNB) and methoxide ions readily form the 1:1 sigma-complex (1.3) (eqn.1.1.1).

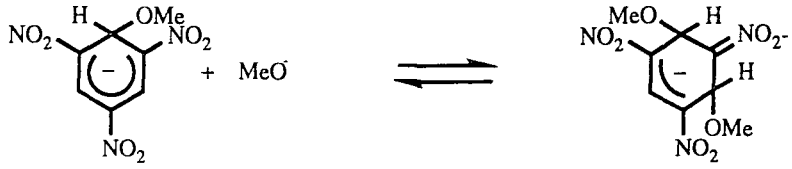
Eqn.1.1.1

TNB

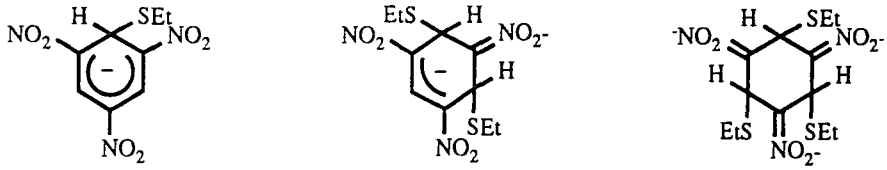
(1.3)

This is the typical activated aromatic-base interaction yielding a sigma-complex. There is stopped-flow evidence [11] that in methanol-water systems it is possible for TNB and methoxide to form the 1:2 sigma-complex (1.4) from the 1:1 complex (1.3) (eqn.1.1.2).

Indeed, with thiolate ions TNB is able to form the 1:1, 1:2 and 1:3 complexes [12] (1.5-7). There is evidence that di-anions and tri-anions are better solvated by water than by dipolar aprotic solvents.

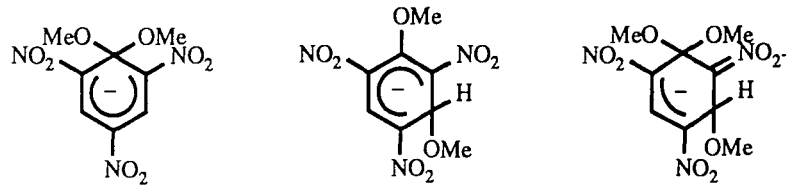


(1.3) (1.4) Eqn.1.1.2



(1.5) (1.6) (1.7)

In DMSO-methanol mixtures both the C-1 (1.8) and C-3 (1.9) dimethoxy sigma-adducts from 2,4,6-trinitroanisole and methoxide are observable by NMR.[8] In methanol only (1.9) is so short lived that a stopped-flow temperature-jump method [13] has to be used to observe it. With high concentrations of nucleophile in DMSO the 1:2 sigma-complex (1.10) is observable using NMR.[14]



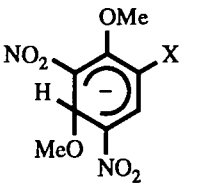
(1.8) (1.9) (1.10)

Methoxide addition to substituted 4-X-2,6-dinitroanisoles (X = NO_2, SO_2CF_3, CN, SO_2Me, CHO, CO_2Me.) in methanol-DMSO mixtures has been the subject of many investigations.[1] In all cases addition to the unsubstituted C-3 to give the 1,3-dimethoxy sigma-complexes is kinetically favoured, but rearrangement occurs to give the 1,1-dimethoxy complexes. The reasons for this are discussed in section 1.2.1 below.

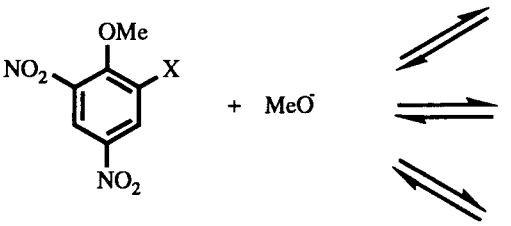
Due to the nonequivalence of the 3- and 5- positions, 2-X-4,6-dinitroanisoles may react with methoxide to give complexes (1.11), (1.12) and (1.13) (Scheme 1.1) which are designated 1,5, 1,3 and 1,1 complexes respectively. Under conditions where they can be observed, (1.11) and (1.12) which both result from methoxide addition to an unsubstituted carbon, are formed under kinetic control. In all cases, these undergo complete conversion into the thermodynamically more stable 1,1 complex (1.13).

NMR measurements have confirmed the structure of the transient complexes (1.11) and (1.12) when X = CN and CF_3.[15]

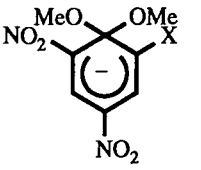
Scheme 1.1



(1.11)



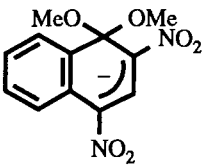
(1.12)



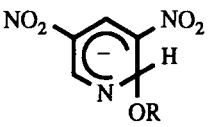
(1.13)

X = SO_2CF_3, CN, CF_3, CO_2Me, Cl, F.

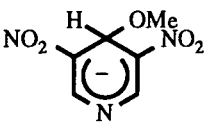
1-Methoxy-2,4-dinitronaphthalene reacts with dilute methoxide solutions in methanol to give directly the 1,1 complex (1.14).[1] Equilibria measurements show that the 1,1-dimethoxy-2,4-dinitronaphthalene is $5x10^6$ times more stable than that from 2,4-dinitroanisole, but 75 times less stable than that from 2,4,6-trinitroanisole.[16]



(1.14)



(1.15)



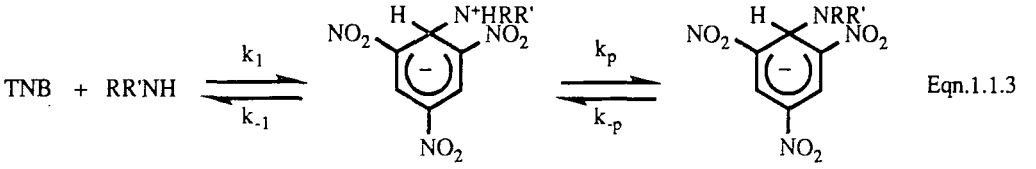
(1.16)

In agreement with the well known activating effect of the aza group in nucleophilic heteroaromatic substitution reactions, activated pyridines and pyrimidines easily form stable hydroxy and alkoxy sigma-complexes.[1] Hydroxide and methoxide ions react with 3,5-dinitropyridine in water or methanol to form the yellow addition complex (1.15).[17,18] In methanol-DMSO mixtures rich in DMSO it is possible using stopped-flow spectrophotometry to observe the rapid formation and decay of the 1,4 complex (1.16). In DMSO, it is possible to observe (1.16) by NMR measurements.[17]

It is possible to form sulphur-bonded sigma-complexes using sulfite, thiophenoxide or thiolate nucleophiles.[1] Examples of the latter have been given above.

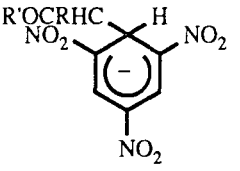
Addition of primary or secondary amines to TNB initially yields a zwitterion (1.17) which then loses an alkylammonium proton to give the anionic sigma-complex

(1.18) (eqn.1.1.3).[1] Similar work has been carried out on 2,4-dinitrobenzene derivatives to elucidate the mechanism of base catalysis in S_NAr reactions.[19]

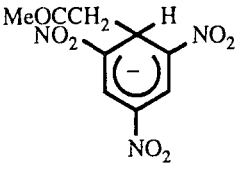


(1.17) (1.18) Eqn.1.1.3

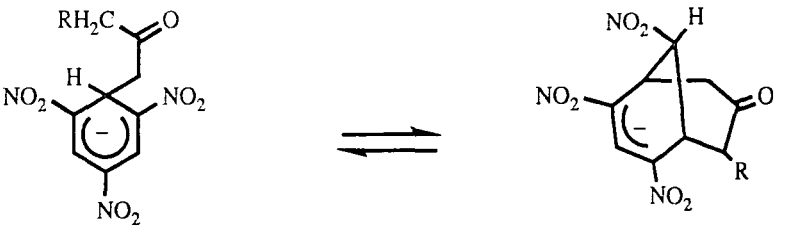
Activated aromatics and heteroaromatics react with the enolate carbanions from ketones, aldehydes, keto-esters, esters or amides [1] to form complexes of general structure (1.19), also called Janovsky complexes. When methoxide is added to a solution of TNB in acetone, the NMR spectrum of the solution shows resonances for both acetonate (1.20) and methoxy complexes (1.3). The former increases with time at the expense of the latter.[5,8] When complexes have a potential nucleophilic site γ to the sp^3 ring carbon (1.21), intramolecular cyclisation may occur to give the bicyclic analogues (1.22).[19]



(1.19)



(1.20)



(1.21) (1.22)

1.1.2 The Mechanism of Sigma-Complex Formation.

Molecular orbital (MO) calculations predict that in the methoxy sigma-complex of 2,4,6-trinitroanisole (1.8) the C-1 is truly sp^3 hybridised,[5] and the C-1 - oxygen bonds are equivalent and have no π -character. MO calculations have been able to predict the number of absorption bands in the visible region for adducts from mono-, di- and tri-nitro substrates.[5,21,22] HMO treatments have been attempted for sigma-complexes,[23] but have been contradicted by more recent and sophisticated methods.[24,25] Both the

method of composite molecules [24] and Pariser-Parr-Pople type self consistent field calculations [25] predict a significant increase in negative charge both on the nitro groups and on the ring carbons during adduct formation.

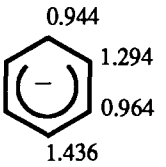
Figure 1.1

Valence structures of the cyclohexadienyl anion

Ab initio calculations with the minimal STO-3G basis set [26] have confirmed that the cyclohexadienyl ion may be represented by the valence structures shown in fig.1.1. The π-electron population is greatest at the *para*-position (fig.1.2).

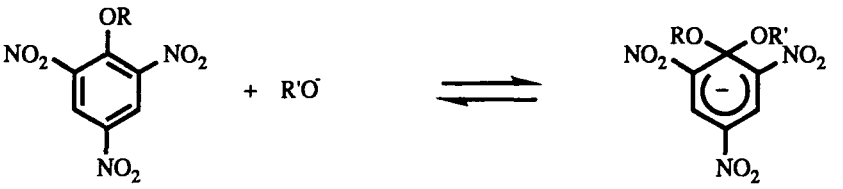
Figure 1.2

π–Electron populations of the cyclohexadienyl anion.



The relative stabilisation energies of various substituents on the cyclohexadienyl anion, regardless of position are NO_2 > CN > COOH > F > OH > NH_2. The π-acceptors (NO_2, CN) stabilise better at the *para*-position than at the *ortho*-position, than at the *ipso*-position. The π-donors (F, OR, NH_2) stabilise better at the *ipso*- and *meta*-positions, and actually destabilise at the *para*-position.[26] A recent review [27] describes attempts of MO calculations on neutral un-, mono- and disubstituted benzenes.

Steric effects are usually only significant in the attack of nucleophiles at substituted carbons; but when using particularly bulky nucleophiles, such as *tert*-butoxide, attack at an unsubstituted carbon between two nitro groups is sterically hindered.[10] The reactions of the picryl ethers with alkoxide nucleophiles (eqn.1.1.4) can be explained by steric effects and π-donation by the *ipso* substituent. This is also discussed in section 1.2.1.

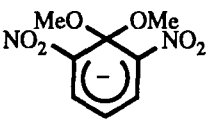


Eqn.1.1.4

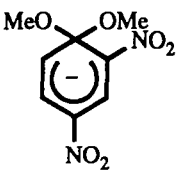
R = Me, Et, Pr, *etc.*

Because in the neutral substrate both the nitro groups and the alkoxy group wish to be in the plane of the ring there is considerable strain, resulting in the nitro groups being forced out of that plane.[28] Formation of a 1,1-adduct produces tetrahedral geometry at the C-1, relieving the strain. Due to the release of this tension, and the greater stabilising influence of a double-alkoxy substitution over a mono-alkoxy substitution (section 1.2.1),[26] these adducts are more stable than the corresponding products from TNB and alkoxides.[5,29] Also, formation of the 1,3-adduct, although much faster than 1,1-adduct formation because of less steric hindrance,[2,30] yields a complex less thermodynamically stable.

From the work of the previous decades it is well substantiated that the stabilities of the sigma-complexes mirror the degree to which the ring is activated by electron-withdrawing groups.[1,2,5,31] Replacing a nitro group in the *ortho* or *para* position to the sp^3 carbon with a group of less electronegativity reduces the stability of the sigma-complex. However, the position *para* to the sp^3 carbon is the more important.[32] The exception to this rule is the replacement of a nitro group by hydrogen.[33] This is demonstrated by the greater stability of the 1,1-methoxy adduct of 2,6-dinitroanisole (1.23) compared with that of 2,4-dinitroanisole (1.24).

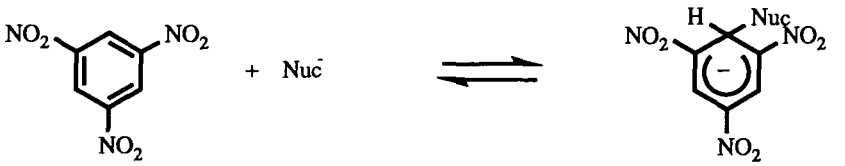


(1.23)



(1.24)

This is because 2,4-dinitroanisole is less sterically crowded at the site of attack and so there is less strain to release. Here, steric effects take precedence over substituent electronegativity effects. As expected, replacement of a nitro group by a trifluoromethylsulphonyl group, the strongest known neutral electron-withdrawing group, enhances the stability of a sigma-complex.[1] Attempts to quantify substituent effects in terms of free energy values have been made,[1,5,34] and these results confirm the experimental observations described above.



TNB

Eqn.1.1.5

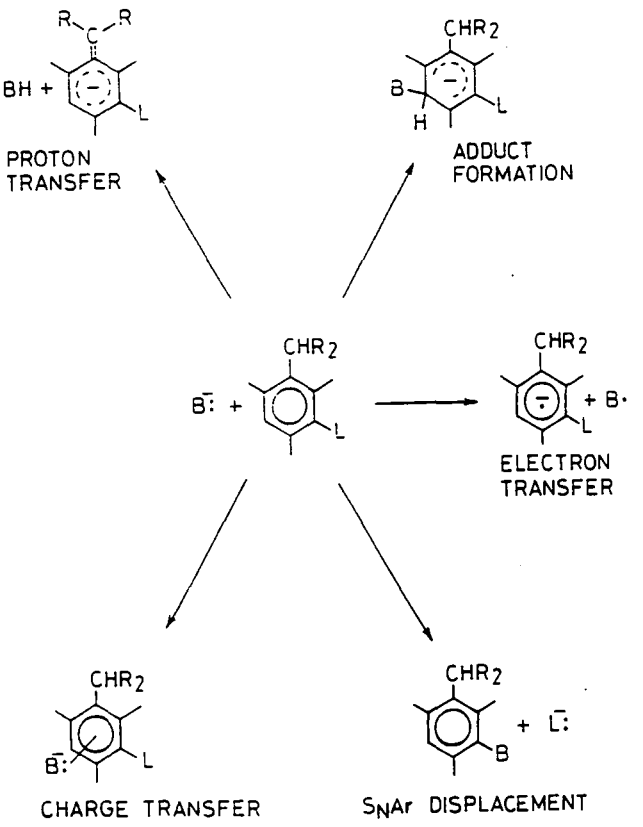
The adduct forming reactions of TNB are the most commonly used to study the effects of varying the nucleophile because of the lack of steric effects and the wealth of data that has been collected.[1,2,5,31] The general equation for the formation of a 1:1 complex (eqn.1.1.5) indicates that the stability of the complex will be affected by the affinity of the nucleophile for the carbon at the electrophilic site, often called the carbon basicity. The carbon basicity may well be very different to the Bronsted basicity, the affinity for a proton. This is exemplified by the series of oxygen nucleophiles: hydroxide, methoxide and ethoxide.[30] In this case the relative stabilities of the adducts in eqn.1.1.5 are ethoxide > methoxide > hydroxide. The relative Bronsted basicities of hydroxide, methoxide and ethoxide in water are 1:0.62:1.80.[35] This result is in accordance with the general pattern found in other nucleophilic reactions and is attributed to the greater solvation of the hydroxide ion compared to the alkoxide ions.[2] Similarly, we can compare the nucleophiles methoxide and thioethoxide;[36] for methoxide (pK_{MeOH} = 16.7) the equilibrium constant for eqn.1.1.5 is 15dm^3mol^{-1}, for the thioethoxide (pK_{EtSH} = 15) the equilibrium constant is 3 500 dm^3mol^{-1}. The methoxide has the higher Bronsted basicity, but the carbon basicity is in the reverse order. The irrelevance of Bronsted basicities as a measure of nucleophilic strength in eqn.1.1.5 is also demonstrated by the cyanide ion. In ethanol, where ethoxide is approximately 10^6 times more basic than cyanide, the TNB-cyanide complex is slightly more stable than the TNB-ethoxide adduct.[30,37,38]

Some common possible electron-deficient aromatic/base interactions are shown in scheme 1.2.

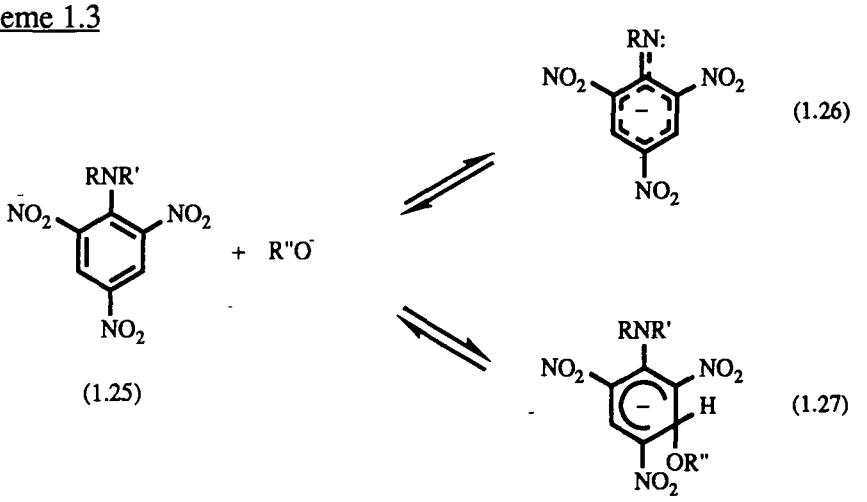
The competition between complex formation and proton extraction when the aromatic has an exocyclic ionisable group can be seen by comparing the reactions of picramide (2,4,6-trinitroaniline) (1.25, R = R' = H) (scheme 1.3) and 2,4,6-trinitro-toluene (1.28) (scheme 1.4).[2] In scheme 1.3 both products are present at equilibrium, but production of the conjugate base (1.26) is very fast,[39] with adduct (1.27) formation much slower. If neither R or R' are hydrogen then only the slow adduct formation occurs.[40]

In scheme 1.4 the complex (1.30) forms prior to the anion (1.29), which is the thermodynamically more stable product.[41]

Scheme 1.2 [2]

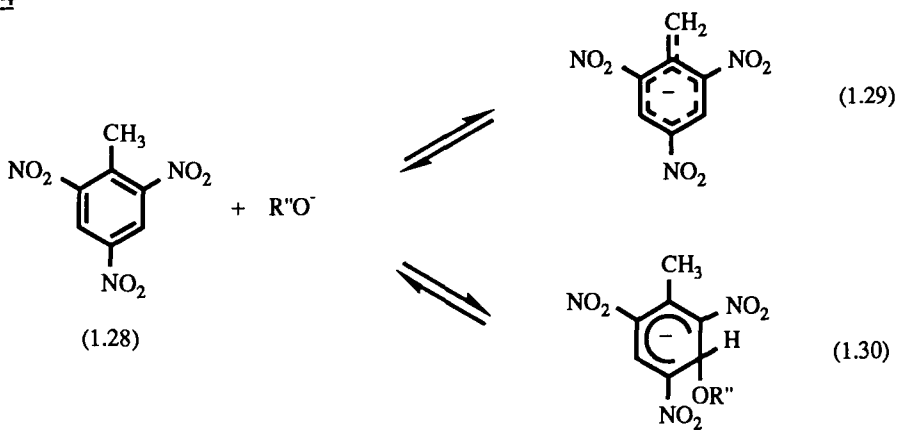


Scheme 1.3



As shown in scheme 1.2 benzylic hydrogen transfer and electron transfer are feasible under the conditions usually employed for sigma-complex formation. Competition between the three processes in a given system will depend on factors such as the relative rates and the stabilities of the species generated. In the nitrotoluene series, the stabilities of the sigma-complexes increase *para*-nitrotoluene < *meta*-

Scheme 1.4

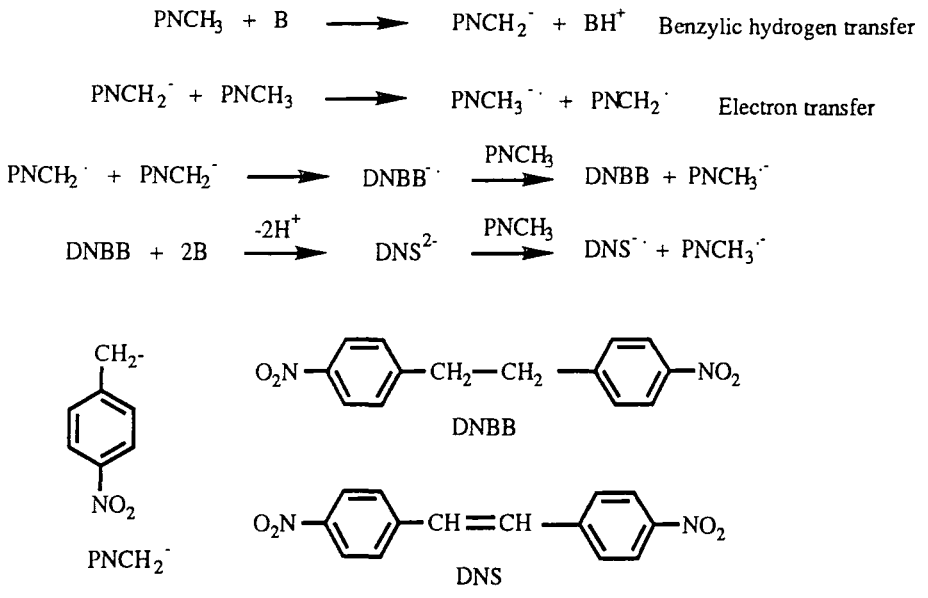


dinitrotoluene < 2,4,6-trinitrotoluene, and the carbanion stabilities increase in the same order.[2] It is also reasonable to assume that the stabilities of the respective radical anions follow the same order. However, complex formation is rare with *para*-nitrotoluene and yet facile with 2,4,6-trinitrotoluene. Both electron and benzylic hydrogen transfer are common with *para*-nitrotoluene, but unusual with 2,4,6-trinitrotoluene. *meta*-Dinitrotoluene is intermediate in most cases.

para-Nitrotoluene reacts with bases [45] for which the pKa value of the corresponding conjugate acids are greater than that for *para*-nitrotoluene, *eg.* potassium hydride and potassium fluoride, to form 4,4'-dinitrostilbene (DNS) or 4,4'-dinitrobibenzyl (DNBB) as the final products (scheme 1.5). 2,4,6-Trinitrotoluene exhibits isotopic exchange of methyl protons under basic conditions, (*eg.* 2,4,6-trinitrotoluene (0.5M) and sodium deuterio-oxide (0.1M) in 90% DMF / 10% D_2O).[46] In methoxide/methanol/DMSO media 2,4,6-trinitrotoluene exhibits radical anions through electron-spin resonance spectroscopy.[47]

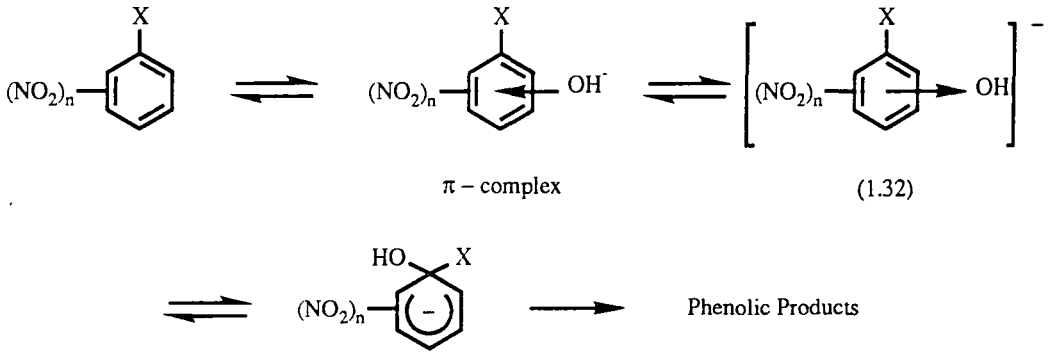
The conditions under which *meta*-dinitrobenzene (13DNB) and TNB exhibit nuclear hydrogen abstraction have been reviewed.[2] We are interested in whether abstaction of an aromatic proton is a preliminary step to sigma-complex formation and subsequent nucleophilic aromatic substitution; or an initial side equilibrium. Buncel and Symons [48] have demonstrated that proton exchange and complex formation are in competition in TNB-base systems. The two processes were shown to have a different solvent dependence. Sigma-complexes do not exchange their protons. Other studies [49-51] have shown that the same is true for 13DNB systems.

Scheme 1.5 [2,45]



It has been reported that this isotopic exchange occurs through free TNB *via* the aryl carbanion as a steady-state intermediate.[2] However, recent workers [52-54] have suggested that aromatic hydrogen exchange is *via* a charge transfer complex (1.32) which is an intermediate along the pathway to the sigma-complex (scheme 1.6).

Scheme 1.6

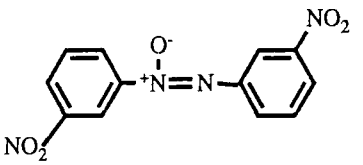


There is agreement that the actual exchange is still in competition with complex formation. Similar pathways are supported by recent MNDO studies [55] for *para*-chloronitrobenzene and halide nucleophiles.

1.1.3 Single Electron Transfers in Nucleophilic Aromatic Substitution.

The ability of aromatic compounds carrying electron-withdrawing groups to act as electron acceptors in basic solutions is well established,[56-58] and radical anions are accepted to be intermediates in $S_{RN}1$ substitutions [59] and in reductions of such compounds.[60] However, as the number of electron-withdrawing groups in the ring is increased, the formation of anionic sigma-adducts becomes increasingly favoured at equilibrium relative to the formation of anion radicals.[2,56,58]

ortho- And *para*-dinitrobenzene form the respective phenols and anisoles from reaction with hydroxide or methoxide in water or methanol respectively.[61] The reaction of *meta*-dinitrobenzene is complicated by the formation of 3,3'-dinitro-azoxybenzene (1.33).[61,62] The formation of (1.33) in methanol is *via* the radical anion of *meta*-dinitrobenzene, the only radical anion observed by e.s.r. in the system. The radical then forms a nitroso-like intermediate to yield the observed product.



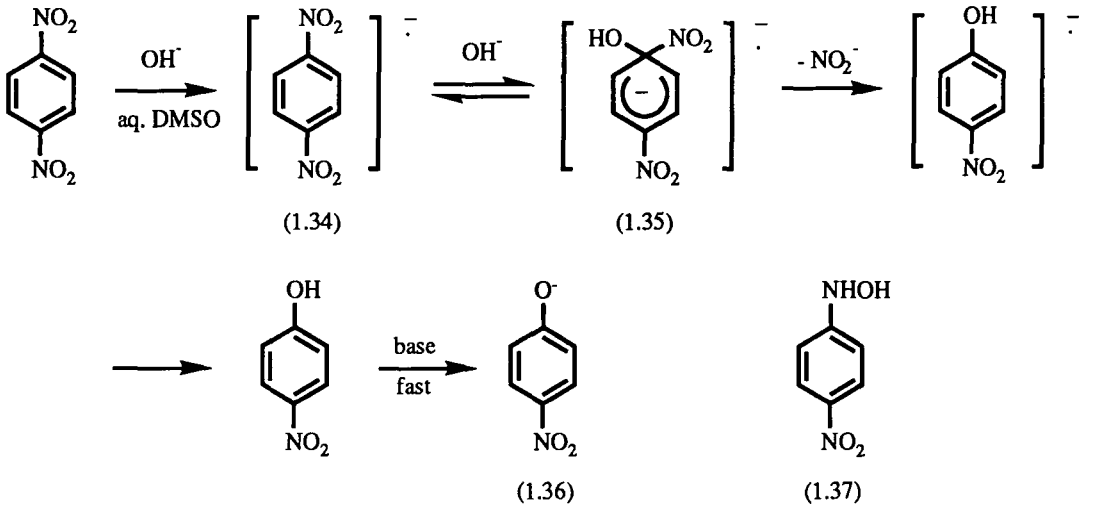
(1.33)

More recent studies [63,64] present uv/vis spectroscopic and e.s.r. evidence for the formation of *ortho*- and *para*-dinitrobenzene anion radicals in the reaction of the respective neutral parent with hydroxide ions in aqueous DMSO. It has been postulated that there is an initial electron transfer from the nucleophile to the substrate, (scheme 1.7) creating the anion radical (1.34); this is followed by formation of a radical dianion (1.35), then the formation of the phenoxide product (1.36).

The anion radical of *para*-dinitrobenzene (1.34) is the main product when *para*-dinitrobenzene reacts with cyanide ion in dry DMF,[65] if water is present *para*-nitrophenoxide (1.36) is produced. *para*-Nitrophenylhydroxylamine (1.37) is formed in a secondary reaction from the radical anion (1.34). There is polarographic evidence [66] that (1.34), generated electrochemically, is stable in dry and degassed DMF. In solvent containing any oxygen or water, *para*-nitrophenol and (1.37) are produced. The rate law for the formation of the radical anion (1.34) is first order with respect to both substrate and cyanide. Direct reduction by cyanide, however, is unfeasible. Eberson demonstrated [67] that hydroxide is not likely to reduce *para*-dinitrobenzene directly. Taking this into account the fact that cyanide has a more positive normal potential than does hydroxide (*eg.* 1.9V and 2.59V in water [68] and 0.8V and 1.1V in acetonitrile [67] for hydroxide and cyanide respectively), reduction by cyanide is even less likely.

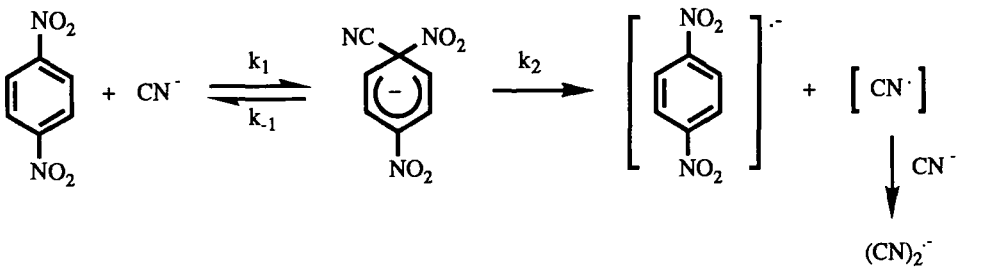
acetonitrile [67] for hydroxide and cyanide respectively), reduction by cyanide is even less likely.

Scheme 1.7



A scheme is proposed [65] for the formation of (1.34) from cyanide and *para*-dinitrobenzene in dry DMF (scheme 1.8). It is proposed that there is initial formation of a sigma-complex (1.35). This subsequently loses a cyanide radical which combines with a second cyanide ion to form the cyanogen radical anion. Kinetic data indicate that $k_2 >> k_1$, so it is not expected that the steady-state concentration of the sigma-complex will be sufficient for spectroscopic detection.

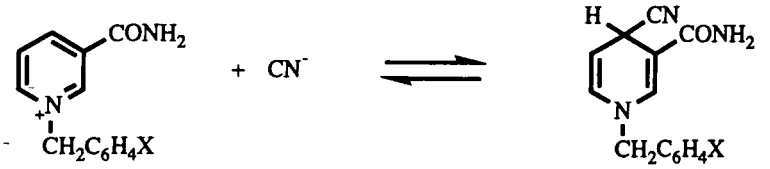
Scheme 1.8



It has been suggested from NMR and uv/vis spectroscopic evidence [52-54,69,70] that π - complexes and charge-transfer complexes are precursors to sigma-complexes between 1-X-2,4,6-trinitrobenzenes (X = H, Cl, SO_3^-) and hydroxide ions in aqueous DMSO. It is proposed [54] that the reaction involves an interaction between nucleophile and substrate to form a π – complex (scheme 1.6). This is followed by a single electron transfer from the nucleophile to the substrate to form a charge-transfer complex

(1.32). Interaction of the two partners in the charge-transfer complex leads to the new bond in a 1,1- or 1,3-sigma-complex.

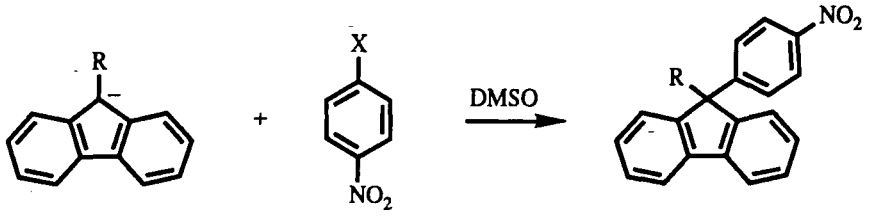
However, there is by no means universal agreement that one electron transfers are precursors to sigma-complex formation in the interactions of nucleophiles with activated aromatic compounds. Recent kinetic evidence [71] has confirmed that, as has been thought for many years,[2] the reaction of hydroxide ions with tri- and dinitro compounds to form hydoxy adducts occurs without the observation of spectrophotometrically detectable intermediates. A MNDO study [72] of nucleophilic aromatic substitution has indicated that the formation of a charge-transfer complex by a nucleophile and substrate is an unproductive side-reaction, and does not lead to sigma-complex formation. Such calculations have been confirmed by experiment with the addition of cyanide to 1-substituted nicotinamide cations [73] (1.38) (eqn.1.1.6) in acetonitrile. The observed rapid formation of a charge-transfer complex is not a promotive step in the process of adduct formation, but rather contributes to initial-state stabilisation of the nicotinamide cation, and is therefore counter-productive to adduct formation.



Eqn.1.1.6

(1.38, X = OMe, Me, H, F, CN)

A kinetic study [74] has ruled out the possibility of a charge-transfer mechanism in the nucleophilic aromatic substitution reactions between substituted fluorenide carbanions (1.39) and *para*-substituted nitrobenzenes (1.40) in DMSO (eqn.1.1.7).

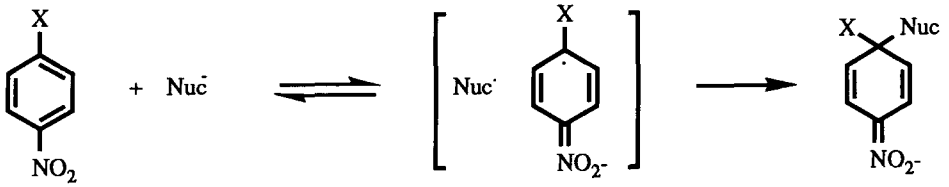


Eqn.1.1.7

(1.39) (1.40)

R = Me, Ar, ArS X = F,Cl, Br, I , PhO

The observation of good second order kinetics is inconsistent with an electron transfer chain mechanism; but this does not preclude production of a sigma-complex by a non-chain single electron transfer (eqn.1.1.8).



(1.40)

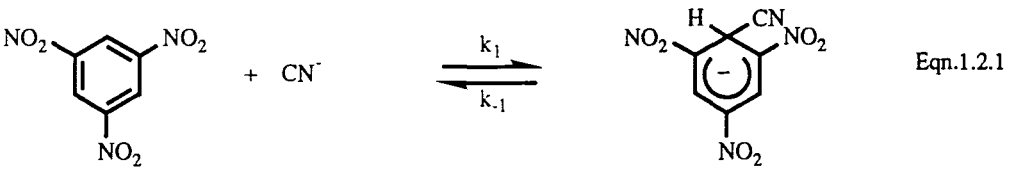
Eqn.1.1.8

1.2 CYANIDE SIGMA-ADDUCTS.

In reactions with alkyl and acyl halides,[7] and olefins [75] the cyanide ion behaves as a typical nucleophilic reagent. Similarly the reactions of aromatic halides with cuprous cyanide (discussed in section 1.3.2) generally produce the expected nitriles. However, the cyanide ion in alcoholic media readily forms sigma-complexes with suitably activated aromatic compounds, but hardly ever effects straightforward substitution.[6]

1.2.1 - With Trinitro-substrates.

The 1:1 TNB-cyanide sigma-complex (1.41) can be observed by uv/vis spectrophotometry by mixing cyanide and TNB in many non-aqueous solvents (eqn.1.2.1) such as acetone,[76] chloroform,[76] alcohols [77] and DMSO.[76] The absorption spectrum of the complex in acetone at 25.3°C is typified by maxima at 437 and 555nm, with a ratio of optical densities at these two wavelengths of 1.75. Typical kinetic and thermodynamic parameters are given in table 1.1.[1] Over some minutes in systems with excess cyanide, or those open to the air at room temperature, the red colour fades to give a yellow-brown solution . The cyanide stretch in the complex (1.41) is at 2350cm^{-1}, while in the decayed yellow-brown solution it is at 2200cm^{-1}. These absorbances should be compared with that for the free cyanide ion of 2080cm^{-1}.[76] Cooling to -40°C prevents the decay of the complex.



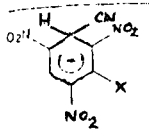
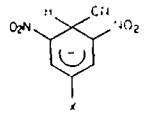
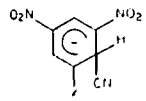
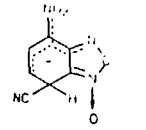
TNB (1.41) Eqn.1.2.1

With lower alcohols (methanol or ethanol) as solvents cyanide-complex formation is complicated by the alcoholysis of the cyanide ion which yields the corresponding alkoxide ion and consequently the 1:1 TNB-alkoxide sigma complex (*e.g.* 1.3).[37] The effects of alcoholysis are discussed in chapter 3. In higher alcohols (*iso*-propanol and *tert*-butanol) little alcoholysis is observed.

Values of rate constants,[37] k_1, and equilibrium constant,[77] for the formation of (1.41) decrease as the solvent is changed from *tert*-butanol to *iso*-propanol to *n*-propanol, to ethanol, to methanol. This has been explained by considering solvent effects. In the systems studied, using tetraphenylarsonium cyanide, the concentration of cyanide does not exceed 0.002M; hence ion pair formation between the bulky tetraphenylarsonium ion and the cyanide ion will be small in the alcohols above. The equilibrium measurements are therefore considered to apply to the reaction of free

Table 1.1

Kinetic and Thermodynamic Parameters for Formation and Decomposition of Cyanide Sigma-Complexes at 25°C [1]

	Cpx	X	solvent	k_f, L mol^{-1} s^{-1}	k_d, s^{-1}	K, L mol^{-1}	activation and thermodynamic parameters;[c] conditions and comments[d]
	198	H	$CHCl_3$	225	6.7×10^{-4} [e]	3.35×10^5	isnc
			CH_3COCH_3			1.44×10^5	isnc
			MeOH			39	isnc; $\Delta H^\ddagger \simeq 0$; $\Delta S^\ddagger = 30$
			EtOH			1265	isnc; $\Delta H^\ddagger = -32.6$; $\Delta S^\ddagger = -36$; cd
				442	0.042	1.05×10^4	isnc
			PrOH			1470	isnc; $\Delta H^\ddagger = -29.7$; $\Delta S^\ddagger = -42$
				932	<0.01	$>9 \times 10^4$	isnc
			i-PrOH	2450	0.245[e]	10^4	isnc; $\Delta H^\ddagger = -29.7$; $\Delta S^\ddagger = -23$; cd
				2450	0.048	5.1×10^4	isnc; $\Delta H_f^\ddagger = 49$; $\Delta S_f^\ddagger = -5$; $\Delta H_d^\ddagger = 78.7$; $\Delta S_d^\ddagger = 11.7$; $\Delta H^\circ = -29.7$; $\Delta S^\circ = -16.7$
			BuOH			2020	isnc; $\Delta H^\ddagger = 32.6$; $\Delta S^\ddagger = 44$; cd
			t-BuOH			5×10^5	isnc; $\Delta H^\ddagger = 65$; $\Delta S^\ddagger = -105$; cd
				1.06×10^5	2.5	4.24×10^4	isnc
	199a	OMe	*i*-PrOH	344	0.031[e]	1.12×10^4	isnc; $\Delta H_f^\ddagger = 38.9$; $\Delta S_f^\ddagger = -47.6$; $\Delta H_d^\ddagger = 42.2$; $\Delta S_d^\ddagger = 113.6$; $\Delta H^\circ = -3.3$; $\Delta S^\circ = 66$
	199b	Me	*i*-PrOH	32.6	0.002	2.01×10^4	isnc; $\Delta H_f^\ddagger = 49.3$; $\Delta S_f^\ddagger = -39.3$; $\Delta H_d^\ddagger = 69.8$; $\Delta S_d^\ddagger = -53.5$; $\Delta H^\circ = -20.5$; $\Delta S^\circ = 14.2$
	201a	CN	$MeOH-Me_2SO$ 28:72	721	4.28×10^{-3}	1.68×10^5	isnc
	201b	COOMe	$MeOH-Me_2SO$ 28:72	142.5	7.2×10^{-3}	1.98×10^4	isnc
	202a	CN	$MeOH-Me_2SO$ 28:72	259	5.4×10^{-4}	4.8×10^5	isnc
	202b	COOMe	$MeOH-Me_2SO$ 28:72	57.5	4.5×10^{-4}	1.28×10^5	isnc
	203		*i*-PrOH	274	<0.01	$>2.74 \times 10^4$	isnc; $\Delta H_f^\ddagger = 36.8$; $\Delta S_f^\ddagger = -75.7$

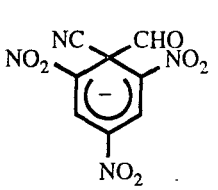
[c] Enthalpies in kJ mol^{-1}, entropies J mol^{-1} K^{-1}. [d] Abbreviations: isnc = ionic strength not calculated, cd = calorimetric determination.

cyanide ion and TNB. The solvation of reactants and products may vary considerably between solvents. The cyanide ion is small with relatively localised negative charge and is strongly solvated by polar solvents such as methanol and ethanol .[78] The charge on the sigma-complex is dispersed and hydrogen bonding between the complex and polar protic solvents is fairly weak. Thus, formation of the sigma-complex requires desolvation of the cyanide ion and this is likely to be a major factor in determining enthalpy and entropy change for reaction in methanol.

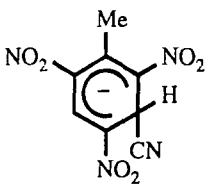
tert-Butanol solvates the cyanide ion only to a limited extent and solvation effects are of minor importance. An equilibrium constant of $5x10^5$ dm^3mol^{-1} is observed in *tert*-butanol; there is a large negative enthalpy change and the effect of the enthalpy term on the equilibrium constant is only partially compensated for by the large entropy decrease. Hence *tert*-butanol typifies a weakly interacting solvent, and values of ΔH and ΔS are comparable to those in chloroform and acetone.[76]

The hydroxy groups of the lower alcoholic solvents are considerably less shielded by methyl groups and solvation by these alcohols has a considerable effect on the equilibrium constant. The equilibrium constant in methanol at 25°C is some 10 000 times smaller than in *tert*-butanol. In methanol the enthalpy change is approximately zero, and the desolvation of the small cyanide ion leads to a small positive entropy change. The equilibrium constants at 25°C in other alcohols are all in the range of 1-$2x10^4$ dm^3mol^{-1}. They show intermediate behaviour between the extremes of methanol and *tert*-butanol. Desolvation of the cyanide ion is likely to be the main factor causing a decrease in equilibrium constant from that in *tert*-butanol, but the effect is smaller than in methanol.

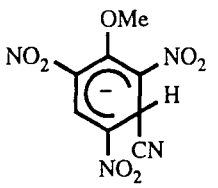
Cyanide ion is also known to react with a number of related 1-X-2,4,6-trinitrobenzenes (X = Me, OMe and CHO) in acetone, chloroform and alcohols.[38] In *d*-chloroform proton NMR shows that for X = CHO, addition of cyanide ion occurs exclusively at the C-1 position to yield (1.42) [79] while with 2,4,6-trinitrotoluene addition occurs exclusively at the C-3 position (1.43).



(1.42)



(1.43)

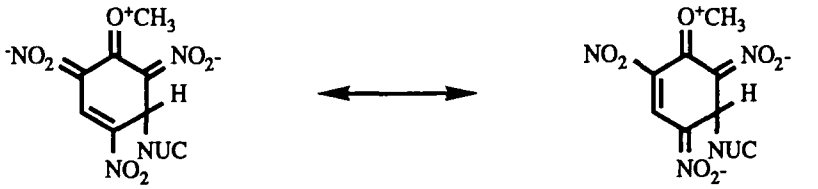


(1.44)

With 2,4,6-trinitroanisole in *d*-chloroform addition occurs at both C-1 and C-3 positions, however the C-3 complex (1.44) is the thermodynamically more stable.[80] When 2,4,6-trinitroanisole reacts with methoxide ions in methanol there is NMR evidence [49,50] that both C-1 and C-3 adducts are formed, however in this case the C-1 complex (1.8) is the more thermodynamically stable. With cyanide ion in *iso*-propanol

only the C-3 adduct is formed with 2,4,6,-trinitroanisole. The equilibrium constants for 1:1 sigma-complex formation with cyanide ion at 25°C in *iso*-propanol increase in the order 2,4,6-trinitroanisole < 2,4,6-trinitrotoluene < TNB, however the difference is small (11 200 dm^3mol^{-1} and 51 000 dm^3mol^{-1} for 2,4,6-trinitroanisole and TNB respectively).[38]

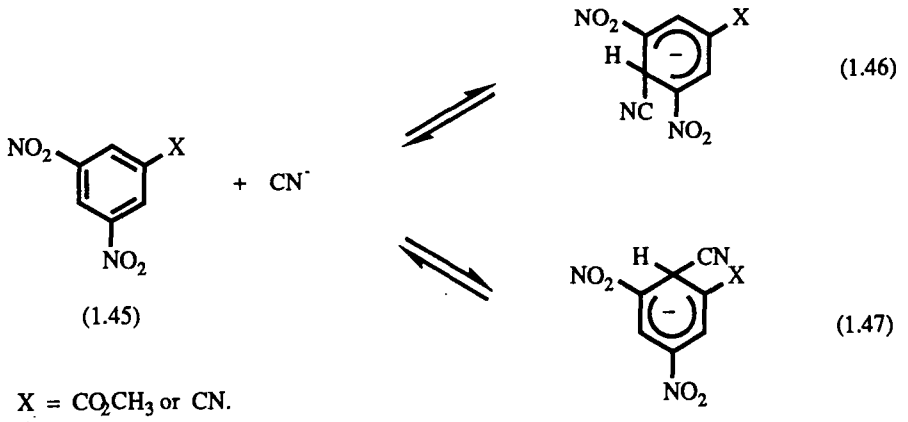
The reason why the 1,1-dimethoxy complex of 2,4,6-trinitroanisole (1.8) is more stable than the 1,3 isomer (1.9) (section 1.1.2) is that multiple alkoxy substitution has a large stabilising effect on sp^3 carbon relative to a non- or little-substituted sp^3 carbon as well as relative to an equally substituted sp^2 carbon.[81] Obviously this effect does not apply in nucleophilic cyanide attack on 2,4,6-trinitroanisole. 1,3-complexes of 2,4,6-trinitroanisole benefit from resonance stabilisation involving the methoxy group (eqn.1.2.2), and so do the transition states leading to the 1,3-complexes.[30] This effect is independent of the nature of the nucleophile, hence the 1,3-cyanide complex of 2,4,6-trinitroanisole (1.44) is prefered over the 1,1-isomer.



Eqn.1.2.2

Cyanide ions in methanol-DMSO mixtures form sigma-complexes with 1-carbomethoxy- and 1-cyano-3,5-dinitrobenzenes (1.45) (scheme 1.10).[82] Addition of cyanide ion to the 4-position of both substrates is approximately 3 times faster than at the 2-position. The symmetrical complex (1.46) formed is less stable thermodynamically, and it mostly undergoes isomerisation into the unsymmetrical complex (1.47). Both complexes are decomposed in the reaction medium; decomposition is catalysed by the cyanide ion.

Scheme 1.10



(1.45)

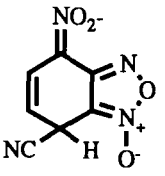
(1.46)

(1.47)

X = CO_2CH_3 or CN.

The reaction of 4-nitrobenzofuroxan (1.48) and cyanide in *iso*-propanol proceeds in two distinct fast steps.[83] The initial reaction is the formation of the C-7 sigma-complex (1.49). The nature of the second and subsequent species produced remains unknown. Stable sigma-complexes from similar substrates have been produced by the reaction of 7-methoxy-4-nitrobenzofuroxan and methoxide in methanol-DMSO mixtures.[84]

(1.48)

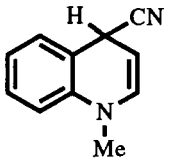


(1.49)

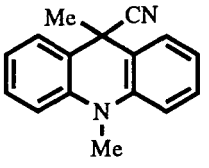
When solutions of cyanide ions are mixed with TNB in water, no formation of an anionic sigma-complex is observed. However, when the same reaction is carried out in the presence of the cationic micelle hexadecyltrimethylammonium cyanide,[85] the red colouration of the TNB-cyanide sigma-complex developes.

1.2.2. - With Other Activated Substrates.

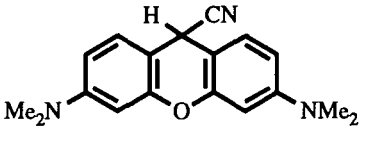
Addition compounds can be formed from the solvated cyanide ion and hetero-aromatic cations.[6] The action of cyanides on 1-methylquinolinium iodide,[86] 9,10-dimethylacridinium chloride [87] and tetramethyldiaminoxanthylium chloride yields the compounds (1.50), (1.51) and (1.52) respectively.[88]



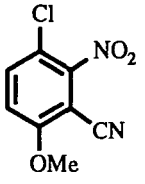
(1.50)



(1.51)

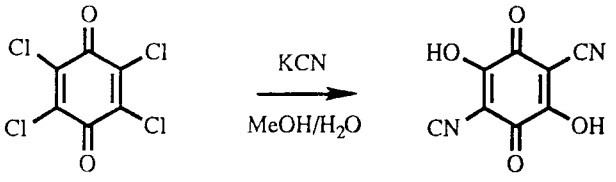


(1.52)



(1.53)

In the reaction of 1-chloro-2,4-dinitrobenzene with cyanide in methanol the nucleophile has been reported to replace the C-3 hydrogen rather than the more obvious halo-nucleofuge. This is then followed by replacement of the C-4 nitro group to yield 3-chloro-6-methoxy-2-nitrobenzonitrile (1.53).[6] Similar to this is the reaction of *meta*-dinitrobenzene with methanolic cyanide [89] to produce 2-methoxy-6-nitrobenzonitrile which is investigated further in chapter 4 below. Early literature [90] reported that aqueous methanolic potassium cyanide will replace two chloro-substituents of chloranil to yield 2,5-dicyano-3,6-dihydroxyquinone (eqn.1.2.3).



Eqn.1.2.3

1.3 OTHER METHODS OF AROMATIC CYANATION.

1.3.1 Photocyanation and Electrocyanation - Electron transfer pathways.

Aromatic nucleophilic substitution occuring by the $S_{RN}1$ mechanism [91] has been studied during the last two decades.[92] It is described by scheme 1.11, which requires an electron transfer reduction (the electron source may be an electrode, solvated electrons, or other redox reagents), or a photoreduction of the substrate ArX (step 1). Cleavage of the anion radical thus generated produces the sigma-aryl radical (Ar·) (step 2), which is the actual electrophilic reactant rather than the starting substrate. The key step of the reaction is then the coupling of the aryl radical and the nucleophile (step 3), leading to the anion radical of the target product. This species is then reoxidised into the final product; the oxidant being any electron sink present in the reaction medium, *e.g.* an electrode (step 4) or the substrate itself (step 5). In the latter case, the reaction continues on a chain mechanism. In the organic solvents commonly used in organic electrochemistry such as DMSO and acetonitrile,[93] cyclic voltametry shows that an important side reaction is the abstraction of a hydrogen atom from the solvent by the aryl radical (step 6). (The solvent radical is further reduced at the electrode or in the solution).

Scheme 1.11

$$ArX + e^- \rightleftharpoons ArX^{\cdot -} \quad (1)$$

$$ArX^{\cdot -} \longrightarrow Ar^{\cdot} + X^- \quad (2)$$

$$Ar^{\cdot} + Nuc^- \longrightarrow ArNuc^{\cdot -} \quad (3)$$

$$ArNuc^{\cdot -} - e^- \rightleftharpoons ArNuc \quad (4)$$

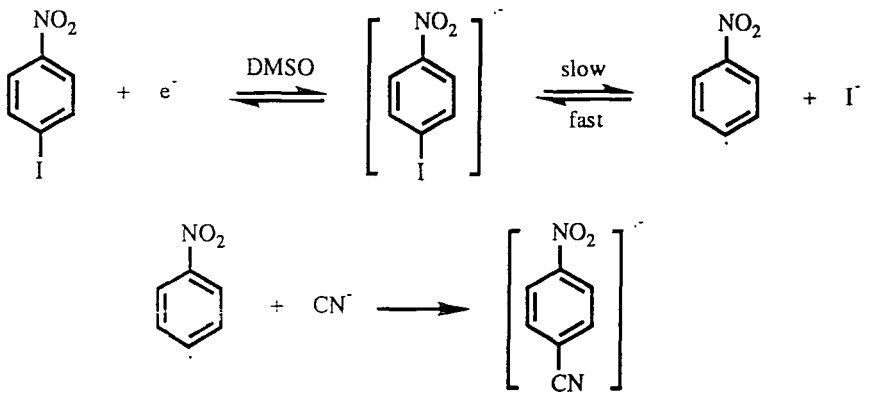
$$ArNuc^{\cdot -} + ArX \rightleftharpoons ArNuc + ArX^{\cdot -} \quad (5)$$

$$Ar^{\cdot} + Solv.H \longrightarrow ArH + Solv^{\cdot} \quad (6)$$

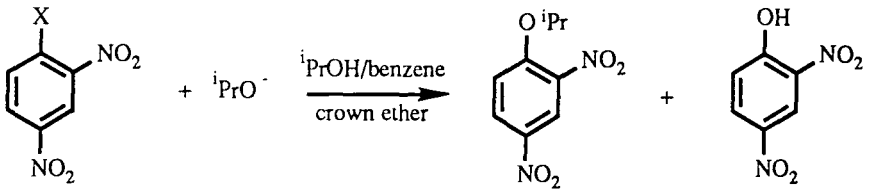
There is evidence from cyclic voltametry [93,94] and e.s.r. spectroscopy [94] for the substitution of halogens by cyanide *via* a $S_{RN}1$ mechanism (scheme 1.12).

Competition between normal nucleophilic aromatic substitution and single electron transfer pathways has been demonstrated [60] by the reactions of 1-chloro- and 1-iodo-2,4-dinitrobenzene (1.54) with potassium *iso*-propoxide in propan-2-ol/benzene in the presence of crown ethers (eqn.1.3.1).

Scheme 1.12



In the absence of crown ethers, the expected product of nucleophilic aromatic substitution, 1-*iso*-propoxy-2,4-dinitrobenzene (1.55), is obtained. The addition of crown ethers induces the formation, together with (1.55), of significant amounts of 2,4-dinitrophenol (1.56). The formation of (1.56) is accompanied by the appearance of an e.s.r. signal which has been assigned to the radical anion of the parent.



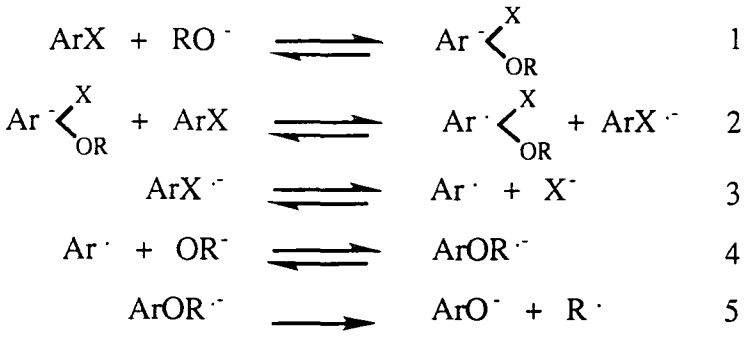
Eqn.1.3.1

(1.54, X = Cl, I) (1.55) (1.56)

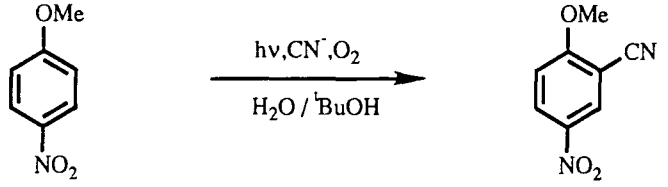
It is proposed that the mechanism of the phenol producing reaction is as shown in scheme 1.13. The sigma-complex (from step 1) may also evolve to give the normal substitution product (1.55). Alternatively the sigma-complex may donate an electron to the parent substrate producing the sigma-aryl radical and the radical anion of the parent (step 2). Production of the phenoxide anion of (1.56) from the radical anion of the parent then proceeds by reaction with alkoxide followed by fragmentation of the radical anion (steps 3-5).

Since the discovery and classification of the $S_{RN}1$ mechanism aromatic cyanations have been achieved by photochemically induced radical reactions.[91,95] Photocyanation of benzene and naphthalene can be performed in the presence of potassium cyanide and ammonium in a *tert*-butanol/water solvent.[95] With nitrobenzene, the cyanide ion does not give photosubstitution; instead the cyanide ion attacks the nitro group to form nitrosobenzene and the cyanate ion.[96] The methoxy group of *meta*-nitroanisole can be substituted by cyanide,[97] however, *para*-nitroanisole gives 2-cyano-4-nitroanisole.[98]

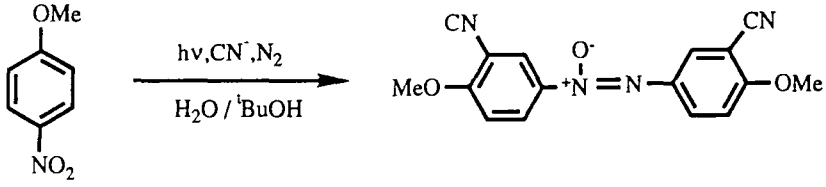
Scheme 1.13



Such selectivity for the position *meta* to the nitro group is because in the excited state this position is the most reactive. When cyanide attacks, a strong carbon-carbon bond is formed so the resulting intermediate survives long enough to react with oxygen to form 2-cyano-4-nitroanisole (eqn.1.3.2), or in the absence of oxygen, to disproportionate to form the azoxybenzene derivative (eqn.1.3.3). Note that preference for the position *meta* to the nitro group and *ortho* to the methoxy group is the opposite of the preference in normal nucleophilic aromatic substitution.[2]



Eqn.1.3.2



Eqn.1.3.3

1.3.2 Copper Effected Aromatic Substitution.

Nucleophilic aromatic substitution usually requires a suitable leaving group and activation of the ring by electron-withdrawing groups. Nucleophilic aromatic substitution on unactivated rings is relatively rare, but may be effected in the presence of copper.

There are two types of copper mediated reactions. In Ullmann condensations the copper is present as a metal, salt or oxide (eqn.1.3.4). The Rosenmund-von Braun nitrile synthesis is an example of this type; the bromo-derivatives of high-boiling point aromatic hydrocarbons are converted to their nitriles by treatment with a slight excess of

cuprous cyanide at 260°C.[6,7] Experiments in the solid phase [99] have made advances in unravelling the mechanism of this reaction.

$$NucH + ArX \xrightarrow{Cu^+} ArNuc + HX \qquad \text{Eqn.1.3.4}$$

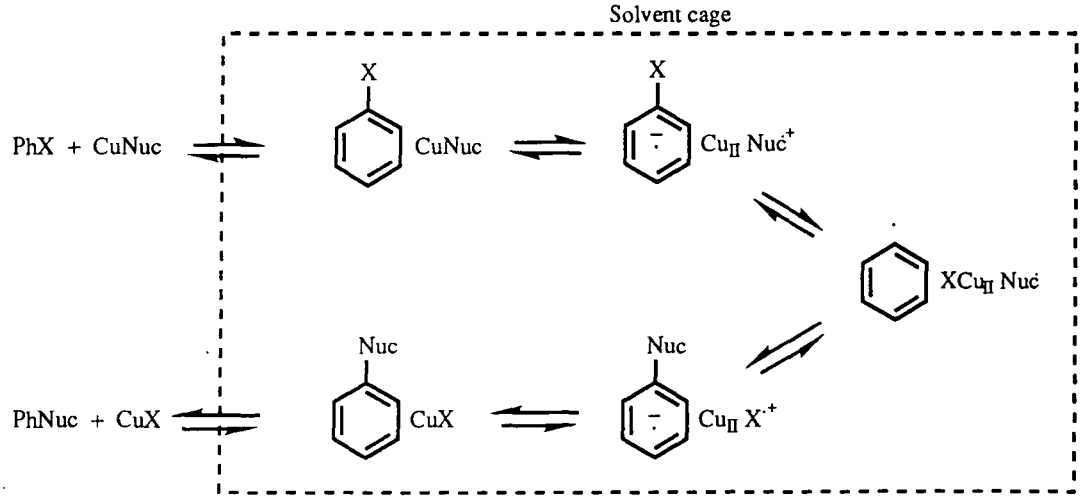
$$CuNuc + ArX \longrightarrow CuX + ArNuc \qquad \text{Eqn.1.3.5}$$

Nuc = Cl, Br, I, CN, SCN, OAc, OH, *etc.*
X = Cl, Br, I.

$$ArN_2Cl + KCu(CN)_2 \longrightarrow ArCN + N_2 + KCl + CuCN \qquad \text{Eqn.1.3.6}$$

Copper ligand exchange reactions use cuprous cyanide, which exchanges the cyanide for the leaving group of the aromatic substrate (eqn.1.3.5). The ligand exchange reaction has provoked the most interest but as yet the mechanism is not well understood. Recent work [100] has outlined a number of unusual characteristics of the reaction: autocatalysis by the copper halide product; retardation by both excess nucleophile and excess halide, *e.g.* as the potassium salts; only cuprous nucleophiles are active; a large halogen effect (I > Br > Cl) but a Hammett ρ value of zero; *ortho*-alkyl groups (even *tert*-butyl groups) do not hinder the reaction, but slightly accelerate it; and an *ortho*-carboxylate group accelerates the reaction by 10^4-10^5 times.

Scheme 1.14

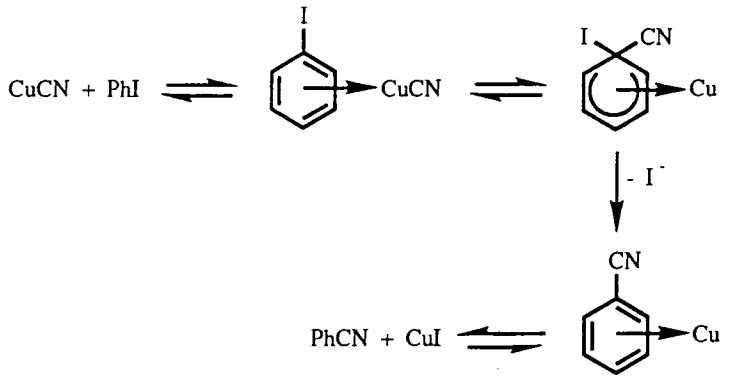


Two possible mechanisms are tentatively suggested. The first involves a very rapid "intimate" electron transfer from the cuprous nucleophile to the aromatic halide within a solvent cage (scheme 1.14); consequently no free radicals are observed. This produces the radical anion of the aromatic halide, which then exchanges nucleophiles with the copper to yield the radical anion of the aromatic product. Intimate electron

transfer occurs again from the product radical anion to the cuprous halide cation radical generating the observed product, which is then released from the solvent cage.

The second possibility proceeds *via* π-complexed organo-cuprate intermediates (scheme 1.15). The key intermediate is the 18-electron complex between the cuprous nucleophile and the six π-electrons of the aryl halide (cuprous ion is d_{10}). From this complex intramolecular attack of the nucleophile gives the tetrahedral intermediate, where the negative charge that would otherwise be borne in the ring, is neutralised by the 16-electron π-complexed copper atom, which sucks all of the excess electron density out of the ring. The rate determining step would be loss of halide, followed by rapid collapse to the final products.

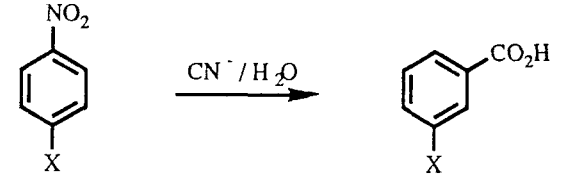
Scheme 1.15



The Sandmeyer reaction (eqn.1.3.6) uses aqueous solutions of cuprous cyanide and potassium cyanide to produce aromatic nitriles from the diazonium salts.[7,101] Other double salts can be used, and this reaction remains an important method for the preparation of aromatic nitriles.[102]

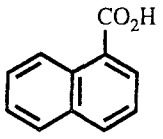
1.3.3 The Von Richter Reaction.

An aromatic nitro compound, when treated with cyanide ion, may give a substituted benzoic acid, [103,104] with the carboxyl group located *ortho* to the position vacated by the nitro group (eqn.1.3.7). Doubt that a rearranged *meta* nitrile was an intermediate first arose when Bunnett and Rauhut [105] were unable to obtain 1-naphthoic acid (1.57) from 1-naphthyl cyanide (1.58) under conditions which converted 2-nitronaphthalene (1.59) to (1.57).

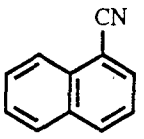


Eqn.1.3.7

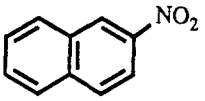
X = Cl, Br.



(1.57)



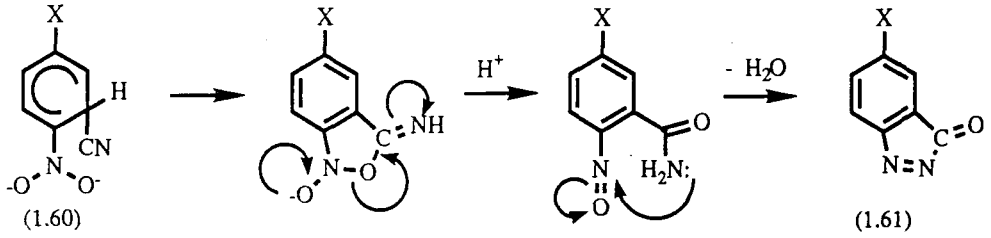
(1.58)



(1.59)

A mechanism that accounts for all the experimental observations to date [106] has been proposed [107] which proceeds *via* an intermediate sigma-complex (1.60).

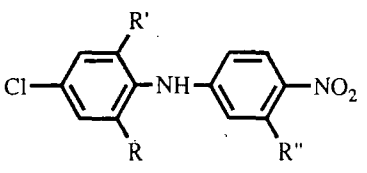
Scheme 1.16



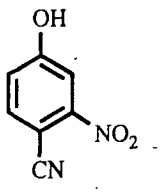
(1.60) (1.61)

It is proposed that an intramolecular cyclisation between an oxygen of the nitro group and the cyano carbon produces (1.61) *via* scheme 1.16. Basic hydrolysis followed by evolution of nitrogen gas gives the carboxylic acid product.

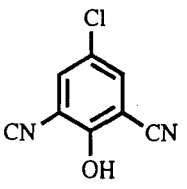
A wide variety of aromatic mono-nitro compounds will undergo the von Richter reaction in boiling alcoholic potassium cyanide.[108] However, *para*-chloronitrobenzene with excess potassium cyanide in DMSO produces five different products (1.62-64).[109] The phenols are not produced when the solvent is thoroughly dried. The initial intermediate is the sigma-complex (1.65). Reduction of (1.65) by intermolecular



(1.62 a) R = CN, R' = R'' = H,)
b) R = $CONH_2$, R' = R'' = H,)
c) R = R'' = $CONH_2$, R' = H.)



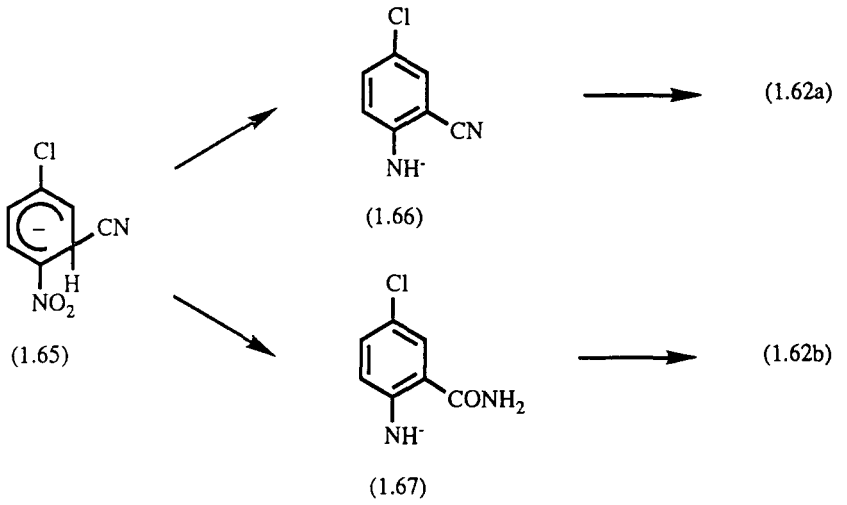
(1.63)



(1.64)

hydride transfer from (1.65) yields (1.66) (scheme 1.17). Intramolecular oxygen transfer from nitro group to nitrile group, followed by reduction produces (1.67). Condensation of (1.66) and (1.67) with parent yields (1.62a) and (1.62b) respectively. The mechanism for the formation of (1.62c) is unknown.

Scheme 1.17

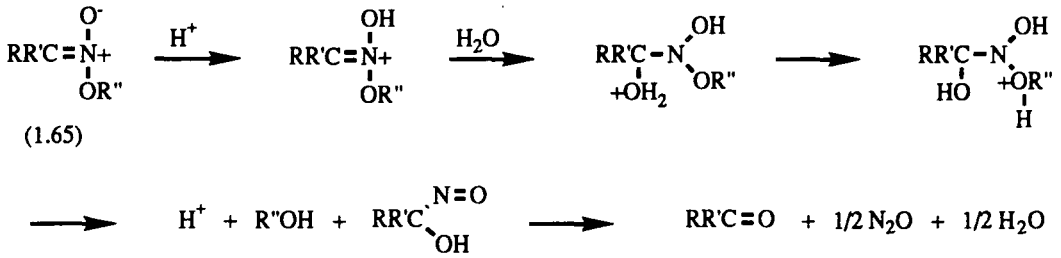


1.4 SUBSTITUTION OF A NITRO GROUP.

The reaction [89] of *meta*-dinitrobenzene with potassium cyanide in methanol yielding 2-methoxy-6-nitrobenzonitrile is considered later (chapter 4).

1.4.1 The Nef Reaction.

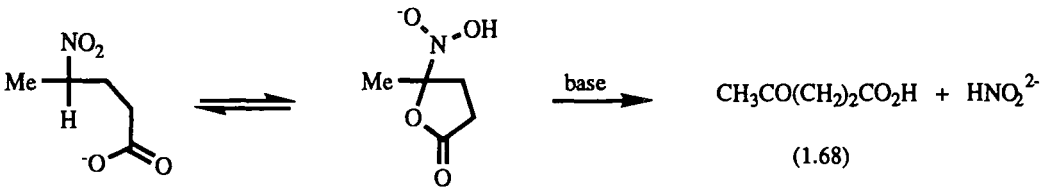
Scheme 1.18



(1.65)

One of the most important reactions of nitro-alkanes is the Nef reaction.[110,111] This reaction is the hydrolysis of a nitronic acid or ester (1.65) derived from a primary or secondary nitro-alkane to yield an aldehyde or a ketone, characteristically with the expulsion of nitrous oxide gas. The Nef reaction is usually thought of as an acid-catalysed transformation [112,113] (scheme 1.18), but there is kinetic evidence [114] that the formation of levalinic acid (1.68) from 4-nitrovalerate (1.66) is an example of the Nef reaction occuring in basic media (scheme 1.19).

Scheme 1.19



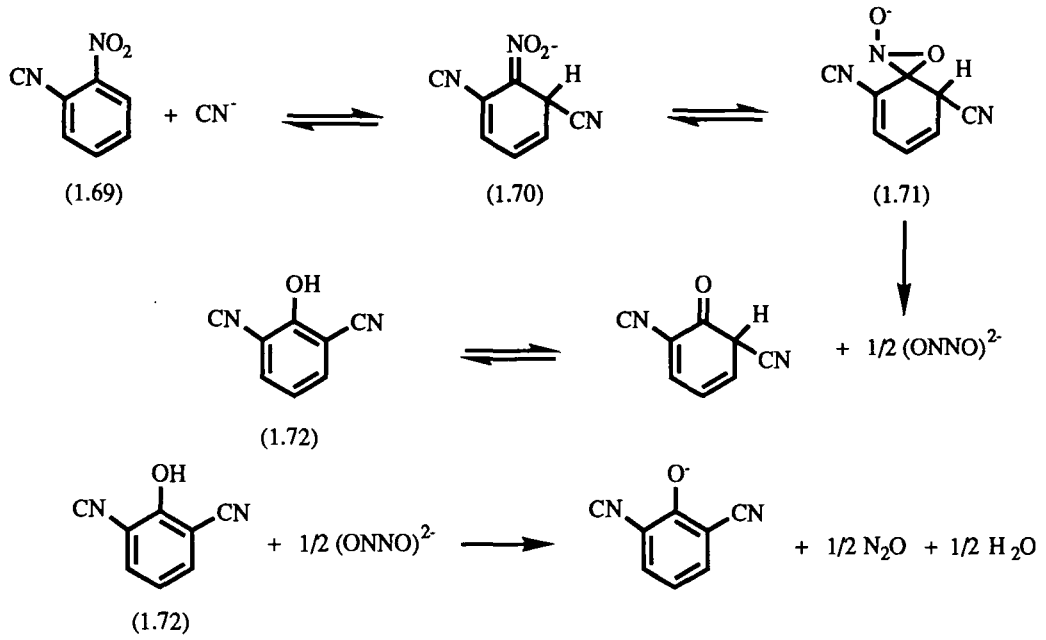
(1.66) (1.67) (1.68)

1.4.2 Hydroxydenitration Using Cyanide.

Such a Nef-type transformation in basic solution has been proposed [115] in explanation of the formation of 2-hydroxyisophthalonitrile (1.72) by the action of sodium cyanide on *ortho*-nitrobenzonitrile (1.69) in DMSO (scheme 1.20). The key step in the reaction may be the ejection of hyponitrite ion from the sigma-type adduct

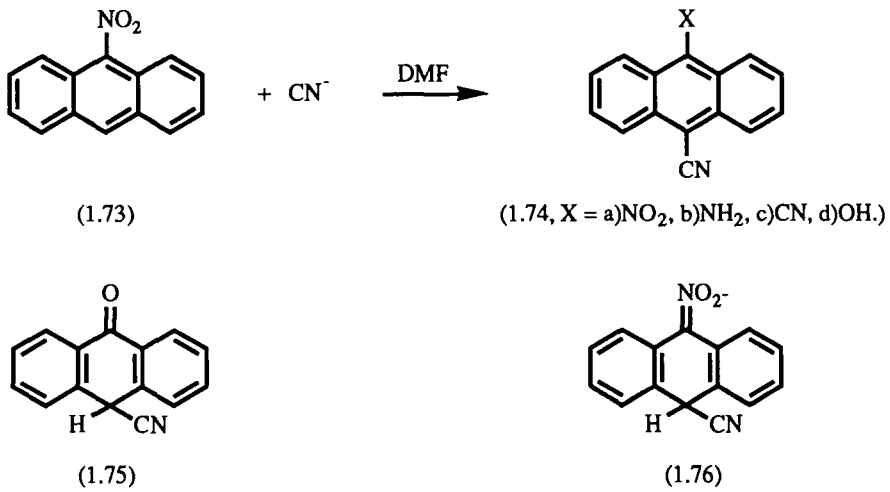
(1.70), perhaps *via* the oxiridine isomer (1.71), leading to the hydroxyisophthalonitrile (1.72) which can liberate nitrous oxide by protonating the hyponitrite anion.

Scheme 1.20



Treatment of 9-nitroanthracene (1.73) with sodium cyanide in DMF under nitrogen at room temperature results in the formation of a series of compounds [116] (scheme 1.21): 9-cyano-10-nitroanthracene (1.74a), 9-amino-10-cyanoanthracene (1.74b), 9,10-dicyanoanthracene (1.74c), 9-cyano-10-anthranol (1.74d) and 9-cyano-10-anthrone (1.75).

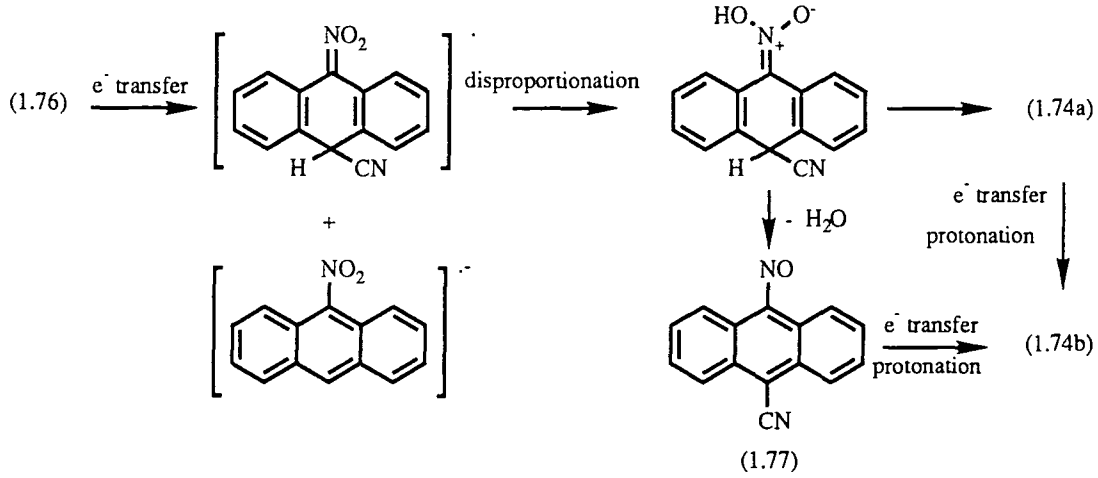
Scheme 1.21



When the reaction was allowed to proceed in an oxygen atmosphere, anthraquinone was also formed. A sample of (1.73) in the presence of cyanide ion in DMF gave rise to an

e.s.r. signal which reached maximum intensity after 45 minutes and then grew weaker until it was of negligible intensity after 3 hours. The variety of products observed suggests a complicated series of simultaneous and consecutive processes. The initial step is the formation of the sigma-complex (1.76). Species (1.74) are oxidation and reduction products of (1.76) (scheme 1.22). 9-Nitroanthracene is known to be a good electron acceptor [117] and furthermore (1.74) and (1.77) may also compete for electrons.[116]

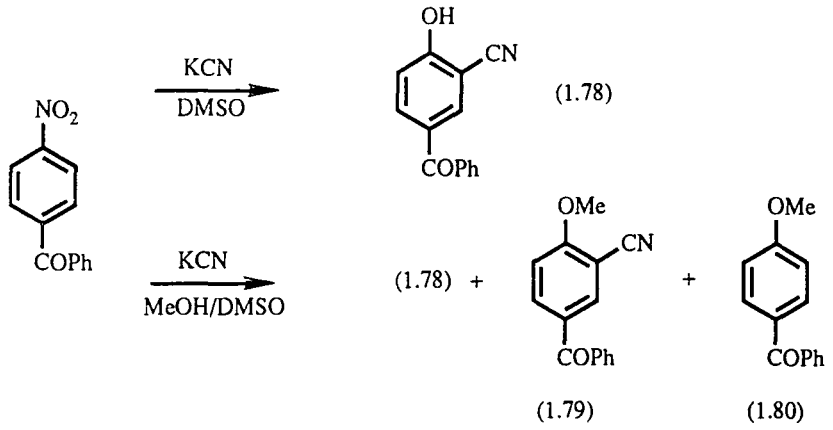
Scheme 1.22



Other simple benzene derivatives [115] (*e.g. meta*-nitrobenzonitrile, nitrobenzene and *para*-dinitrobenzene) all give strong e.s.r. signals on reaction with sodium cyanide in DMSO, but give deeply coloured reaction solutions from which no pure compounds can be isolated, probably because the radical process converts each substrate into a large number of products. In contrast, a solution of *ortho*-nitrobenzonitrile (1.69) and sodium cyanide gives no detectable e.s.r. signal, suggesting that the adduct (1.70) is rapidly removed from the solution by another process (*e.g.* scheme 1.20).

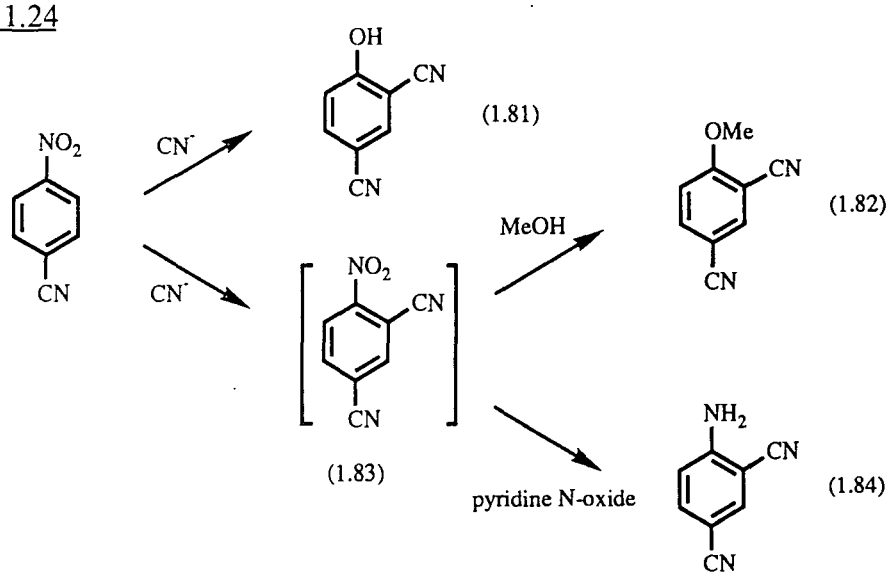
More recently [118,119] hydroxydenitration by a Nef-type process has been postulated as a general pathway from activated mono-nitroaromatics to activated phenols. Thus, in a typical reaction,[118] when 4-nitrobenzophenone is heated with potassium cyanide (3 moles) in DMSO at 100°C for 3 hours the acidic fraction of the product consists of 5-benzoylsalicylonitrile (1.78) (55-60%) (scheme 1.23); a complex mixture of azoxy- and azo-compounds are formed as a neutral fraction. If methanol (10 moles) is added to the initial reaction mixture the yield of (1.78) is reduced and the neutral azo-fraction contains 5-benzoyl-2-methoxybenzonitrile (1.79) (10%) in addition to 4-methoxybenzophenone (1.80). Similarly, in DMSO, the reaction of *para*-nitrobenzonitrile with cyanide [120] yields 2,4-dicyanophenol (1.81) as the major product. In the presence of methanol, 2,4-dicyanoanisole (1.82) is also formed.

Scheme 1.23



In their reaction with moderately activated nitro-compounds in DMSO, cyanide ions resemble aromatic nitranions [121-3] in that direct displacement of NO_2 is impeded; initial attack normally occurs *ortho* to the nitro group.[115,118,119] There is recent synthetic evidence [121] that suggests *ortho*-nitrobenzonitriles (1.83) exist transiently in these systems before reacting with methoxide, hydride or other trapping agents to yield the observed products (1.82, 1.84) (scheme 1.24).

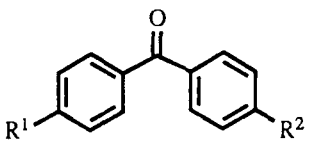
Scheme 1.24



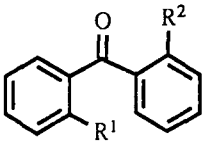
1.4.3 Methoxydenitration.

Aromatic nitro-groups, if sufficiently activated by *ortho* or *para*-carbonyl groups, are displaced by oxy-anions in dipolar aprotic solvents.[124] In DMSO, the benzophenones (1.85a), (1.86a) and (1.87a) react [125] with stoichiometric amounts of methanolic sodium methoxide to yield (1.85c), (1.86b) and (1.87d) *via* isolable

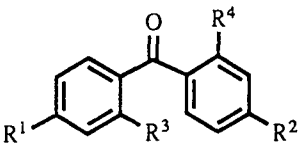
intermediates such as (1.85b) and (1.87b). In 2,2',4,4'-tetranitrobenzophenone (1.87a) the *para*-nitro groups are preferentially displaced.



(1.85, a) $R^1 = R^2 = NO_2$)
b) $R^1 = OMe$, $R^2 = NO_2$)
c) $R^1 = R^2 = OMe$)



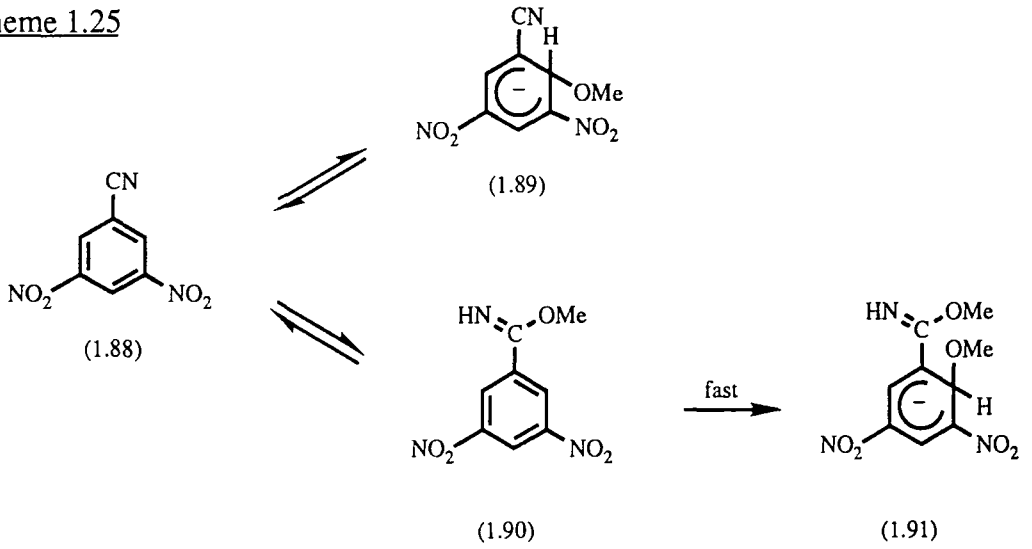
(1.86, a) $R^1 = R^2 = NO_2$)
b) $R^1 = OMe$, $R^2 = NO_2$)



(1.87, a) $R^{1-4} = NO_2$)
b) $R^1 = OMe$, $R^{2-4} = NO_2$)
c) $R^1 = R^2 = OMe$, $R^3 = R^4 = NO_2$)
d) $R^{1-3} = OMe$, $R^4 = NO_2$)

Addition of a large excess of methanolic methoxide to 3,5-dinitrobenzonitrile (1.88) [126] results in the immediate formation of the methoxy sigma-complex (1.89). There is also slower attack of the cyano group by methoxide to yield the imidate (1.90),[127] which in high concentrations of methoxide remains activated enough to form the sigma complex (1.91) (scheme 1.25). Solvation of aromatic cyano groups by methoxide is discussed further in chapter 4.

Scheme 1.25



(1.88) (1.89) (1.90) (1.91)

1.5 REFERENCES

1 F.Terrier, *Chem. Revs.*, (1982), **82**, 77.

2 E.Buncel, M.R.Crampton, M.J.Strauss & F.Terrier, *"Electron Deficient Aromatic- and Heteroaromatic-Base Interactions"*, Elsevier, Oxford, 1984.

3 C.L.Jackson & F.H.Gazzalo, *Amer. Chem. J.*, (1900), **29**, 376.

4 J.Meisenheimer, *Ann.*, (1902), **323**, 205.

5 M.J.Strauss, *Chem. Revs.*, (1970), **70**, 667.

6 J.F.Bunnett & R.E.Zahler, *Chem. Revs.*, (1951), **49**, 273.

7 D.T.Mowry, *Chem. Revs.*, (1948), **42**, 189.

8 M.R.Crampton & V.Gold, *J. Chem. Soc.*, (1964), 4293.

9 R.Foster & C.A.Fyfe, *Tetrahedron*, (1965), **21**, 3363.

10 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1971), **49**, 2490.

11 C.F.Bernasconi & R.G.Bergstrom, *J. Am. Chem. Soc.*, (1974), **96**, 2397.

12 M.R.Crampton & J.A.Stevens, *J. Chem. Soc., Perkin Trans. II*, (1990), 1097.

13 C.F.Bernasconi, *J. Am. Chem. Soc.*, (1971), **93**, 6975.

14 K.L.Servis, *J. Am. Chem. Soc.*, (1967), **89**, 1508.

15 F.Terrier, J.C.Hall & M.P.Simmonis, *Org. Magn. Reson.*, (1971), **3**, 361.

16 J.H.Fendler, E.J.Fendler, W.E.Byrne & C.E.Griffin, *J. Org. Chem.*, (1968), **33**, 977.

17 R.Schaal, F.Terrier, J-C.Halle & A-P.Chatrousse, *Tetrahedron Lett.*, (1970), **17**, 1393.

18 C.A.Fyfe, *Tetrahedron Lett.*, (1968), **6**, 659.

19 C.F.Bernasconi, *Acc. Chem. Res.*, (1978), **11**, 147.

20 M.J.Strauss, *Acc. Chem. Res.*, (1974), **7**,181.

21 T.Abe, *Bull. Chem. Soc. Jpn.*, (1964), **37**, 508.

22 T.Abe, *Bull. Chem. Soc. Jpn.*, (1966), **39**, 627.

23 P.Caveng, P.B.Fischer, E.Heilbronner, A.L.Miller & H.Zollinger, *Helv. Chim. Acta,* (1967), **50**, 848.

24 H.Hoseya, S.Hoseya & S.Nagakura, *Theor. Chim. Acta*, (1968), **12**, 117.

25 H.Wennerstrom & O.Wennerstrom, *Acta Chem. Scand.*, (1972), **26**, 2883.

26 A.J.Birch, A.L.Hinde & L.Radom, *J. Am. Chem. Soc.*, (1980), **102**, 6430.

27 A.Pross & L.Radom, *Progress in Phys. Org. Chem.*, Wiley-Interscience, (1981), **13**, 1.

28 H.Ueda, N.Sakeabe, J.Tanaka & A.Furasaki, *Bull. Chem. Soc. Jpn.*, (1968), **41**, 2866.

29 M.R.Crampton, *Adv. Phys. Org. Chem.*, (1969), **7**, 211.

30 C.F.Bernasconi, *J. Am. Chem. Soc.*, (1970), **92**, 4682.

31 E.Buncel, *Supp.F, The chemistry of amino, nitroso, and nitro compounds and their derivatives., Part 2*, Ed. S.Patai, J.Wiley & Sons, Chichester, (1982), 1225.
32 M.R.Crampton & H.A.Khan, *J. Chem. Soc., Perkin Trans. II*, (1972), 1173.
33 M.R.Crampton, M.A.Ghariani & H.A.Khan, *J. Chem. Soc., Perkin Trans. II*, (1972), 1178.
34 J.H.Feudler, W.L.Hinze & L.J.Liu, *J. Chem. Soc., Perkin Trans. II*, (1975), 1751.
35 P.Ballinger & F.A.Long, *J. Am. Chem. Soc.*, (1960), **82**, 795.
36 M.R.Crampton, *J. Chem. Soc., B*, (1968), 1208.
37 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1974), **52**, 1.
38 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1974), **52**, 8.
39 M.R.Crampton & B.Gibson, *J. Chem. Soc., Perkin Trans. II*, (1980), 752.
40 R.H.de Rossi, O.D.Madoery & E.B.de Vargas, *J. Org. Chem.*, (1980), **45**, 649.
41 A.R.Norris, *Can. J. Chem.*, (1980), **58**, 2178.
42 C.H.Rochester, *J. Chem. Soc.*, (1965), 2404.
43 H.J.Shine, *Aromatic Rearrangements*, Elsvier, New York, (1967), 307.
44 M.J.Strauss & F.Terrier, *Tetrahedron Lett.*, (1979), 313.
45 E.Buncel & B.C.Menon, *J. Am. Chem. Soc.*, (1980), **102**, 3499.
46 E.Buncel, K.E.Russel & J.Ward, *Chem. Comm.*, (1968), 252.
47 C.A.Fyfe, C.D.Malkiewich, S.W.H.Damji & A.R.Norris, *J. Am. Chem. Soc.*, (1976), **98**, 6983.
48 E.Buncel & E.A.Symons, *J. Org. Chem.*, (1973), **38**, 1201.
49 M.R.Crampton & V.Gold, *J. Chem. Soc., B*, (1966), 498.
50 E.Buncel & A.W.Zabel, *Can. J. Chem.*, (1981), 3168.
51 E.Buncel & A.W.Zabel, *Can. J. Chem.*, (1981), 3177.
52 R.Bacaloglu, C.A.Bunton & G.Cerichelli, *J. Am. Chem. Soc.*, (1987), **109**, 621,
53 R.Bacaloglu, C.A.Bunton & F.Ortega, *J. Am. Chem. Soc.*, (1988), **110**, 3495.
54 R.Bacaloglu, C.A.Bunton & F.Ortega, *J. Am. Chem. Soc.*, (1988), **110**, 3503.
55 S.K.Dotterer & R.L.Harris, *J. Org. Chem.*, (1988), **53**, 777.
56 G.A.Russell & E.G.Janzen, *J. Am. Chem. Soc.*, (1962), **84**, 4153.
57 G.A.Russell , E.G.Janzen & E.T.Strom, *J. Am. Chem. Soc.*, (1962), **84**, 4155.
58 G.A.Russell , E.G.Janzen & E.T.Strom, *J. Am. Chem. Soc.*, (1964), **86**, 1807.
59 J.F.Bunnett, *Acc. Chem. Res.*, (1978), **11**, 413.
60 C.Mariani, G.Modena, G.P.Pizzo, G.Scorrano & L.Kistenbrugger, *J. Chem. Soc., Perkin Trans. II*, (1979), 1187.
61 E.Tommila & J.Murto, *Acta Chem. Scand.*, (1962), **16**, 53.
62 I.R.Bellobono, A.Gamba, G.Sala & M.Tompieri, *J. Am. Chem. Soc.*, (1972), **94**, 5781.
63 T.Abe & Y.Ikegami, *Bull. Chem. Soc. Jpn.*, (1976), **49**, 3227.

64 T.Abe & Y.Ikegami, *Bull. Chem. Soc. Jpn.*, (1978), **51**, 196.
65 A.Sauer, F.Wagestian & B.Barabasch, *J. Chem. Soc., Perkin Trans. II*, (1990), 1317.
66 A.Sauer, F.Wagestian & U.Nickel, *Bull. Chem. Soc. Jpn.*, (1989), **62**, 2688.
67 L.Eberson, *Acta Chem. Scand., Ser. B*, (1984), **38**, 439.
68 D.M.Stanbury, *Adv. Inorg. Chem.*, (1989), **33**, 70.
69 R.Bacaloglu, C.A.Bunton & F.Ortega, *J. Am. Chem. Soc.*, (1988), **110**, 3513.
70 R.Bacaloglu, C.A.Bunton & F.Ortega, *J. Am. Chem. Soc.*, (1989), **111**, 1041.
71 M.R.Crampton, A.B.Davies, C.Greenhalgh & A.J.Stevens, *J. Chem. Soc., Perkin Trans. II*, (1989), 675.
72 S.K.Dotterer & R.L.Harris, *J. Org. Chem.*, (1988), **53**, 777.
73 J.F.J.Engberson, A.Koudijs, H.M.Sleiderink & M.C.R.Franssen, *J. Chem. Soc., Perkin Trans. II*, (1990), 79.
74 F.G.Bordwell & D.L.Hughes, *J. Am. Chem. Soc.*, (1986), **108**, 5991.
75 C.F.Bernasconi, *Tetrahedron*, (1989), **45**, 4017.
76 A.R.Norris, *Can. J. Chem.*, (1967), **45**, 2703.
77 E.Buncel, A.R.Norris, W.Proudlock & K.E.Russel, *Can. J. Chem.*, (1969), **47**, 4129.
78 R.Alexander, E.C.F.Ko, A.J.Parker & T.J.Broxton, *J. Am. Chem. Soc.*, (1968), **90**, 5049.
79 E.Buncel, A.R.Norris & K.E.Russel, *Can. J. Chem.*, (1968), **46**, 2759.
80 A.R.Norris, *Can. J. Chem.*, (1969), **47**, 2895.
81 J.Hine, L.G.Mahone & C.L.Liotta, *J. Am. Chem. Soc.*, (1967), **89**, 5911.
82 J.Kavalek, I.Kolb, V.Machacek & V.Sterba, *Collect. Czech. Chem. Commun.*, (1975), **40**, 3879.
83 M.E.Moir & A.R.Norris, *Can. J. Chem.*, (1980), **58**, 1691.
84 E.Buncel, N.Chuaqui-Offermanns & A.R.Norris, *J. Chem. Soc., Perkin Trans. I*, (1977), 415.
85 L.H.Gan, *Aust. J. Chem.*, (1985), **38**, 1141.
86 A.Kaufmann & A.Albertini, *Ber.*, (1909), **42**, 3776.
87 A.Kaufmann & A.Albertini, *Ber.*, (1911), **44**, 2052.
88 P.Ehrlich & L.Benda, *Ber.*, (1913), **46**, 1931.
89 A.Russell & G.Tebbens, *Org. Synth., Coll. Vols.*, **3**, 293.
90 V.von Richter, *Ber.*, (1911), **44**, 3472.
91 J.K.Kim & J.F.Bunnett, *J. Am. Chem. Soc.*, (1970), **92**, 7463 & 7465.
92 C.Amatore, C.Combellas, S.Robveille, J-M.Saveant & A.Thiebault, *J. Am. Chem. Soc.*, (1986), **108**, 4754.
93 C.Amatore, J.Pinson, J-M.Saveant & A.Thiebault, *J. Am. Chem. Soc.*, (1982), **104**, 817.

94 D.E.Bartak, W.C.Danen & M.D.Hawley, *J. Org. Chem.*, (1970), **35**, 1206.
95 J.Cornelisse & E.Havinga, *Chem. Revs.*, (1975), **75**, 353.
96 W.C.Petersen & R.L.Letsinger, *Tetrahedron Lett.*, (1971), 2197.
97 R.L.Letsinger & J.H.McCain, *J. Am. Chem. Soc.*, (1966), **88**, 2884.
98 R.L.Letsinger & J.H.McCain, *J. Am. Chem. Soc.*, (1969), **91**, 6425.
99 J.H.Clark *et.al.*, *J.Chem.Soc., Chem. Comm.*, (1986), 877.
100 C.Couture & A.J.Paine, *Can. J. Chem.*, (1985), **63**, 111.
101 K.Friedrich & K.Wallenfels, *The chemistry of the cyano group*, (Ed. Z.Rappoport), Interscience, London, (1970).
102 H.H.Hodgeson, *Chem. Revs.*, (1947), **40**, 251.
103 V.von Richter, *Ber.*, (1874), **7**, 1145.
104 V.von Richter, *Ber.*, (1875), **8**, 1418.
105 J.F.Bunnnett & M.M.Rauhut, *J. Org. Chem.*, (1956), **21**, 944.
106 J.Casanova, *The chemistry of the cyano group*, (Ed. Z.Rappoport), Interscience, London, (1970), 885.
107 M.Rosenblum, *J. Am. Chem. Soc.*, (1960), **82**, 3796.
108 J.F.Bunnett, J.F.Cormack & F.C.McKay, *J. Org. Chem.*, (1950), **15**, 481.
109 G.T.Rogers & T.L.V.Ulbricht, *Tetrahedron Lett.*, (1968), **9**, 1029.
110 E.Breuer, *Supp.F, The chemistry of amino, nitroso, and nitro compounds and their derivatives., Part 1*, Ed. S.Patai, J.Wiley & Sons, Chichester, (1982).
111 W.E.Noland, *Chem. Revs.*, (1955), **55**, 136.
112 M.F.Hawthorne, *J. Am. Chem. Soc.*, (1957), **79**, 2510.
113 N.Kornblum & R.A.Brown, *J. Am. Chem. Soc.*, (1965), **87**, 1742.
114 H.Wilson & E.S.Lewis, *J. Am. Chem. Soc.*, (1972), **94**, 2283.
115 R.B.Chapas, R.D.Knudsen, R.F.Nystrom & H.R.Snyder, *J. Org. Chem.*, (1975), **40**, 3746.
116 R.G.Landolt & H.R.Snyder, *J. Org. Chem.*, (1968), **33**, 403.
117 A.Ishitani & S.Nagakura, *Bull. Chem. Soc. Jpn.*, (1965), **38**, 367.
118 J.H.Gorvin, *J. Chem. Soc., Chem. Comm.*, (1971), 1120.
119 J.H.Gorvin, *J. Chem. Soc., Chem. Comm.*, (1976), 972.
120 J.H.Gorvin, *J. Chem. Res.*, (1991), (S) 88, (M) 738.
121 J.H.Gorvin, *J. Chem. Res.*, (1990), (S) 198, (M) 1662.
122 J.H.Gorvin, *J. Chem. Soc., Perkin Trans. I*, (1988), 1331.
123 J.H.Gorvin, *J. Chem. Soc., Chem. Comm.*, (1985), 238.
124 J.H.Gorvin, *Chem. & Ind.*, (1967), 1525.
125 J.H.Gorvin & D.P.Whalley, *J. Chem. Soc., Perkin Trans. I*, (1979), 1365.
126 E.J.Fendler, J.H.Fendler, N.L.Arthur & C.E.Griffin, *J. Org. Chem.*, (1972), **37**, 812.
127 T.Abe, *Bull. Chem. Soc. Jpn.*, (1983), **56**, 1206.

CHAPTER 2

EXPERIMENTAL.

2.1 MATERIALS.

2.1.1. Solvents.

Acetone:	General purpose reagent was used for washing apparatus.
Acetonitrile:	B.D.H. "HiPerSolv" was used for HPLC after filtration and degassing. Analytical grade was used for uv/vis spectroscopy without further treatment.
Chloroform:	Analytical grade, used without further treatment.
d-Chloroform:	99.8% D-atom, commercial grade, used as supplied.
Cyclohexane:	Analytical grade, used without further treatment.
Dichloromethane:	General purpose reagent, used without further treatment.
Dimethylsulphoxide:	Analytical grade, dried with calcium hydride then distilled at reduced pressure.
d_6-DMSO:	99.9% D-atom, commercial grade, used as supplied.
p-Dioxan:	Commercial grade, used without further treatment.
Ethanol:	Analytical grade, used without further treatment.
Methanol:	Analytical grade, used without further treatment.
d_4-Methanol:	99.8% D-atom, commercial grade, used as supplied.
Petroleum Spirit:	(b.pt. 60-80°C), commercial grade, used without further treatment.
iso-Propanol:	Analytical grade, used without further treatment.
Water:	Distilled, filtered and degassed for HPLC.

2.1.2. Substrates.

1-Bromo-2,4-dinitrobenzene:	Commercial grade, used as supplied.
1-Chloro-2,4-dinitrobenzene:	Commercial grade, used as supplied.
2,4-Dimethoxybenzonitrile:	Commercial grade, used as supplied.
2,6-Dimethoxybenzonitrile:	Commercial grade, used as supplied.
2,4-Dinitroanisole:	Commercial grade, used as supplied.
meta-Dinitrobenzene:	Commercial grade, used as supplied.

2,6-Dinitrobenzonitrile:	From I.C.I., m.pt. 147°C (lit:[2] 149-51°C).
1-Fluoro-2,4-dinitrobenzene:	Commercial grade, used as supplied.
1-Iodo-2,4-dinitrobenzene:	Commercial grade, used as supplied.
2-Methoxy-4-nitrobenzonitrile:	From I.C.I., m.pt. 158-60°C (lit:[3,4] 180°C).
2-Methoxy-6-nitrobenzonitrile:	From I.C.I., m.pt. 175°C (lit:[5] 175-7°C).
4-Methoxy-2-nitrobenzonitrile:	From I.C.I., m.pt. 138°C (lit:[6] 139°C).
Picric Acid:	Commercial grade, used as supplied.
1,3,5-Trinitrobenzene:	Commercial grade, used as supplied.

2.1.3 Reagents.

Potassium Cyanide:	Commercial grade, used as supplied.
Sodium Cyanide:	Commercial grade, used as supplied.
Sodium Methoxide:	Commercial grade sodium metal dissolved in methanol.
Hydrochloric Acid:	37% Aqueous solution, analytical grade, used as supplied.

2.2 MEASUREMENT TECHNIQUES.

2.2.1 UV/Vis Spectrophotometry.

All uv/vis spectra were recorded using fresh solutions in 1cm quartz cells on either Perkin-Elmer Lambda 2 or Lambda 3 instruments. These same instruments were also used for kinetic and equilibrium measurements (made at 25°C), except in the case of the fast reactions, in which case the stopped-flow spectrophotometer was used (see below).

All kinetic measurements were made under pseudo first order conditions and observed rate coefficients were determined by following the change in absorbance at an appropriate wavelength. Absorbance values measured on the Lambda 3 instrument were entered into a suitable program running on an Apple IIe microcomputer; those from the Lambda 2 instrument were entered into a suitable program running on an Epson personal computer. These programs calculated the observed rate coefficient based on the following derivation (calculation 2.1).

Calculation 2.1

For a decrease in absorbance:

$$\frac{-d[A]}{dt} = k_{obs}[A] \qquad [A] = \text{absorbance}$$

$$\int_{[A]_0}^{[A]_t} \frac{d[A]}{[A]} = -k_{obs}\int_0^t dt$$

$$\ln\left\{\frac{[A]_t}{[A]_0}\right\} = -k_{obs}.t$$

$[A]_0$ = initial absorbance

$[A]_t$ = absorbance at time t

Assuming absorbance does not fade to zero, $[A]_0$ becomes $([A]_0-[A]_\infty)$ and $[A]_t$ becomes $([A]_t-[A]_\infty)$ where $[A]_\infty$ is the absorbance at "infinite" time. Therefore:

$$\ln\left\{\frac{([A]_t-[A]_\infty)}{([A]_0-[A]_\infty)}\right\} = -k_{obs}.t$$

$$([A]_0-[A]_\infty) = \text{constant}$$

Thus a plot of $\ln([A]_t-[A]_\infty)$ *vs.*time has a gradient of $-k_{obs}$. If following an increase in absorbance a plot of $\ln([A]_\infty-[A]_t)$ *vs.*time has a gradient of $-k_{obs}$.

For measurements of rate coefficients of reactions too fast for the conventional machines a Hi-Tech Scientific SF-3L stopped-flow spectrophotometer was used. This is shown schematically in fig.2.1.

The two solutions A and B, which undergo reaction, are stored in glass reservoirs, and from there enter identical syringes, so that equal volumes of each solution are mixed at point M (halving the concentration of each solution) before passing into a thermostatted 2mm quartz cell at point O. When the plunger of the third syringe hits the stop the flow of reactants stops and the trigger causes monitoring of the reaction at O to begin. This is accomplished by passing a beam of monochromatic light of the appropriate wavelength through the cell. The reaction within the cell causes an increase or decrease in the transmitted light which is fed through a photomultiplier and displayed on an oscilloscope screen, from where voltage changes can be read. Although the output of the photomultiplier is not linear, for a small percentage change the voltage can be assumed to be proportional to the absorbance of the reaction mixture, and therefore a plot of log $(V_t - V_\infty)$ *vs.* time gives k_{obs} from gradient.

2.2.2 Mass Spectrometry.

Mass spectrometric measurements were made using a 7070E instrument supplied by V.G.Analytical Ltd. Electron ionisation, chemical ionisation or direct current ionisation methods were employed, the most suitable for any compound being determined empirically.

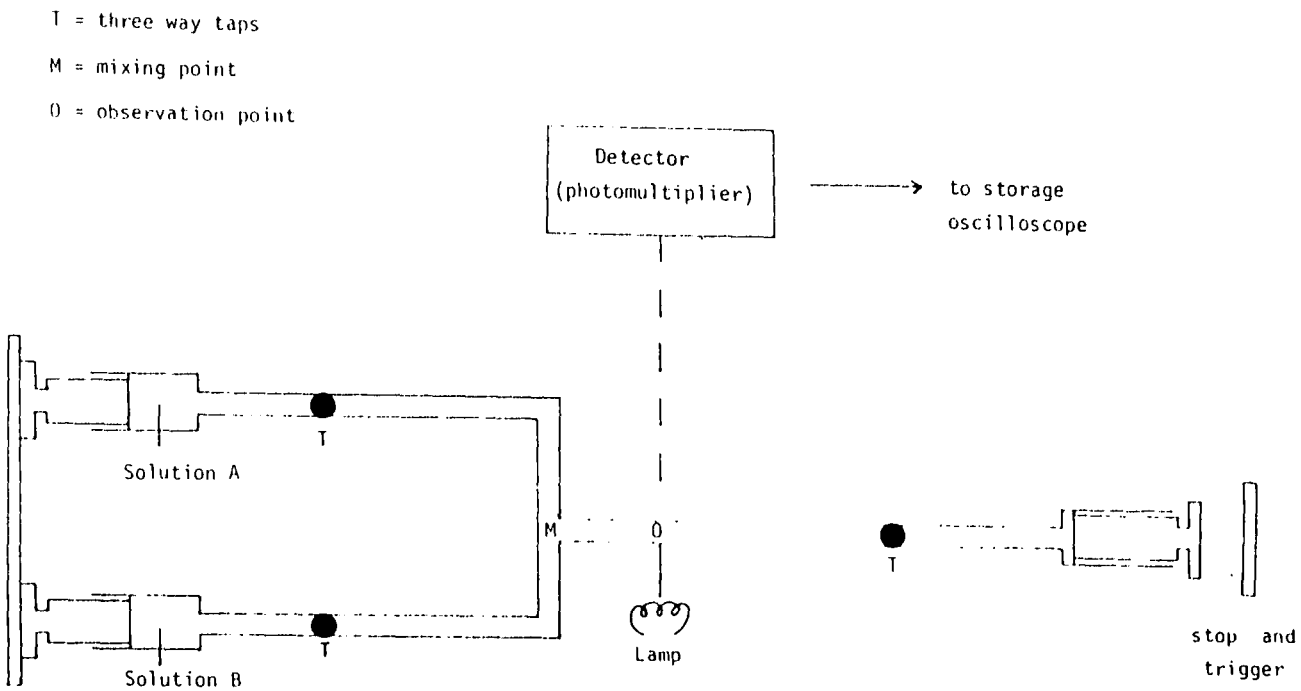
2.2.3 NMR Spectrometry.

Proton NMR spectra were recorded on either a Bruker AC250 (250MHz) or a Varian 400MHz instrument. Chemical shift measurements are quoted as "δ" values relative to tetramethylsilane (TMS).

2.2.4 HPLC Measurements.

Reverse-phase HPLC was performed using a Gilson Modular Gradient HPLC System, with an ODS-2 column supplied by HiChrome. For all HPLC runs an isocratic eluent (35%/65% v/v acetonitrile/water) was used with a flow of 2ml/min and an observing wavelength of 240nm. Identification was by doping experiments, and molar

Figure 2.1 Schematic representation of stopped-flow UV/visible spectrophotometer



ratios of products were found by comparing signal areas in the product mixture with signal areas of samples of known concentration.

2.2.5 Electron Spin Resonance Spectrometry.

E.S.R. spectra were recorded on a Bruker ESP 300 and Varian E-104 spectrometers, each equipped with X-band microwave bridges and 100KHz modulation. Hyperfine splittings were measured directly from the field scan, which had previously been calibrated with a signal from an aqueous solution of Fremy's salt (a_N=1.3091mT, g=2.0055).

2.2.6 Polarography.

Polarography experiments were performed on a Metrohm polarographer. The reference used was silver/silver chloride in aqueous potassium chloride (3M). The electrodes and background electrolytes used in the experiments are given in the text.

2.3 REFERENCES.

1 R.S.Storrie, *J. Chem. Soc.*, (1937), 1746.

2 J.R.Beck, *J. Org. Chem.*, (1972), **37**, 3224.

3 A.H.Cook, I.M.Heilbron, K.J.Reed & M.N.Stachan, *J. Chem. Soc.*, (1945), 861.

4 R.D.Clinton & S.C.Laskowski, *Am. Chem.*, (1952), **74**, 2226.

5 J.R.Beck, R.L.Sobczak, R.G.Suhr & J.A.Yahner, *J. Org. Chem.*, (1974), **39**, 1839.

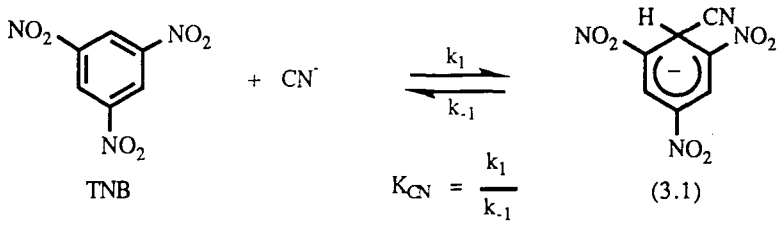
6 M.Jubault & D.Peltier, *Bull. Soc. Chim. Fr.*, (1972), 2365.

CHAPTER 3

THE REACTION OF CYANIDE WITH TRINITRO SUBSTRATES.

3.1 INTRODUCTION.

It is well documented that cyanide adds reversibly to 1,3,5-trinitrobenzene (TNB) to yield a 1:1 sigma-complex (3.1) in many solvents (section 1.2) (eqn.3.1).[1] However there are no reports in the literature of cyanide and TNB forming (3.1) in water without the use of micelles.[2]



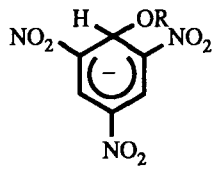
TNB $\qquad K_{CN} = \frac{k_1}{k_{-1}}$ $\qquad$ (3.1) $\qquad$ Eqn.3.1

In DMSO the uv/vis absorbance spectrum of (3.1) has λ_{max} 443 and 526nm (with an optical density ratio of 1.75:1). The equilibrium constant in DMSO, using potassium cyanide in the presence of 18-crown-6 [3] is 1.2×10^5 dm^3mol^{-1} at 25°C. The values of K_{CN} (eqn.3.1) in methanol, ethanol, *n*-propanol, *iso*-propanol, *n*-butanol and *tert*-butanol have been reported [4] as 39, 1265, 1470, 10000, 2020 and 500000 dm^3mol^{-1} respectively at 25°C. The specific rate constants, k_1, for the formation of (3.1) in ethanol, *n*-propanol, *iso*-propanol and *tert*-butanol [5] are 442, 932, 2450 and 106000 $dm^3mol^{-1}s^{-1}$ respectively. In ethanol and *n*-propanol the formation of (3.1) is complicated by alcoholysis producing the respective alkoxide ions, which rapidly attack TNB (section 1.2). An equilibrium constant for ethanolysis (eqn.3.2) has been calculated [5] as 1.33×10^{-6} mol dm^{-3} at 25°C.

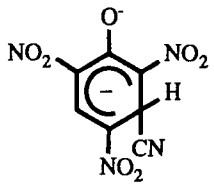
$$CN^- + EtOH \rightleftharpoons EtO^- + HCN \qquad \text{Eqn.3.2}$$

In water and methanol TNB reversibly forms 1:1 sigma-complexes with hydroxide (3.2a) and methoxide (3.2b) respectively.[6] The equilibrium constants for the formation of (3.2) in these respective solvents at 25°C are 2.7 (3.2a) and 18 dm^3mol^{-1} (3.2b).

The author has observed methanolysis in the reaction of TNB with cyanide in methanol, and has calculated a methanolysis constant of $4 \times 10^{-4} dm^3mol^{-1}$ at 25°C.

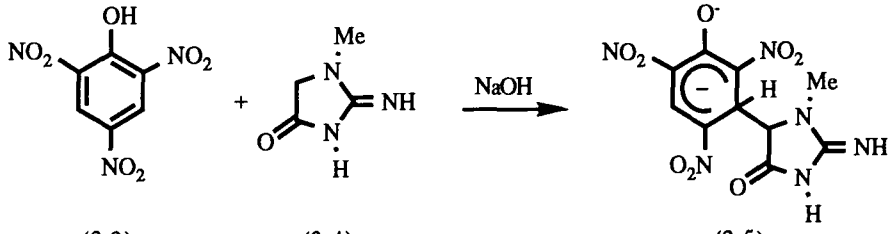


(3.2, a) R = H, b) R = Me.)



(3.6)

There is NMR and uv/vis spectroscopic evidence that picric acid (2,4,6-trinitrophenol) (3.3) forms 1:1 and 1:2 sigma-complexes with nucleophiles such as hydroxide, methoxide, acetate and sulphite.[7-9] Picric acid is also used in the detection of biologically dangerous species such as creatinine [9] (2-imino-1-methylimiazolidin-4-one) (3.4). Creatinine plus the sodium salt of picric acid gives a red coloured species (3.5) (eqn.3.3). Aqueous picric acid is also used in the detection of cyanide in plants.[10] A red coloured complex λ_{max} 510nm is observed. The species responsible has not been identified but a possibility is the sigma-complex (3.6). The author has carried out a similar reaction in methanol, and observed a clean reaction yielding a red coloured species.



Eqn.3.3

(3.3) (3.4) (3.5)

3.2 THE REACTION OF 1,3,5-TRINITROBENZENE WITH CYANIDE.

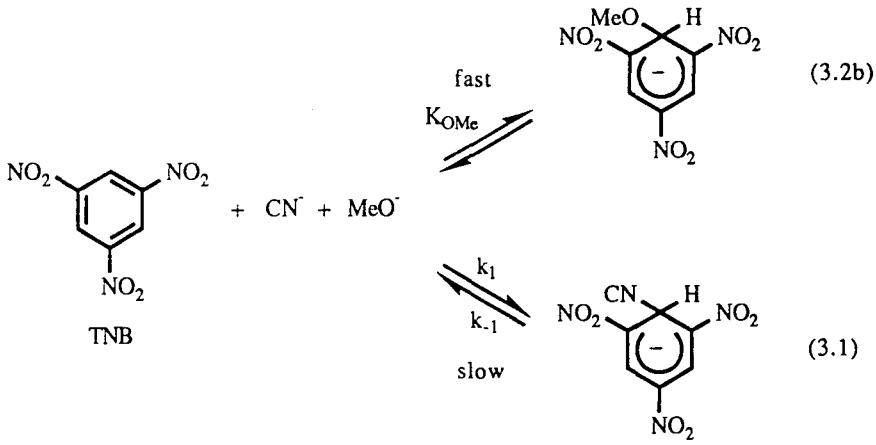
3.2.1 TNB with Cyanide in Water and Aqueous DMSO.

Mixing solutions of TNB ($4x10^{-5}$ M) with excess potassium cyanide in water or in 50%/50% v/v water-DMSO produced no immediate colour. However the solutions slowly became yellow. The visible spectra at completion of the reactions are shown in figure 3.1. They show maxima at 350nm with a shoulder at higher wavelength and are similar to that of picric acid in the same media (fig.3.2).

3.2.2 TNB with Cyanide in Methanol.

In the presence of excess cyanide a very rapid process is observed producing a species with λ_{max} 425 and 495nm (fig.3.3). This is consistent with formation of the sigma-complex (3.2b) by attack of methoxide, produced by methanolysis of the cyanide. A slower reaction produces a species with λ_{max} 435 and 535nm. This is consistent with cyanide attack, forming the adduct (3.1) (scheme 3.1). The final spectrum of the system shows a band at 540nm and the solution was brown in colour. Buncel *et. al.* [4] also reported the fading of colour due to initially formed sigma-complexes to give a yellow solution of unknown composition.

Scheme 3.1



Methanolysis produces methoxide ions when cyanide is dissolved in methanol (eqn.3.4). The concentration of methoxide can be reduced by adding hydrochloric acid to the methanolic cyanide solutions. Care was taken that this was performed in a fume-cupboard because hydrogen cyanide could have been evolved. That added acid reduces the methoxide concentration can be seen from table 3.1; where A_1, the absorbance after the very fast formation of (3.2b) , is reduced.

Figure 3.1

The final products (15min after mixing) of TNB ($4x10^{-5}M$) with:
i) KCN (0.05M) /water, ii) KCN (0.005M) /water,
iii) KCN (0.013M) / 50%/50% v/v water/DMSO.

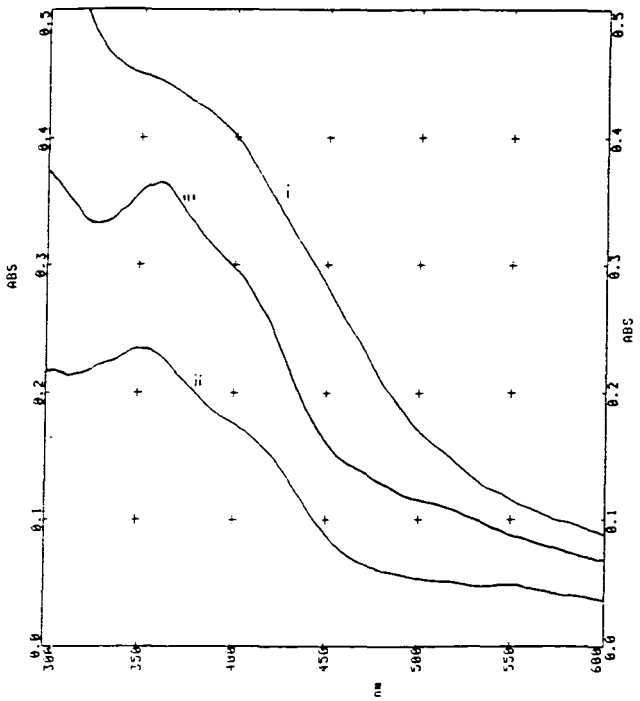


Figure 3.2

Picric acid ($10^{-4}M$) /water.

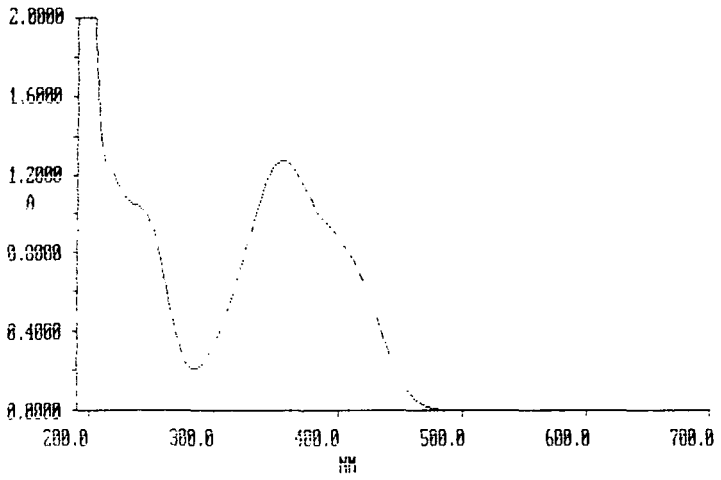
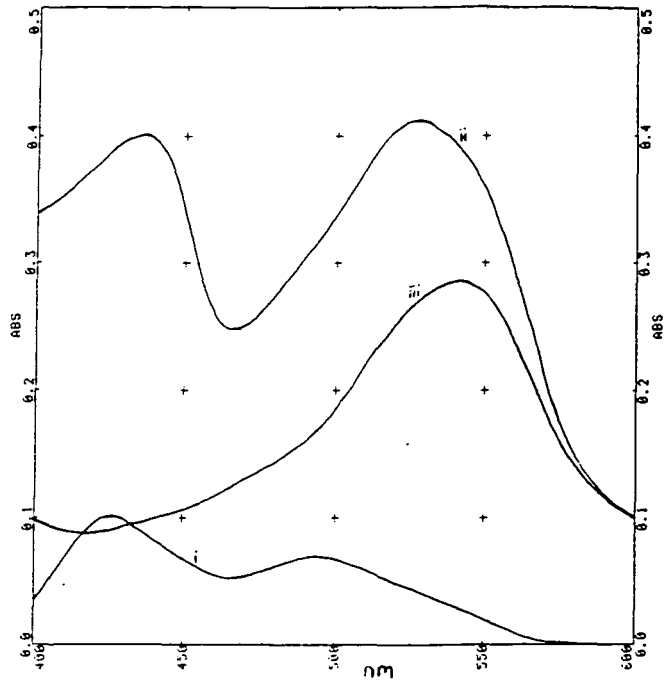


Figure 3.3

TNB (10^{-4}M) + KCN(0.01M):

i) 0.1s after mixing (A_1), ii) maximum absorbance of the system (A_2), iii) final absorbance of the system (A_3).



$$CN^- + MeOH \underset{}{\overset{K_{Meth}}{\rightleftharpoons}} MeO^- + HCN \qquad \text{Eqn.3.4}$$

Table 3.1

Comparison of unbuffered and buffered cyanide solutions.

	KCN (0.005M)	KCN (0.015M) + HCl (0.01M)
A_1	0.042	0.024
A_2	0.229	0.481
A_3	0.151	0.219

At 440nm: A_1 is 0.1s after mixing, A_2 is the maximum absorbance for the system (10-15s), A_3 is the final absorbance of the system (200s) (fig.3.4). [TNB] is $1x10^{-4}$M.

Reactions in degassed and oxygen-rich methanol were investigated. The solvent was degassed by placing in a sonic agitator under reduced pressure followed by passage of helium gas. Degassed solvent was stored under reduced pressure, and both types of solvent were stored in vessels protected by Parafilm. Modifying the solvent by either method had little effect, either on the products, their absorbances or the rates of their formation.

3.2.3 Kinetic Study.

The reaction in methanol of TNB with excess potassium cyanide was examined by stopped-flow spectrophotometry. There was evidence for three processes, and measurements were made at 440nm. The fastest process, too fast for measurement on the stopped-flow time-scale, is attributed to attack by methoxide ions, produced by methanolysis of cyanide. The absorbance, A_1, at completion of this process was measured after 0.1s. This was followed by a slower colour forming reaction attributed to attack by cyanide on the TNB ring (scheme 3.1). The absorbance, A_2, at completion of this reaction and the rate coefficients, k_f, are given in table 3.2. The third, slowest process was measured as a fading process at 440nm. Absorbances, A_3, at the completion of this process and the rate coefficient, k_d, are also given in table 3.2. At the higher cyanide concentrations there was some interference between the latter two processes, so that absorbance verses time plots were similar to figure 3.4. This necessitated extrapolation of data for the slow decay reaction in order to calculate the

infinity value, ∞_f, for the slower colour forming reaction. Because of this the error associated with these rate constants is relatively high (20%).

Table 3.2

Absorbance values, and rate coefficients for the formation and decay of absorbance, at 440nm for the reaction between TNB and KCN in methanol.

$[CN^-]_o$ /M	$[CN^-]_r$ /M	$[CN^-]_x$ /M	A_1	A_2	A_3	k_f	k_d	10^4 x K_{Meth}
0.005	0.004	0.0039	0.032	0.371	0.195	0.26	0.033	1.99
0.010	0.009	0.0088	0.046	0.485	0.195	0.27	0.070	1.97
0.015	0.013	0.0125	0.069	----	----	0.29	0.096	3.03
0.020	0.017	0.0161	0.093	0.524	0.195	0.31	0.13	4.24
0.025	0.022	0.0208	0.106	----	----	0.35	0.15	4.39
0.030	0.027	0.0255	0.115	0.604	0.195	0.41	0.18	4.30
0.040	0.036	0.0335	0.131	0.731	0.212	0.51	0.20	4.20
0.050	0.043	0.0380	0.218	0.842	0.212	0.73	0.20	10.67

$[CN^-]_o$ is the initial (pre-methanolysis) concentration of cyanide.
$[CN^-]_r$ is the residual (after methanolysis) concentration of cyanide.
$[CN^-]_x = [CN^-]_r / (1 + K_{OMe}[OMe^-])$.
$[TNB] = 10^{-4}M$.

Figure 3.4

Typical absorbance - time plot for TNB + KCN in methanol.

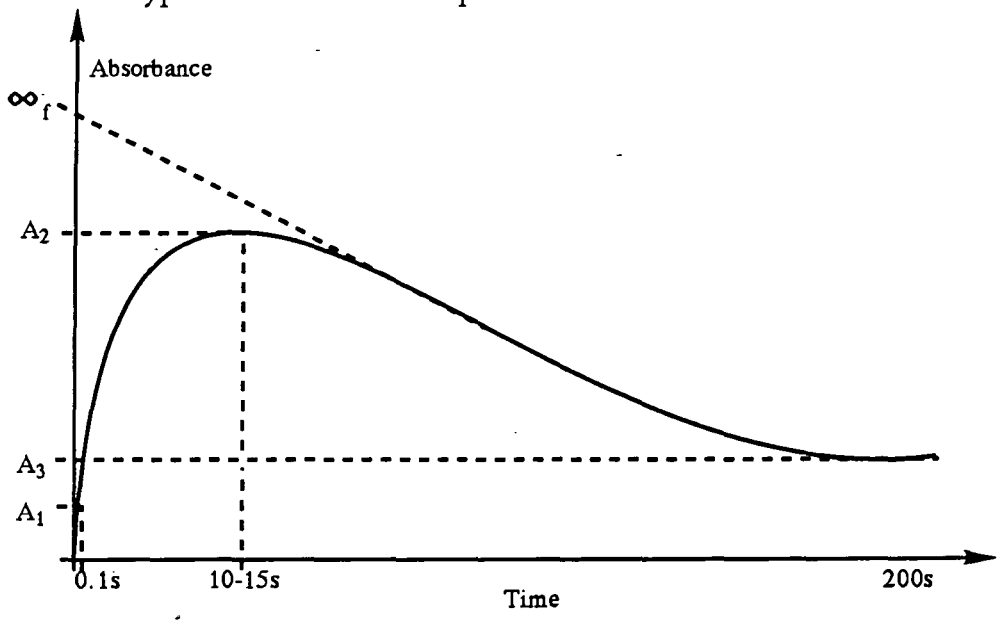


Figure 3.5

The observed rate constants for the formation, k_f, and decay, k_d, of absorbance at 440nm *vs.* $[KCN]_o$. ($[TNB] = 10^{-4}M$).

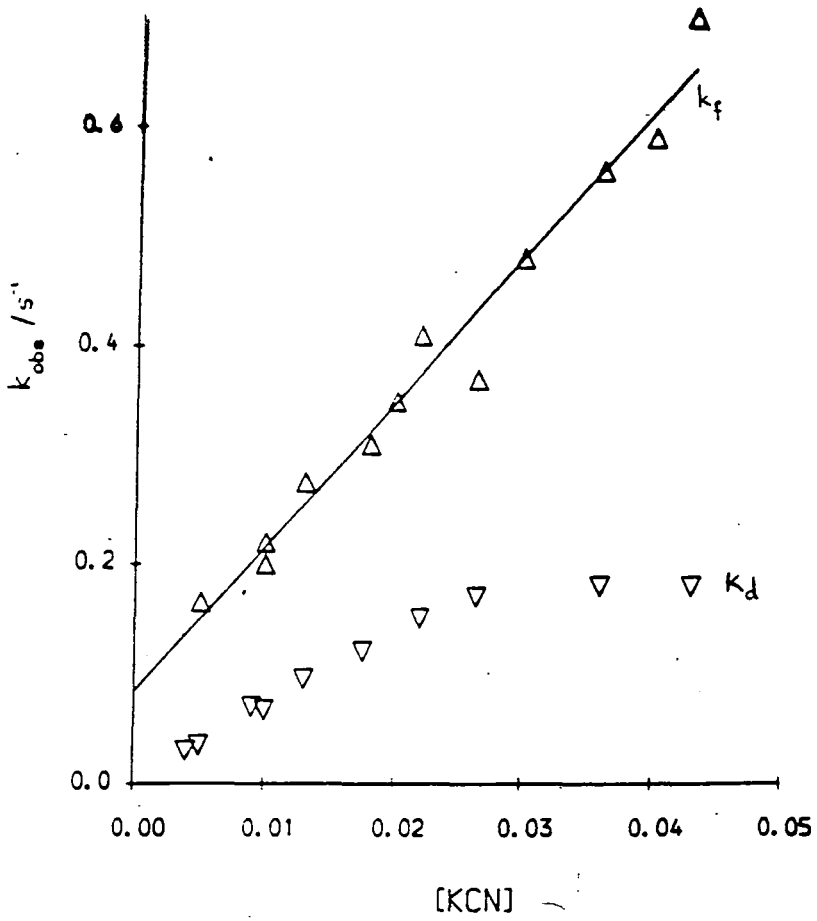
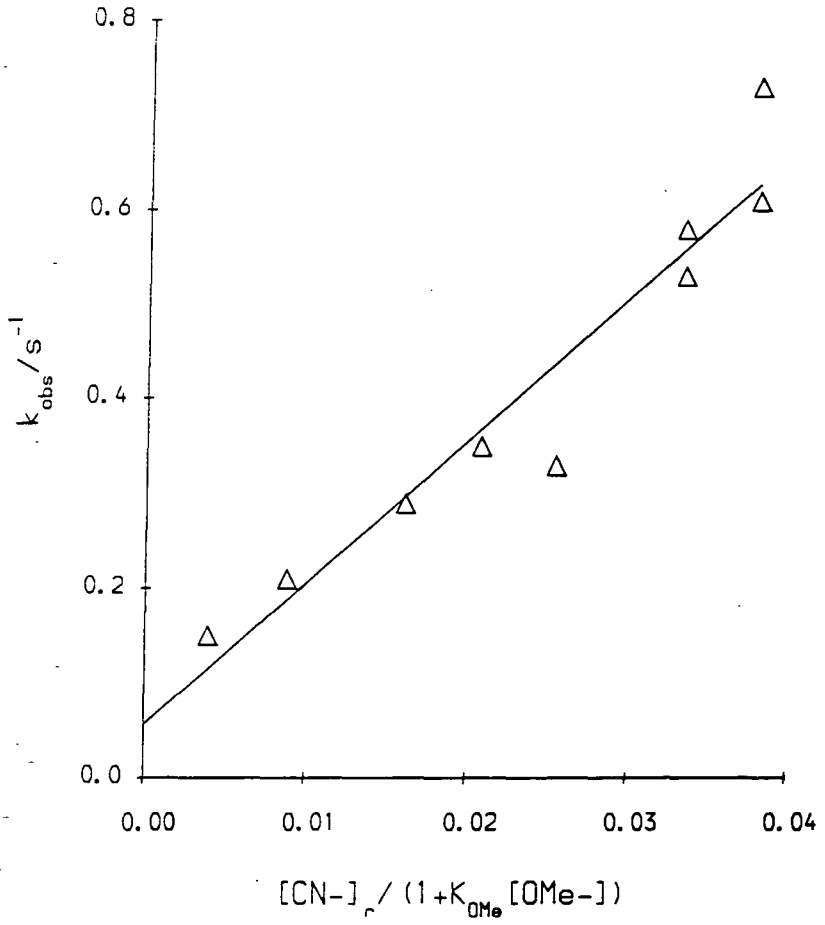


Figure 3.6

The observed rate constants for the formation, k_f, of absorbance at 440nm *vs.* $[CN^-]_r / \{1 + K_{OMe}[OMe^-]\}$. ($[TNB] = 10^{-4}M$).



3.2.4 Calculation of the pK_a value of Hydrogen Cyanide in Methanol.

The results provide evidence for the methanolysis of cyanide ions (eqn.3.4), and it will be shown (calc.3.1) that the data lead to a value of 13.52 for the pK_a of hydrogen cyanide in methanol. This value is in qualitative agreement with literature [5] values in water (11.05), ethanol (13.00) and *n*-propanol (13.76). The value obtained in methanol is derived from the value of $4x10^{-4}$mol dm^{-3} obtained for the methanolysis constant K_{Meth}. This value was obtained from the initial absorbances produced in the reaction with TNB (table 3.2), and uses the literature values of 18 dm^3mol^{-1} for the equilibrium constant,[11] K_{OMe}, (scheme 3.1) for the reaction of TNB with methoxide ions, and $2x10^4$ $dm^3mol^{-1}cm^{-1}$ for the extinction coefficient of (3.2b).

Calculation 3.1:

$$TNB + MeO^- \overset{K_{OMe}}{\rightleftharpoons} TNB.OMe^- \quad (3.2b)$$

$$[OMe^-] = \frac{[TNB.OMe^-]}{[TNB] \times 18} = \frac{A_1}{18\,(2.0 - A_1)}$$

$$CN^- + MeOH \overset{K_{Meth}}{\rightleftharpoons} HCN + MeO^- \quad \text{(eqn.3.4)}$$

$$K_{Meth} = \frac{[MeO^-]^2}{[CN^-]_r} = 4x10^{-4}M \quad \text{(table 3.2)}$$

N.B. $[CN^-]_r = [CN^-]_o - [MeO^-]$

Also $$K_{Meth} = \frac{[MeO^-].[HCN]}{[CN^-]_r} = 4x10^{-4}M$$

$$MeOH \overset{K_a'}{\rightleftharpoons} H^+ + MeO^-$$

$$pK_a' = 16.92\ [12]$$

$$HCN \overset{K_a}{\rightleftharpoons} H^+ + CN^-$$

So $$K_a = \frac{10^{-16.92}}{4x10^{-4}}$$

$$\underline{pK_a = 13.52}$$

The value obtained for K_{Meth} of $4x10^{-4}$ moldm^{-3} may be compared with a literature value[13] of $1.5x10^{-4}$ moldm^{-3}. Examination of the data in table 3.2 shows that the values obtained for K_{Meth} increase with increasing cyanide concentration. It is possible that here, where the rate constants for the reaction with cyanide are fastest, the values obtained for A_1 include a small contribution from the TNB-cyanide reaction.

$$k_f = \frac{k_1 [CN^-]_r}{1 + K_{OMe}[OMe^-]} + k_{-1} \qquad \text{Eqn.3.5}$$

Figure 3.5 shows plots of the raw data for k_f and k_d versus the stoichiometric cyanide concentration ($[CN^-]_o$). However, because of the prior equilibrium involving rapid methoxide attack and also because of the depletion of cyanide concentration by methanolysis, the rate expression appropriate for formation of (3.1) is given in eqn.3.5. A linear plot of k_f according to this equation is shown in figure 3.6 and allows the calculation of values for k_1 of 15.03 dm^{3}mol^{-1}s^{-1} and k_{-1} of 0.055 s^{-1}. Combination of these values gives a value for K_{CN} of 273 dm^{3}mol^{-1}.

The nature of the product of the slowest reaction is uncertain but this will be discussed below (section 3.2.6).

3.2.5 Visible Spectra at Low Cyanide Concentration in Methanol.

Table 3.3

The equilibrium constants, K_o and K_r, for the formation of the TNB.CN^- sigma-complex (3.1).

$[CN^-]_o$[a]/M	$[CN^-]_r$[a]/M	TNB /M	t ∞ /min.[b]	A_{435}[c]	K_o[d]	K_r[d]
$5x10^{-5}$	$2.2x10^{-6}$	0.05	60	0.35	10.8	162
$5x10^{-5}$	$3.8x10^{-6}$	$5x10^{-3}$	130	0.15	35.3	401
$1x10^{-4}$	$1.5x10^{-5}$	$1x10^{-3}$	20	0.12	64.2	392
$5x10^{-4}$	$2.0x10^{-4}$	$1x10^{-3}$	25	0.50	54.0	128
$1x10^{-3}$	$4.9x10^{-4}$	$1x10^{-3}$	5	1.20	67.9	124
$1x10^{-3}$	$5.2x10^{-4}$	$5x10^{-4}$	16	0.55	59.8	107
$1x10^{-3}$	$5.3x10^{-4}$	$5x10^{-5}$	5	0.05	52.8	94

a) As for table 3.2.
b) Time of measuring A_{435} after mixing.
c) Uncorrected for any absorbance of TNB.OMe^- (3.2b) at 435nm.
d) dm^{3}mol^{-1}.

Visible spectra were recorded using conventional spectrophotometry of solutions containing low concentrations of cyanide ($<5x10^{-3}M$). In order to obtain coloured solutions it was necessary to use relatively high concentrations of TNB and in most cases the concentration of TNB was greater than that of cyanide. Three representative sets of spectra are shown in figures 3.7-9, and the final absorbances at 435nm are given in table 3.3.

In these solutions methanolysis must be taken into account, especially at low concentrations of cyanide. A value of $4x10^{-4}$ $moldm^{-3}$ has been calculated (calc.3.1) for the methanolysis constant, K_{Meth}, of the cyanide ion. Table 3.3 gives the absorbance, A_{435}, of (3.1) at 435nm, and both the initial (pre-methanolysis) concentration of cyanide, $[CN^-]_o$, and the concentration of residual (after methanolysis) cyanide concentration, $[CN^-]_r$, and the respective equilibrium constants,K_o and K_r, for the formation of the sigma-complex (3.1). The calculation method is shown in calculation 3.2.

Calculation 3.2:

$$TNB + CN^- \overset{K_{CN}}{\rightleftharpoons} TNB.CN^- \quad (3.1)$$

$$K_o = \frac{[TNB.CN^-]}{[TNB].[CN^-]_o}$$

Assume ε_{435} for (3.1) = $2x10^4$ $dm^3mol^{-1}cm^{-1}$: $[TNB.CN^-] = \frac{A_{435}}{2x10^4}$

$$K_o = \frac{A_{435} / 2x10^4}{([TNB] - A_{435} / 2x10^4)([CN^-] - A_{435} / 2x10^4)}$$

$$[CN^-]_o = [CN^-]_r + [OMe^-] + [TNB.CN^-]$$

and $$K_{Meth} = \frac{[MeO^-]^2}{[CN^-]_r} = 4x10^{-4}M \qquad \text{(table 3.2)}$$

Therefore $$4x10^{-4}[CN^-]_r = \{[CN^-]_o - [TNB.CN^-] - [CN^-]_r\}^2$$

A quadratic equation which can be solved for $[CN^-]_r$, then:

$$K_r = \frac{[TNB.CN^-]}{[TNB].[CN^-]_r}$$

The results obtained for K_{CN} using the residual cyanide concentration, K_r, show quite a wide variation. This can be attributed to the very low cyanide concentrations used, so that any acidity or basicity in the solvent will change the equilibrium concentration.

Figure 3.7

TNB (0.001M) + KCN (10^{-4}M) /methanol.

Interval between scans = 2min.

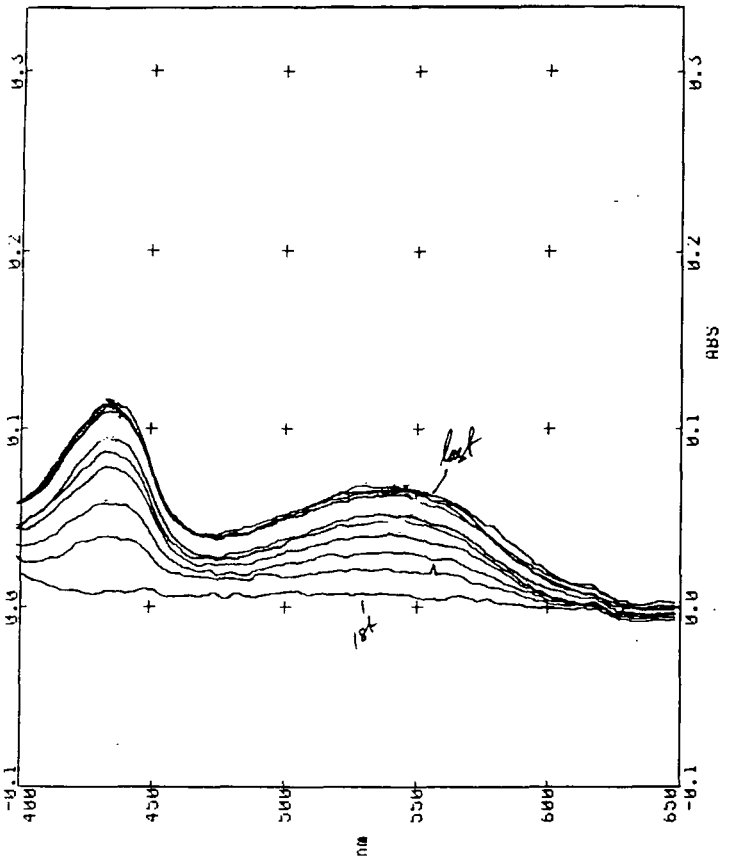


Figure 3.8

TNB (0.001M) + KCN (0.001M) /methanol.

Interval between scans = 2min.

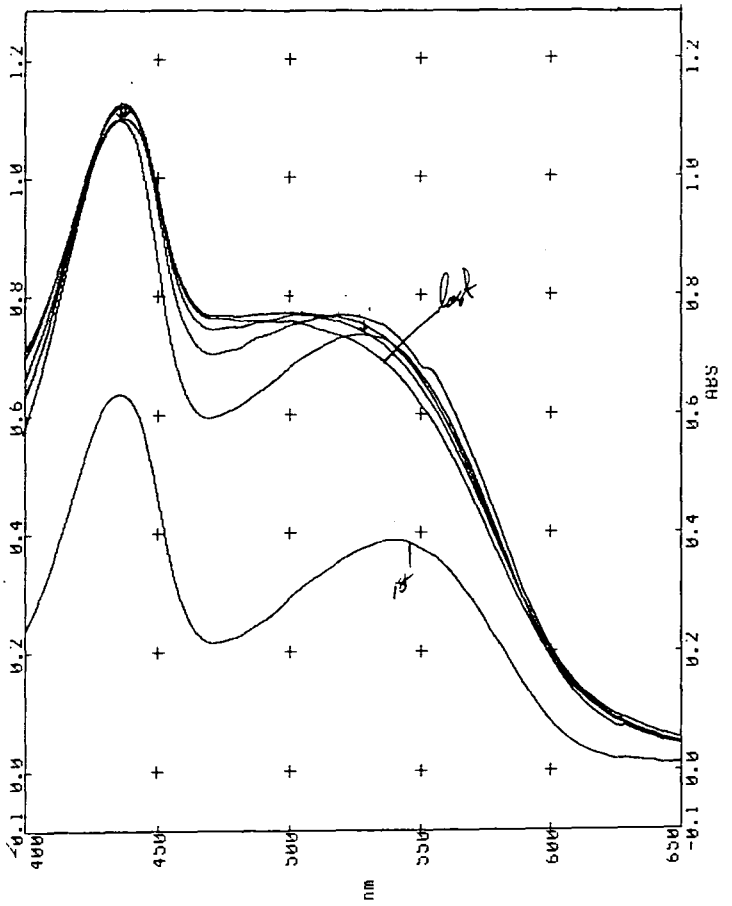
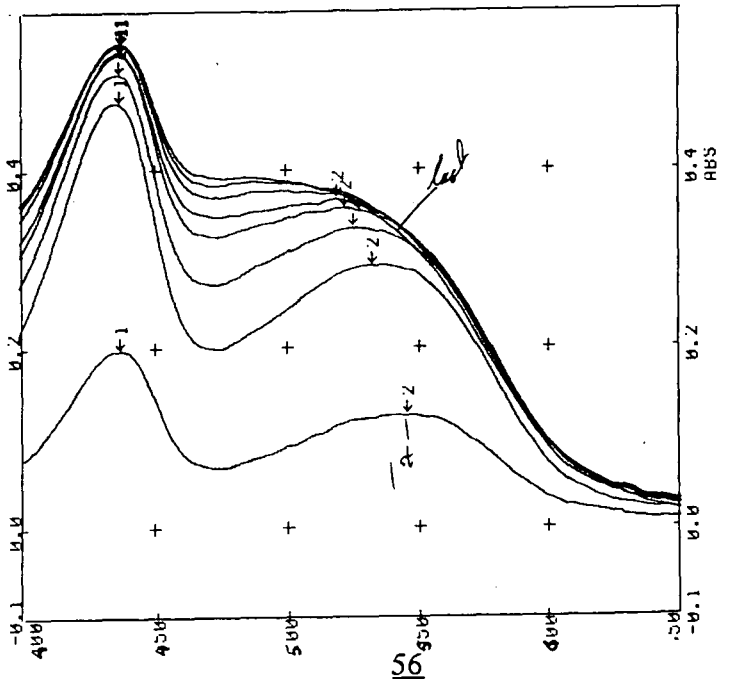


Figure 3.9

TNB ($5x10^{-4}$M) + KCN (0.001M) /methanol.

Interval between scans = 2min.



The values obtained for K_{CN} are not incompatible with the more reliable value of 273 dm^3mol^{-1} obtained from the kinetic data.

Two features of the spectra which are worthy of comment are i) the slowness of adduct formation at very low concentrations of cyanide and ii) the further reaction resulting in increased absorbance at 500nm. These will be dealt with in turn.

The slowness of the reaction is apparent from figure 3.7. The data were not thought to be of sufficient quality to attempt the calculation of a rate coefficient, but a qualitative explanation can be given. The reaction becomes slow when the concentration of TNB is greater than that of cyanide, and at low cyanide concentrations. Rapid methanolysis competes with adduct formation. In the presence of the rapid pre-equilibrium the expression for k_f is given [14] by eqn.3.6. At low concentrations of cyanide when $K_{Meth} >> 2[MeO^-]$ the value of the rate constant will be decreased.

$$CN^- + MeOH \overset{K_{Meth}}{\rightleftharpoons} HCN + MeO^-$$

$$TNB + CN^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} TNB.CN^- \quad (3.8)$$

$$k_f = \frac{k_1[TNB]}{1 + \frac{K_{Meth}}{2[MeO^-]}} + k_{-1} \qquad \text{Eqn.3.6}$$

3.2.6 The Nature of the Fading Reaction.

The plot in figure 3.5 shows that with increasing cyanide concentration the value of k_d increases in a curvilinear fashion reaching a plateau. One possible explanation for this behaviour is a slow competing reaction of cyanide with TNB, as shown in scheme 3.2.

Scheme 3.2

$$TNB + CN^- + MeO^- \overset{K_{CN}}{\rightleftharpoons} TNB.CN^- \quad (3.1)$$

$$TNB.CN^- \overset{k_2}{\longrightarrow} ?$$

$$TNB + CN^- + MeO^- \overset{K_{OMe}}{\underset{\text{fast}}{\rightleftharpoons}} TNB.OMe^- \quad (3.2b)$$

If the sigma-adduct forming reactions with methoxide and cyanide are fast equilibria compared with the further process then the appropriate expression for k_d is eqn.3.7, which will simplify to eqn.3.8 when $[CN^-] >> [OMe^-]$. An equation of this form will

predict the curvilinear dependence observed for k_d, with $k_d = k_2/K_{CN}$ at high cyanide concentration. However the chemical process represented by k_2 is uncertain.

$$k_d = \frac{k_2[CN^-]}{1 + K_{CN}[CN^-] + K_{OMe}[OMe^-]} \qquad \text{Eqn.3.7}$$

$$k_d = \frac{k_2[CN^-]}{1 + K_{CN}[CN^-]} \qquad \text{Eqn.3.8}$$

A further possible explanation is suggested by the increase in absorbance at 500nm shown in figures 3.7-9. It is known [15] that 1:2 adducts typically give a single broad absorbance in this region, so this possibility must be considered. The rate expression for the formation of a dicyano-adduct is eqn.3.9. However, this equation does not predict any levelling-off of the value of k_d obtained at high concentration and must be discarded.

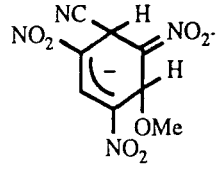
$$TNB.CN^- + CN^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} TNB.(CN)_2^{2-}$$

$$k_d = \frac{k_2K_{CN}[CN^-]^2}{1 + K_{CN}[CN^-]} + k_{-2} \qquad \text{Eqn.3.9}$$

$$TNB.CN^- + OMe^- \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} TNB.(CN)(OMe)^{2-}$$

$$k_d = \frac{k_2K_{CN}[MeO^-][CN^-]}{1 + K_{CN}[CN^-]} + k_{-2} \qquad \text{Eqn.3.10}$$

Nevertheless, a mixed cyano-methoxy di-adduct is a possibility. This would lead to a rate expression given by eqn.3.10. The plot of k_d versus cyanide concentration (fig.3.5) has a small intercept, indicating that k_{-2} has a low value. The rate data were used to calculate values for k_2 as a function of cyanide and methoxide concentrations. The values obtained (table 3.4) show small variation of k_2 with cyanide concentration indicating that this rate expression (eqn.3.10) is not impossible. This, perhaps, is evidence that the slow reaction may involve formation of the adduct (3.7).



(3.7)

Table 3.4

$[CN^-]_r$ /M	$[OMe^-]$ /M	k_d /s^{-1}	k_2 /$dm^3mol^{-1}s^{-1}$
0.0041	0.0009	0.033	70
0.0087	0.0014	0.070	77
0.0130	0.0020	0.096	62
0.0173	0.0027	0.13	59
0.022	0.0030	0.15	59
0.0267	0.0033	0.18	62
0.0361	0.0039	0.20	55
0.0457	0.0043	0.20	50

3.2.7 Other Work.

TNB has been reacted with an excess of potassium cyanide in acetonitrile (fig.3.10) and 5%/95% v/v methanol/chloroform (fig.3.11). In each case the initial reaction appears to be the formation of the sigma-complex (3.1) (λ_{max} 440 and 550nm in acetonitrile, lit:[1] 438 and 555nm; λ_{max} 430 and 530nm in 5%/95% v/v methanol/ chloroform, lit:[1] 442 and 558nm in chloroform, lit:[4] 428 and 540nm in methanol).

An excess of TNB (0.0067M) reacts with potassium cyanide (0.0033M) in methanol to rapidly yield the 1:1 sigma-complex (3.1) λ_{max} 425 and 530nm (fig 3.12). The bands of (3.1) fade to yield a spectra of broad absorbance from 400 to 500nm, caused by a species whose nature remains unknown.

Figure 3.10

TNB (10^{-4}M) + KCN (0.005M) /acetonitrile.
Interval between scans = 2min.

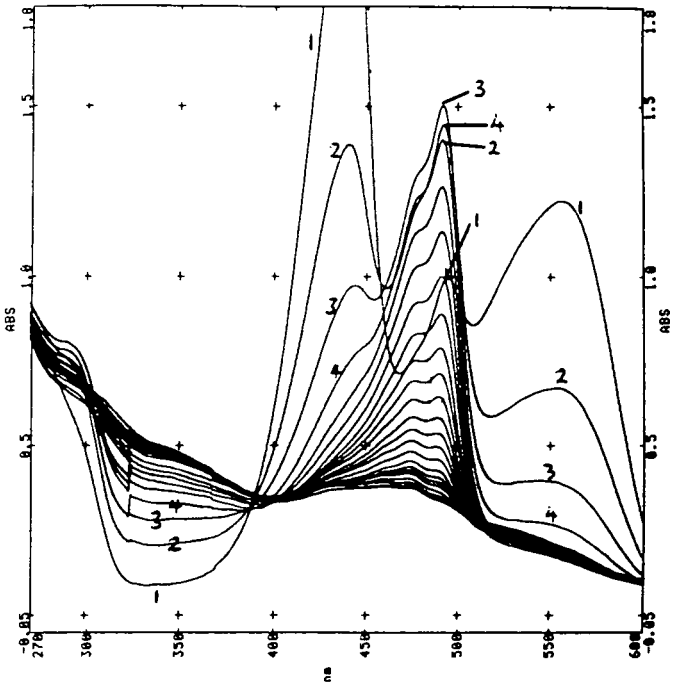


Figure 3.11

TNB (10^{-4}M) + KCN (0.005M) / 5%/95% v/v methanol/chloroform.
Interval between scans = 2min.

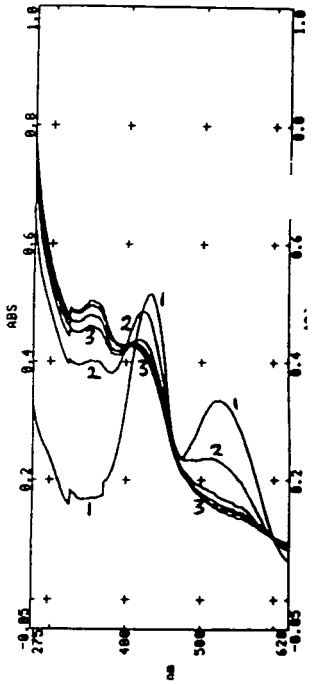


Figure 3.12

TNB (0.0067M) + KCN (0.0033M) /methanol.
Path length = 1mm, interval between scans = 2min.

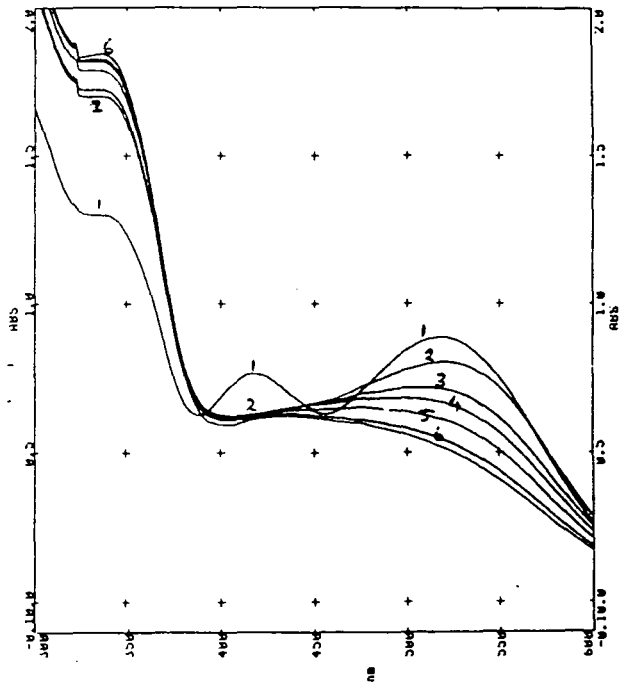
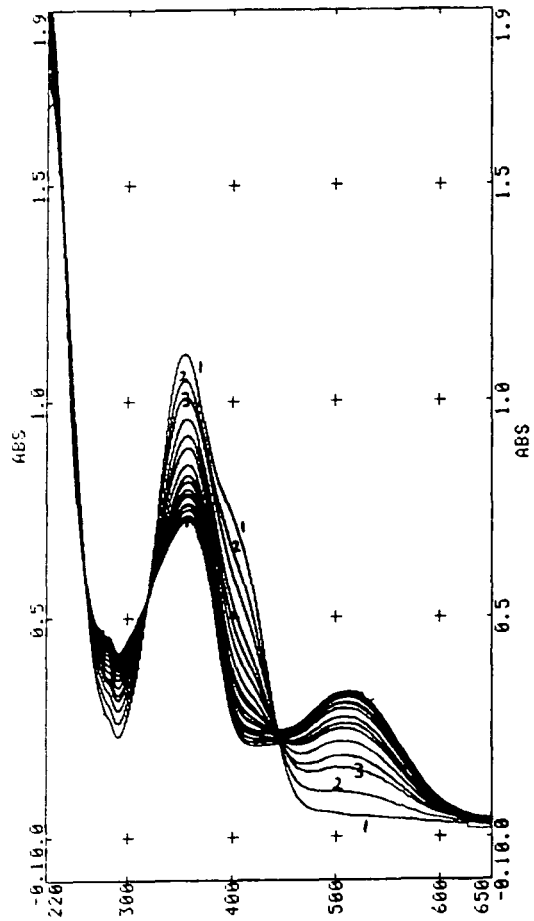


Figure 3.13

Picric acid ($5x10^{-5}$M) + KCN (0.1M) /methanol.
Interval between scans = 2min.



3.3 THE REACTION OF PICRIC ACID WITH CYANIDE.

A small amount of work has been carried out on the reaction of picric acid (2,4,6-trinitrophenol) with potassium cyanide in methanol. In the presence of excess cyanide (0.1M) in methanol picric acid ($5x10^{-5}M$) (λ_{max} 350nm with a shoulder at 410nm) produces a species which causes an absorbance band λ_{max} 505nm (fig.3.13). The isosbestic points (440 and 315nm) indicate a clean reaction with no side reactions. A possible structure of the species giving rise to this new absorbance is discussed in section 3.1.

3.4 CONCLUSION.

In this chapter the reactions of cyanide ion with some trinitro-substituted benzenes have been examined. This work does not present a complete picture, although some headway has been made. A major conclusion is that methanolysis of cyanide ions is an important process in these reactions so that the methoxide ions produced may play an integral part in the overall reactions.

The main thrust of the work in this thesis and the main interest of the sponsor was in the synthesis of new cyano-benzenes. It was felt that further work on the trinitro-benzenes was not justified at this stage.

3.5 REFERENCES.

1 A.R.Norris, *Can. J. Chem.*, (1967), **45**, 2703.

2 L.H.Gan, *Aust. J. Chem.*, (1985), **38**, 1141.

3 V.Gold & W.N.Wassef, *J. Chem. Soc., Perkin Trans. II*, (1984), 1431.

4 E.Buncel, A.R.Norris, W.Proudlock & K.E.Russel, *Can. J. Chem.*, (1969), **47**, 4129.

5 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1974), **52**, 1.

6 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1971), **49**, 2490.

7 M.R.Crampton & V.Gold, *Chem. Commun.*, (1965), 256.

8 M.R.Crampton & M.El-Ghariani, *J. Chem. Soc. (B)*, (1969), 330.

9 A.R.Butler, *J. Chem. Soc., Perkin Trans. II*, (1975), 853.

10 H.J.Williams & T.G.Edwards, *J. Sci. Food Agric.*, (1980), **31**, 15.

11 F.Terrier, *Chem. Revs.*, (1982), **82**, 77.

12 J.Koskikallio, *Suomen. Kem.*, (1957), **30B**, 111.

13 J.Kavalek & V.Sterba, *Collect. Czech. Chem. Comm.*, (1975), **40**, 1932.

14 C.F.Bernasconi, *"Relaxation Kinetics"*, Academic Press, London, (1976).

15 E.Buncel, M.R.Crampton, M.J.Strauss & F.Terrier, *"Electron Deficient Aromatic- and Heteroaromatic-Base Interactions"*, Elsevier, Oxford, 1984.

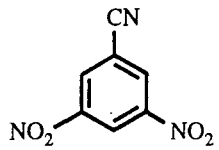
CHAPTER 4

THE REACTIONS OF *META*-DINITROBENZENE AND 2,4- AND 2,6-DINITROBENZONITRILE WITH METHOXIDE, HYDROXIDE AND CYANIDE IN METHANOL OR DMSO.

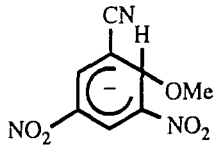
A major product of the reaction between *meta*-dinitrobenzene and potassium cyanide in methanol is known to be [1] 2-methoxy-6-nitrobenzonitrile. It has been demonstrated (chapter 3) that in methanolic cyanide solutions methanolysis produces a significant concentration of methoxide ions, hence a possible route to the reaction product is ring cyanation followed by methoxydenitration. In order to investigate this reaction in further detail, a study of the reactions of the potential intermediates 2,4- and 2,6-dinitrobenzonitrile with cyanide or methoxide ions in methanol has been undertaken.

4.1 REACTIONS WITH METHOXIDE - INTRODUCTION.

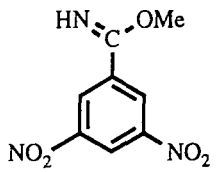
The initial, very fast reaction between 3,5-dinitrobenzonitrile (4.1) and methoxide in methanol or methanol/DMSO mixtures is the formation of the sigma-complex (4.2).[2] The absorbance maxima of (4.2) at 390 and 490nm rapidly fade over several minutes. In the initial work this fading was attributed to the substitution of nitro-groups. However a more recent study [3] has shown that the final product of this reaction is the imidate (4.3), not 3-cyano-5-nitroanisole as originally suggested.[2]



(4.1)



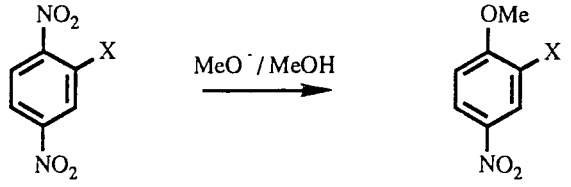
(4.2)



(4.3)

It has been shown [4] that in the presence of methoxide in methanol, a series of 2-X-1,4-dinitrobenzenes (4.4) undergo substitution by methoxide of the nitro-group adjacent to the X-substituent (eqn.1.4). There is kinetic evidence that a cyano-group adjacent to a nitro group promotes this substitution better than either NO_2 or H. For X = CN (4.4) no methoxide attack on the cyano-group was observed, but could not be ruled out as a minor pre-equilibrium to the irreversible formation of the anisole. The bulky nitro group *ortho* to the cyano-group was thought likely to inhibit imidate

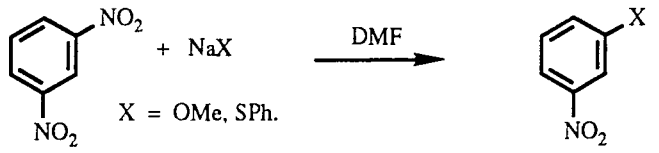
formation. Other examples of methoxydenitration have been discussed above (section 1.4).



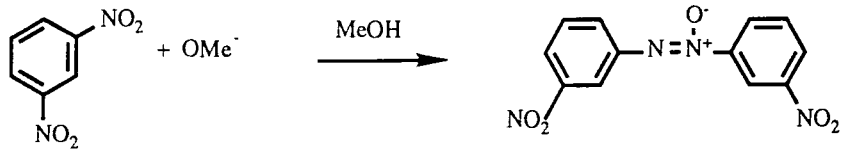
(4.4)

Eqn.4.1

In polar aprotic solvents (DMSO, DMF, hexamethylphosphoramide) the reaction of *meta*-dinitrobenzene with a two-fold excess of either sodium methoxide or thiophenoxide, resulting in the substitution of a nitro group (eqn.4.2), is an example of the behaviour of many substituted nitroaromatics.[5] The reaction is performed at room temperature under nitrogen. However, in methanol, it has been reported [6] that a redox reaction occurs between *meta*-dinitrobenzene and excess methoxide under nitrogen at temperatures between 40-90°C, yielding *trans*-3,3'-dinitroazoxybenzene (eqn.4.3). In the methoxide concentration range 2.9-3.4M with *meta*-dinitrobenzene ($5x10^{-4}$M) the radical anion of the substrate is observed. It has been postulated [7] that 3-nitro-nitrosobenzene is an intermediate in this reaction.



Eqn.4.2



Eqn.4.3

4.2 THE REACTIONS OF 2,4- AND 2,6-DINITROBENZONITRILE WITH METHOXIDE.

4.2.1 In Methanol.

2,4-Dinitrobenzonitrile (1CN24DNB) and 2,6-dinitrobenzonitrile (1CN26DNB) have been reacted with excess methoxide in methanol. The reactions have been followed by proton NMR and uv/vis spectrophotometry; the final products were confirmed by HPLC. There is spectroscopic evidence for attack by methoxide either at i) the cyano group or at ii) the nitro-substituted ring position. The former reaction leads to the solvate (methanol addition to the cyano group) and is reversible, while the latter results in irreversible displacement of a nitro group by methoxide. Kinetic studies indicate that reaction occurs in two well-separated stages; in the first rapid stage the parent is partitioned between solvate and substitution products, while the second slower stage results in the slow conversion of the solvate to substitution products *via* the parent. The final products are isomeric methoxy-nitrobenzonitriles.

The spectrum of 1CN24DNB ($1x10^{-4}$M) shows (fig 4.1) (table 4.1) λ_{max} 225nm, $\varepsilon = 2.7x10^4$ $dm^3mol^{-1}cm^{-1}$ with a shoulder at 300nm. In the presence of base (0.019M), the first stage of the reaction involves a decrease in absorbance at 236nm and an increase at 340nm, while in the second stage there is increase at 340nm and decrease at 250nm. An isosbestic point is observed at 236nm during the slower reaction. The final spectrum is compatible with the formation of a mixture of 1-cyano-2-methoxy-4-nitrobenzene (1CN2MeO4NB) (fig.4.2a) and 1-cyano-4-methoxy-2-nitrobenzene (1CN4MeO2NB) (fig.4.2b) (table 4.1) in the same medium. UV/Vis spectra do not allow the proportions of these isomeric products to be determined. However, HPLC results described later indicate the ratio of 1CN2MeO4NB to 1CN4MeO2NB to be 2:1.

The spectrum of 1CN26DNB ($1x10^{-4}$M) shows (fig 4.3) (table 4.1) λ_{max} 232nm, $\varepsilon = 2.5x10^4$ $dm^3mol^{-1}cm^{-1}$. In the presence of base (0.22M), the first stage of the reaction involves a decrease in absorbance at 227nm and an increase at 335nm, while in the second stage there is increase at 335nm and decrease at 245nm. An isosbestic point is obseved at 227nm during the slower reaction. The spectrum after 30min corresponds to that of 1-cyano-2-methoxy-6-nitrobenzene (1CN2MeO6NB) (fig.4.2c) in the same medium (table 4.1). After 24hrs a shoulder at 301nm is evident due to the very slow production of 2,6-dimethoxybenzonitrile (1CN26DMB) (fig.4.2d) (table 4.1).

The observed rate constants for both the fast (k_f) and slow (k_s) stages of the reaction with excess methoxide of both substrates are shown in tables 4.2 and 4.3; and plots of rate constant against concentration of methoxide are shown in figures 4.4-7.

Figure 4.1

UV/Vis spectra of 1)1CN24DNB($1x10^{-4}$M) /MeOH and 2)1CN24DNB($1x10^{-4}$M) + MeO^-(0.019M) /MeOH (int. = 5min).

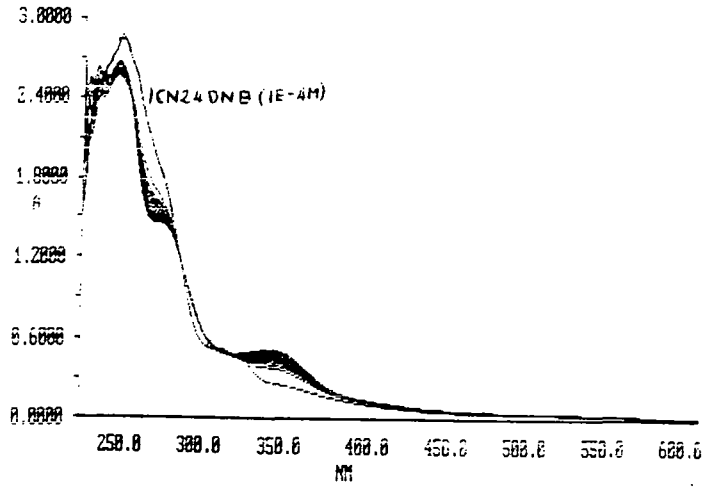


Figure 4.3

UV/Vis spectra of 1)1CN26DNB($1x10^{-4}$M) /MeOH and 2)1CN26DNB($1x10^{-4}$M) + MeO^-(0.22M) /MeOH (int. = 3min).

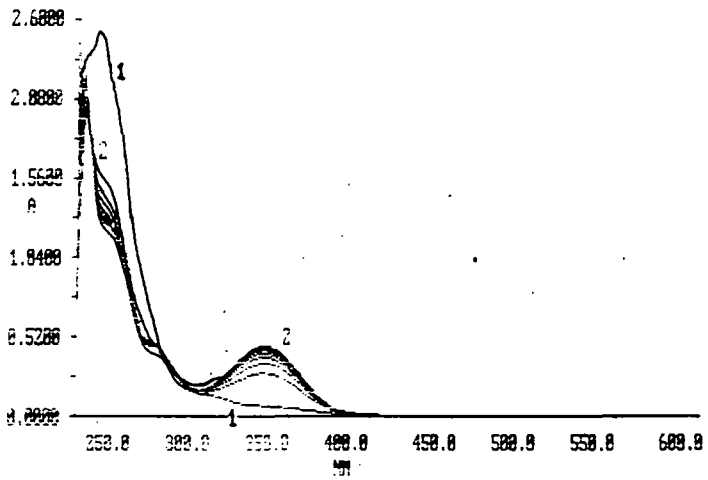
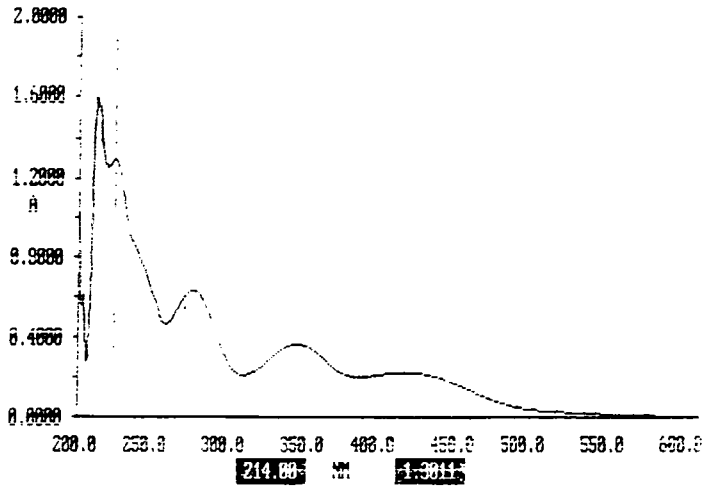
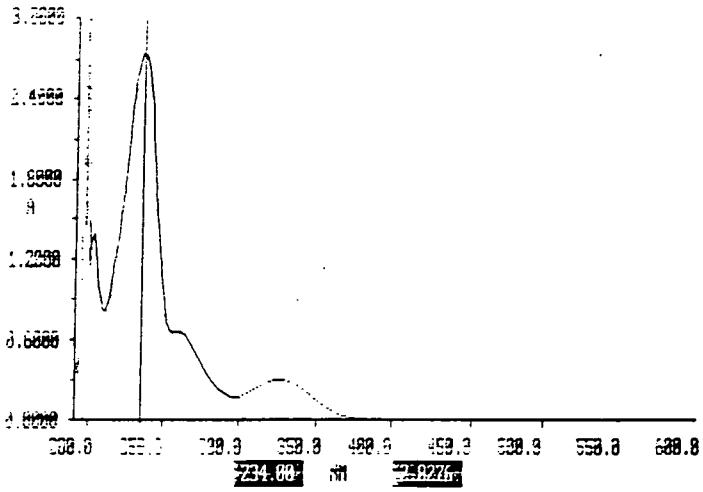


Figure 4.2

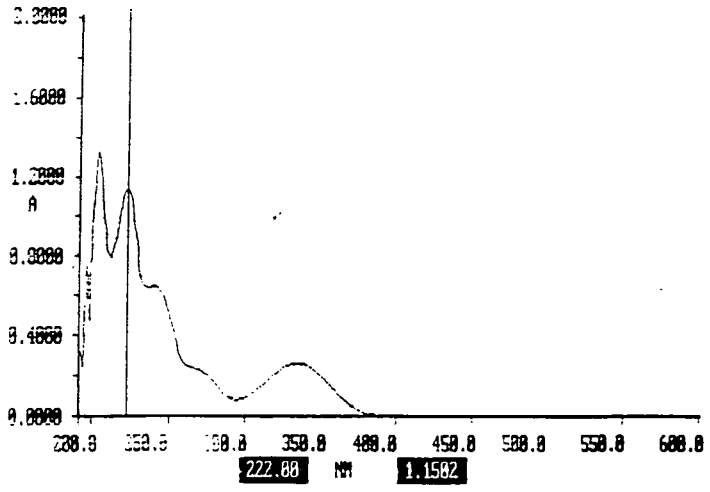
UV/Vis spectra of a) 1CN2MeO4NB b) 1CN4MeO2NB c) 1CN2MeO6NB and d) 1CN26DMB, ($1x10^{-4}$M).



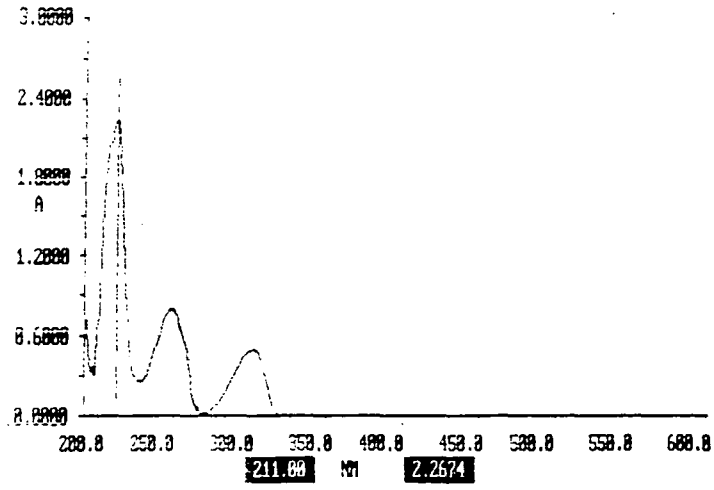
(a)



(b)



(c)



(d)

Table 4.1

The uv/vis spectra of substrates and products in methanol and DMSO.

Solvent	Methanol		DMSO [c]	
	λ_{max} /nm	$10^{-4}\varepsilon$ /dm^{3}mol^{-1}cm^{-1}	λ_{max} /nm	$10^{-4}\varepsilon$ /dm^{3}mol^{-1}cm^{-1}
1CN24DNB	225	2.7	300 (sh) [a]	0.36
1CN26DNB	232	2.5	upto 400 [b]	
1CN2MeO4NB	214	1.3	271	0.59
	267	0.60	343	0.34
	335	0.39	411	0.20
	405	0.25		
1CN4MeO2NB	234	2.8	330	0.34
	325	0.30		
1CN2MeO6NB	222	1.2	271	0.59
	239	0.62	341	0.30
	335	0.39		
1CN26DMB	211	2.3	302	0.80
	247	0.85		
	301	0.40		
1CN24DMB			290	0.76

a) shoulder.
b) no definite peak.
c) DMSO absorbs strongly below 270nm so that substrate absorption is not detectable below this wavelength.

The absorbance at 335nm (A_{335}) of reaction mixtures initially on adding excess methoxide to the substrate (T_0), after the completion of the fast reaction (T_1) and after the completion of the slow stage (T_2) are shown for 1CN24DNB and 1CN26DNB in tables 4.4 and 4.5 respectively. Assuming that the solvate does not absorb at 335nm, these data allow the calculation of the initial fractionation of the parent between the substitution product(s) and the solvate. In terms of scheme 4.3, eqn.4.4 relates the fraction of substituted products formed in the initial stage of reaction to the rate coefficients k_1 and k_2.

$$\frac{A_{335}^{T_1} - A_{335}^{T_0}}{A_{335}^{T_2} - A_{335}^{T_0}} = \frac{k_1}{(k_1 + k_2)} \qquad \text{Eqn.4.4}$$

Figure 4.4

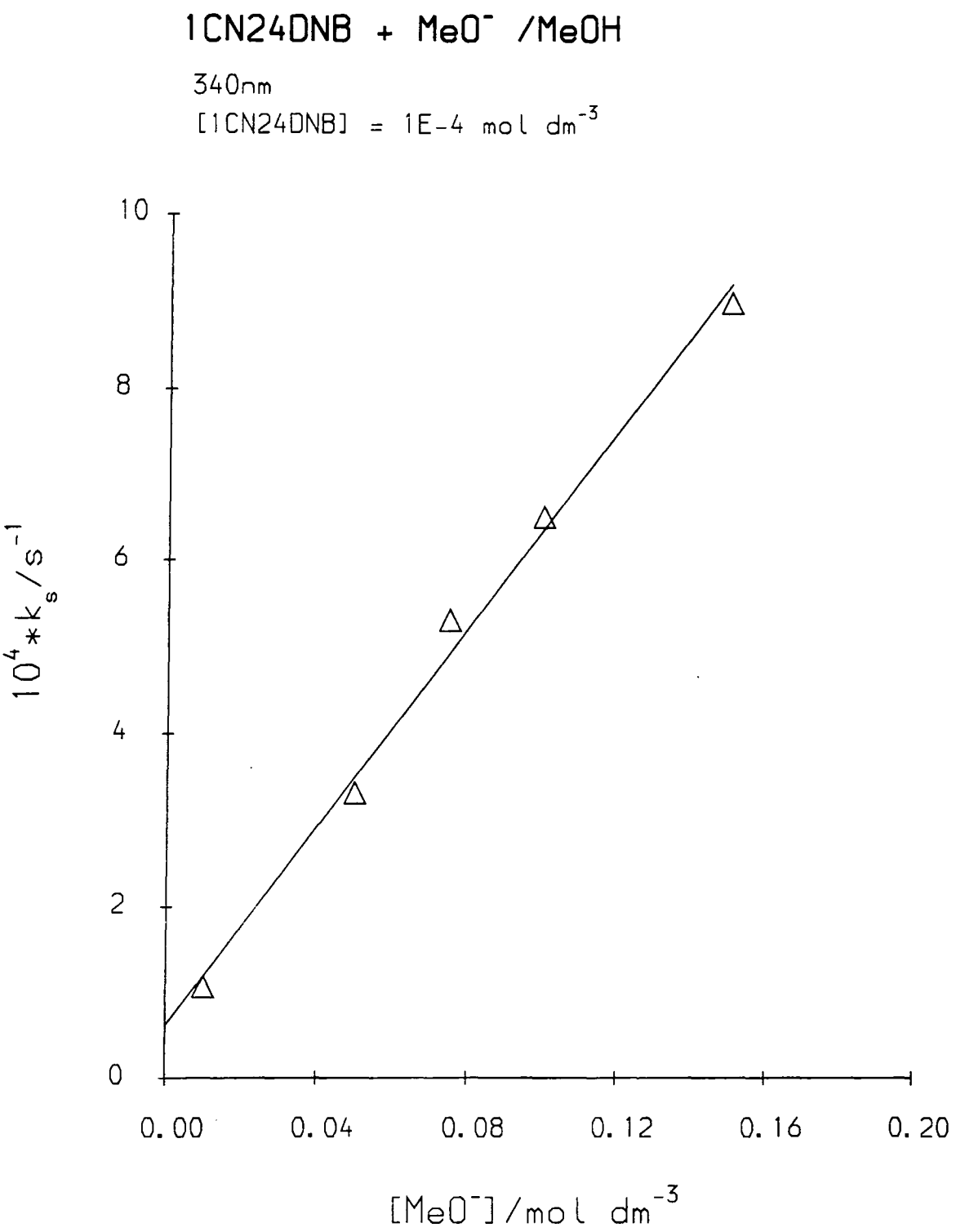

1CN24DNB + MeO⁻ /MeOH
340nm
[1CN24DNB] = 1E-4 mol dm⁻³
10
8
6
4
2
0
10⁴*k_s /s⁻¹
0.00
0.04
0.08
0.12
0.16
0.20
[MeO⁻] /mol dm⁻³

Figure 4.5

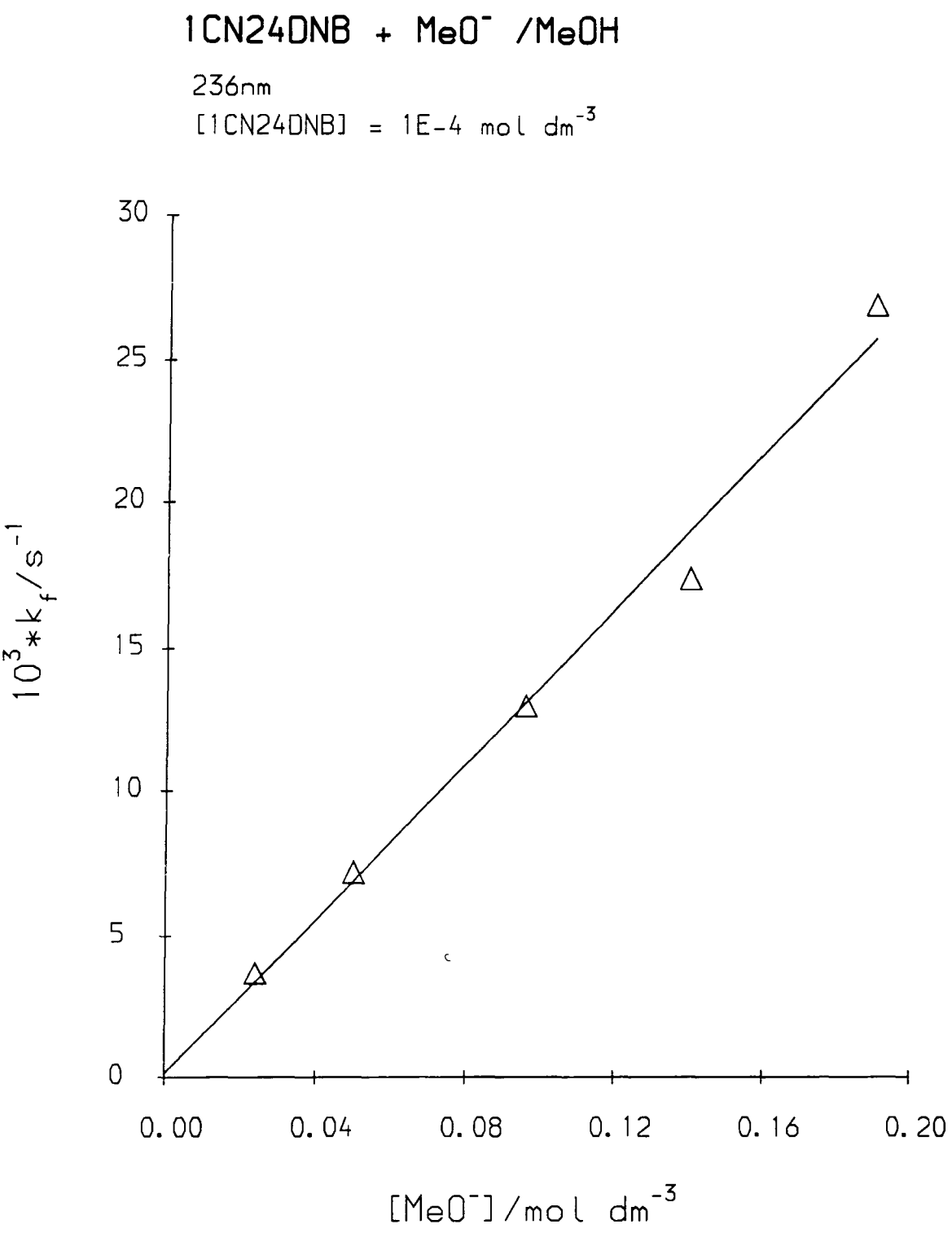

1CN24DNB + MeO⁻ /MeOH
236nm
[1CN24DNB] = 1E-4 mol dm⁻³
30
25
20
15
10
5
0
0.00
0.04
0.08
0.12
0.16
0.20
10³*k_f/s⁻¹
[MeO⁻]/mol dm⁻³

Figure 4.6

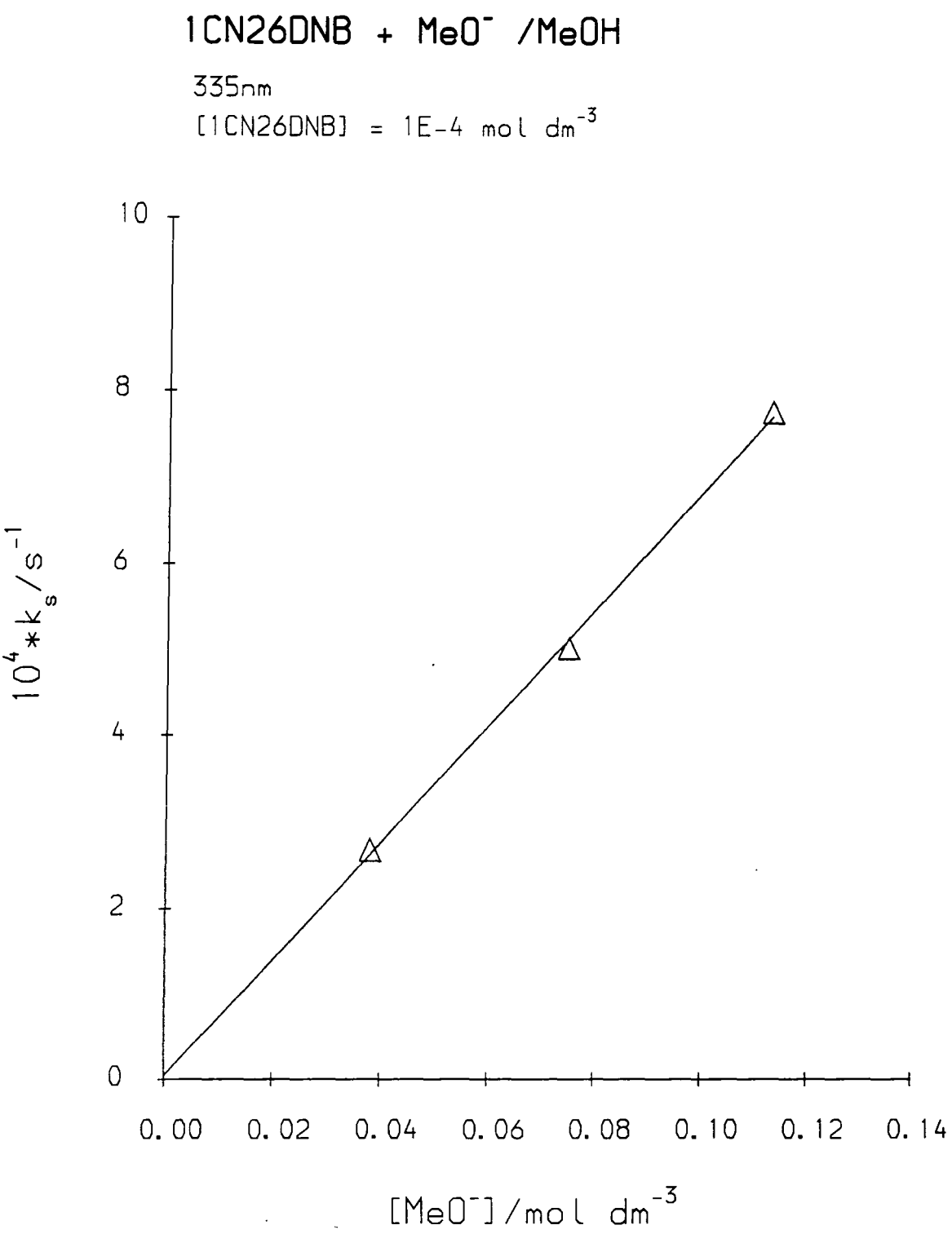

1CN26DNB + MeO⁻ /MeOH
335nm
[1CN26DNB] = 1E-4 mol dm⁻³
10
8
6
4
2
0
10⁴*k_s /s⁻¹
0.00
0.02
0.04
0.06
0.08
0.10
0.12
0.14
[MeO⁻]/mol dm⁻³

Figure 4.7

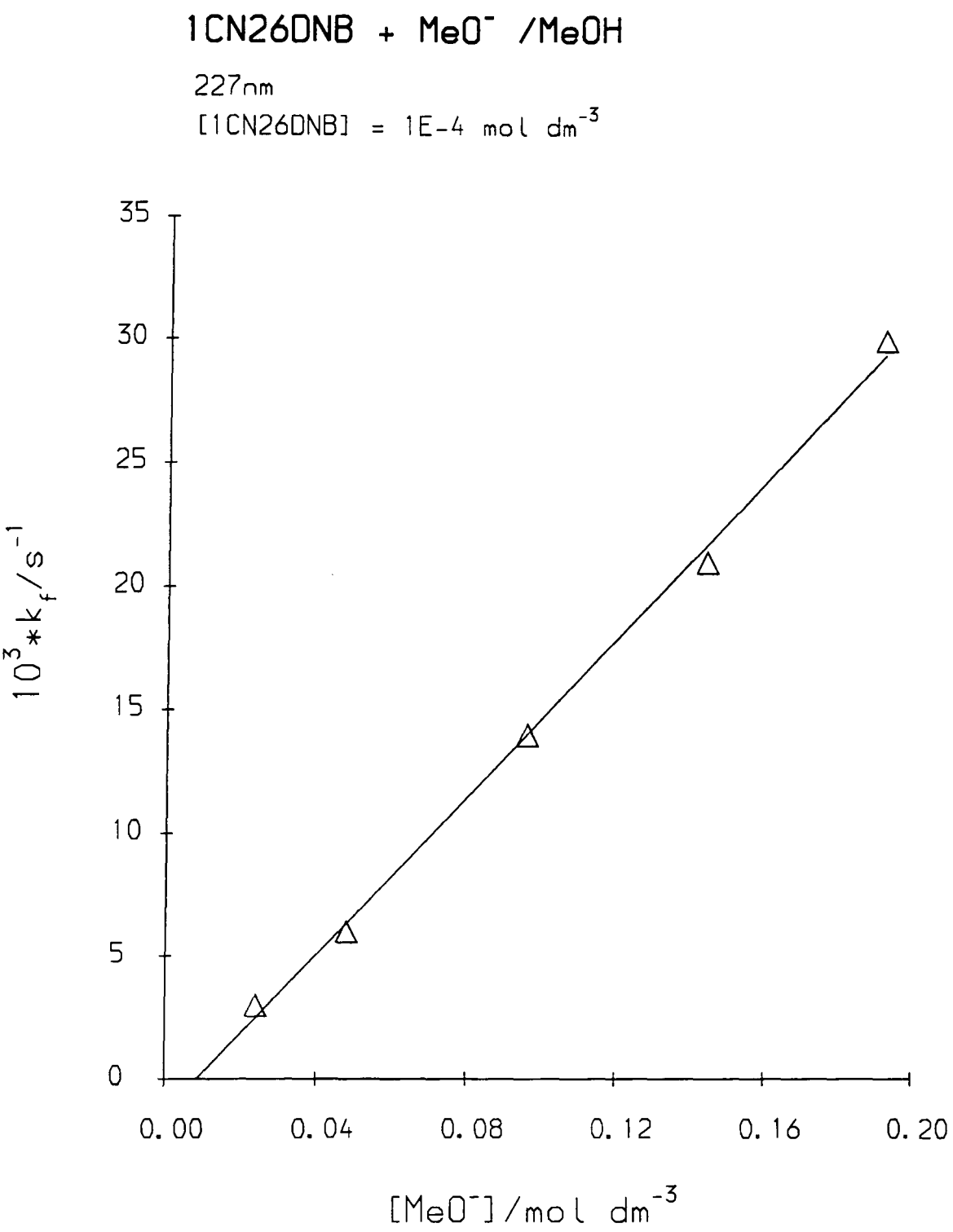

1CN26DNB + MeO⁻ /MeOH
227nm
[1CN26DNB] = 1E-4 mol dm⁻³
35
30
25
20
15
10
5
0
0.00
0.04
0.08
0.12
0.16
0.20
10³*k_f/s⁻¹
[MeO⁻]/mol dm⁻³

Table 4.2

Observed rate constants for the reaction of 1CN24DNB ($1x10^{-4}M$) with excess methoxide in methanol.

$[MeO^-]$ / M	$10^4 k_{slow}$ [a] $/s^{-1}$	$10^3 k_{fast}$ [b] $/s^{-1}$
0.01	1.08	——
0.024	——	3.7
0.05	3.31	7.2
0.075	5.3	——
0.096	——	13.0
0.10	6.5	——
0.14	——	17.4
0.15	9.0	——
0.19	——	27.0

Rate constants measured a) as an increase in absorbance at 340nm and b) as a decrease in absorbance at 236nm on a conventional uv/vis spectrophotometer.

Table 4.3

Observed rate constants for the reaction of 1CN26DNB ($1x10^{-4}M$) with excess methoxide in methanol.

$[MeO^-]$ / M	$10^4 k_{slow}$ [a] $/s^{-1}$	$10^3 k_{fast}$ [b] $/s^{-1}$
0.024	——	3.0
0.038	2.67	——
0.048	——	6.0
0.075	5.02	——
0.096	——	14.0
0.113	7.75	——
0.114	——	21.0
0.192	——	30.0

Rate constants measured a) as an increase in absorbance at 335nm and b) as a decrease in absorbance at 227nm on a conventional uv/vis spectrophotometer.

Table 4.4

1CN24DNB ($1x10^{-4}$M) + MeO^- /MeOH.

Comparison of absorbances at 335nm after the first (T_1) and the second (T_2) reactions.

$[MeO^-]$ /M		T /min	A_{335}	$\frac{k_1}{(k_1 + k_2)}$ [a]
0.096	T_0	0	0.15	0.45
	T_1	5	0.24	
	T_2	60	0.35	
0.048	T_0	0	0.17	0.47
	T_1	10	0.27	
	T_2	120	0.38	
0.024	T_0	0	0.14	0.68
	T_1	20	0.29	
	T_2	240	0.36	

a) from eqn.4.4. An average value of 0.533 is used in calc.4.1.

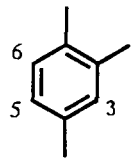
Table 4.5

1CN26DNB ($1x10^{-4}$M) + MeO^- /MeOH.

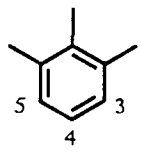
Comparison of absorbances at 335nm after the first (T_1) and the second (T_2) reactions.

$[MeO^-]$ /M		T /min	A_{335}	$\frac{k_1}{(k_1 + k_2)}$ [a]
0.22	T_0	0	0.24	0.52
	T_1	2	0.41	
	T_2	20	0.57	
0.11	T_0	0	0.17	0.59
	T_1	4	0.39	
	T_2	40	0.54	
0.055	T_0	0	0.12	0.60
	T_1	8	0.36	
	T_2	80	0.52	

a) from eqn.4.4. An average value of 0.570 is used in calc.4.1.



(4.4)



(4.5)

Table 4.6

Proton NMR shifts (δ) and coupling constants (J) of 1,2,4-trisusubstituted benzenes. (structure 4.4).

		δ /ppm					J /Hz	
Substrate	Solvent	H^3	H^5	H^6	H^{OMe}	H^{OMe}	J_{35}	J_{56}
1CN24DNB	CD_3OD	9.08	8.71	8.32	—	—	2.20	8.33
	d_6-DMSO	8.93	8.74	8.50	—	—	2.21	8.62
Solvate (4.6)	CD_3OD	8.79	8.54	7.8-9	—	—	2.13	8.54
1CN2MeO4NB	CD_3OD	7.98(s) & 7.91(s)			4.08	—	—	—
	d_6-DMSO	7.97	7.92	8.09	—	—	1.68	8.20
1CN4MeO2NB	CD_3OD	7.86	7.43	7.93	3.98	—	2.55	8.56
	d_6-DMSO	7.87	7.53	8.10	—	—	1.68	8.76
1CN24DMB	d_6-DMSO	6.73	6.66	7.63	3.89	3.85	2.11	8.56
2,4-Dinitro phenoxide	d_6-DMSO	8.54	7.73	6.26	—	—	3.18	9.75

The NMR spectrum of 1CN24DNB in d_4-methanol shows three coupled signals of the ring protons (table 4.6) (fig.4.8i) at 9.08, 8.71 and 8.32ppm. In the presence of an approximately three times excess of methoxide in d_4-methanol the spectrum (fig.4.8ii) shows a mixture of the solvate (4.6) and the substitution products (1CN2MeO4NB) (4.7) and (1CN4MeO2NB) (4.8) (scheme 4.1). The spectrum of the solvate (table 4.6) decreases in intensity during 15mins, as the bands due to the substitution products (4.7-8) (table 4.6) increase (fig.4.8iii). HPLC of the final reaction mixture gives the ratio of (4.7) to (4.8) as 2:1, no solvate is observed.

The NMR spectrum of 1CN26DNB in d_4-methanol shows two coupled signals of the ring protons (table 4.7) (fig.4.9i) at 8.58 and 8.09ppm. In the presence of an approximately three times excess of methoxide in d_4-methanol the spectrum (fig.4.9ii) shows a mixture of the solvate (4.9) and the substitution product (1CN2MeO6NB) (4.10) (scheme 4.2). The spectrum of the solvate (table 4.7) decreases in intensity during 60mins, as the bands due to the substitution product (4.10) (table 4.7) increase. After 24hrs some 1CN26DMB (4.11) is evident, together with (4.10), but there is no

solvate present (fig.4.9iii). 1CN2MeO6NB gives a complicated ABX spin system in methanol, and in DMSO (fig.4.10a), but a clearer picture is obtained in *d*-chloroform where an AMX spin system is obseved (fig.4.10b).

Scheme 4.1

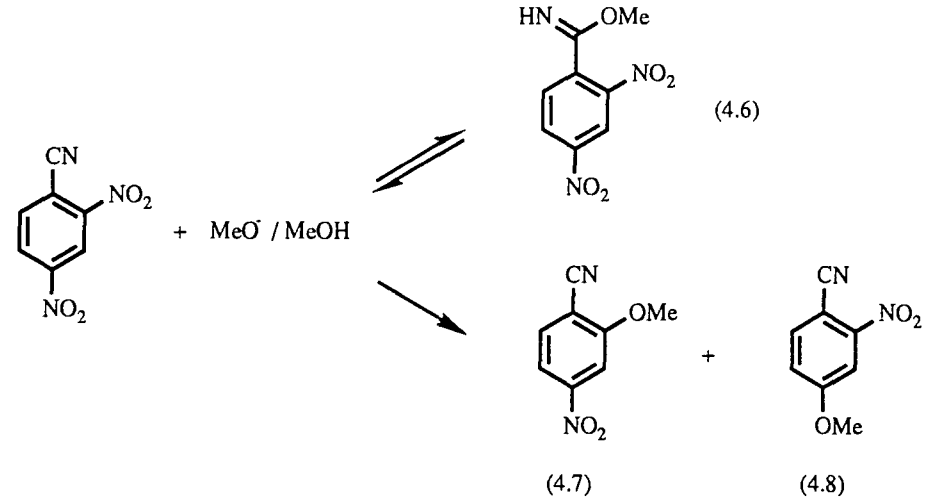


Table 4.7

Proton NMR shifts (δ) and coupling constants (J) of 1,2,6-trisusubstituted benzenes. (structure 4.5).

		δ /ppm				J /Hz	
Substrate	Solvent	H^3	H^4	H^5	H^{OMe}	J_{34}	J_{35}
1CN26DNB	CD_3OD	8.58	8.09	—	—	8.32	—
	d_6-DMSO	8.67	8.19	—	—	8.30	—
Solvate (4.9)	CD_3OD	8.38	7.85	—	—	8.08	—
1CN2MeO6NB	CD_3OD	7.95-87 & 7.74 [a]			4.02	—	—
	$CDCl_3$	7.86	7.73	7.35	4.06	8.25	1.07
	d_6-DMSO	7.95-87 & 7.74 [a]			4.02	—	—
1CN26DMB	CD_3OD	7.52	6.71	—	—	8.55	—
	d_6-DMSO	6.80	7.59	—	—	8.52	—
2,6-Dinitro phenoxide	d_6-DMSO	7.80	6.03	—	—	8.05	—
13DNB	CD_3OD	8.99 (H^2)	8.62	7.90	—	8.20	2.16
	d_6-DMSO	8.85 (H^2)	8.67	7.97	—	8.15	2.17

a) ABX pattern, see text.

Figure 4.8

^{1}H NMR spectra of 1CN24DNB in CD_3OD i) in the absence of methoxide; ii) at completion of the fast reactions with methoxide and iii) at completion of slow reaction with methoxide. Bands labelled "a" are due to parent, "b" are due to solvate (4.6) and "c" are due to the methoxy-nitro-benzonitriles (4.7) & (4.8).

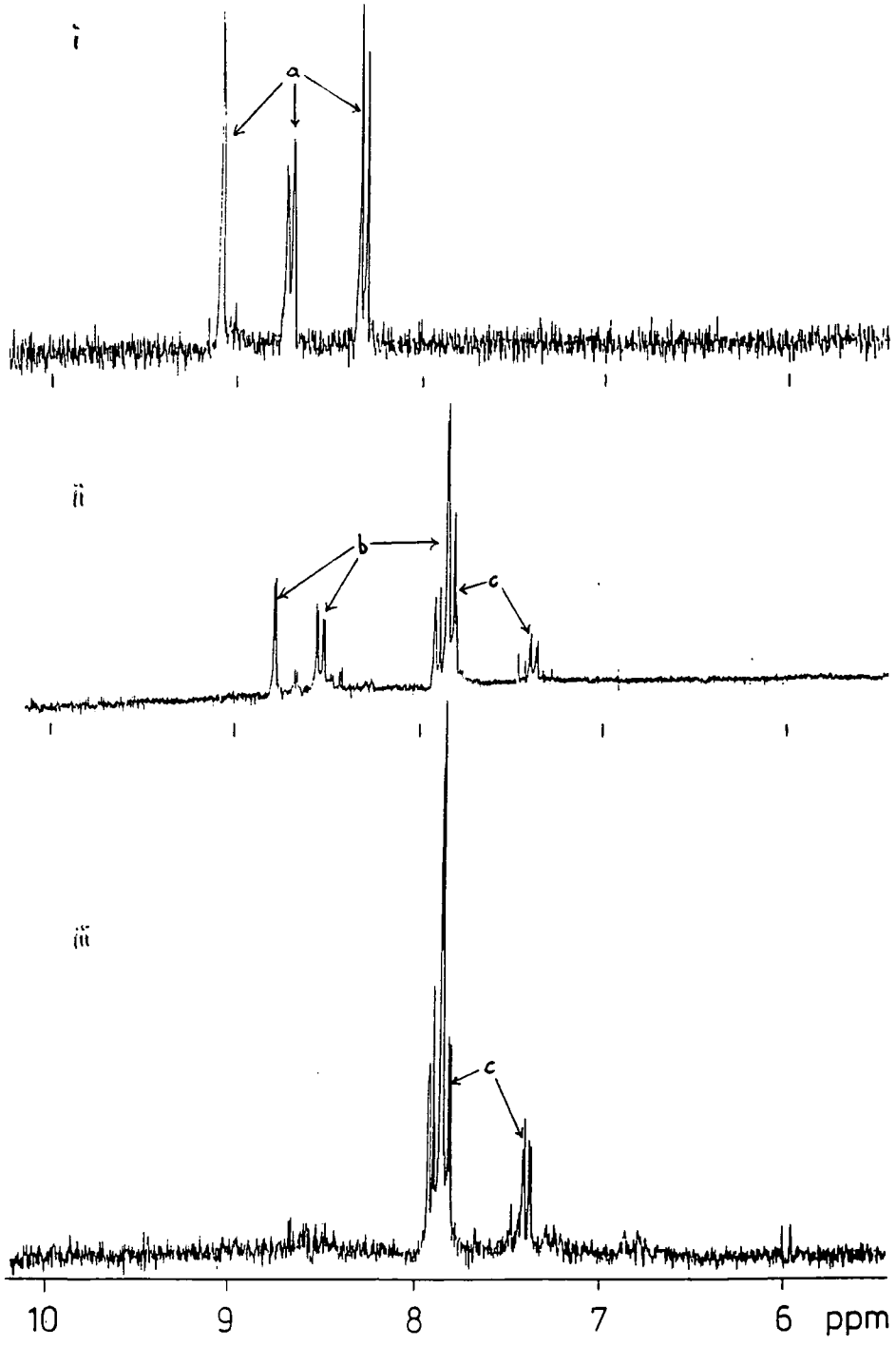
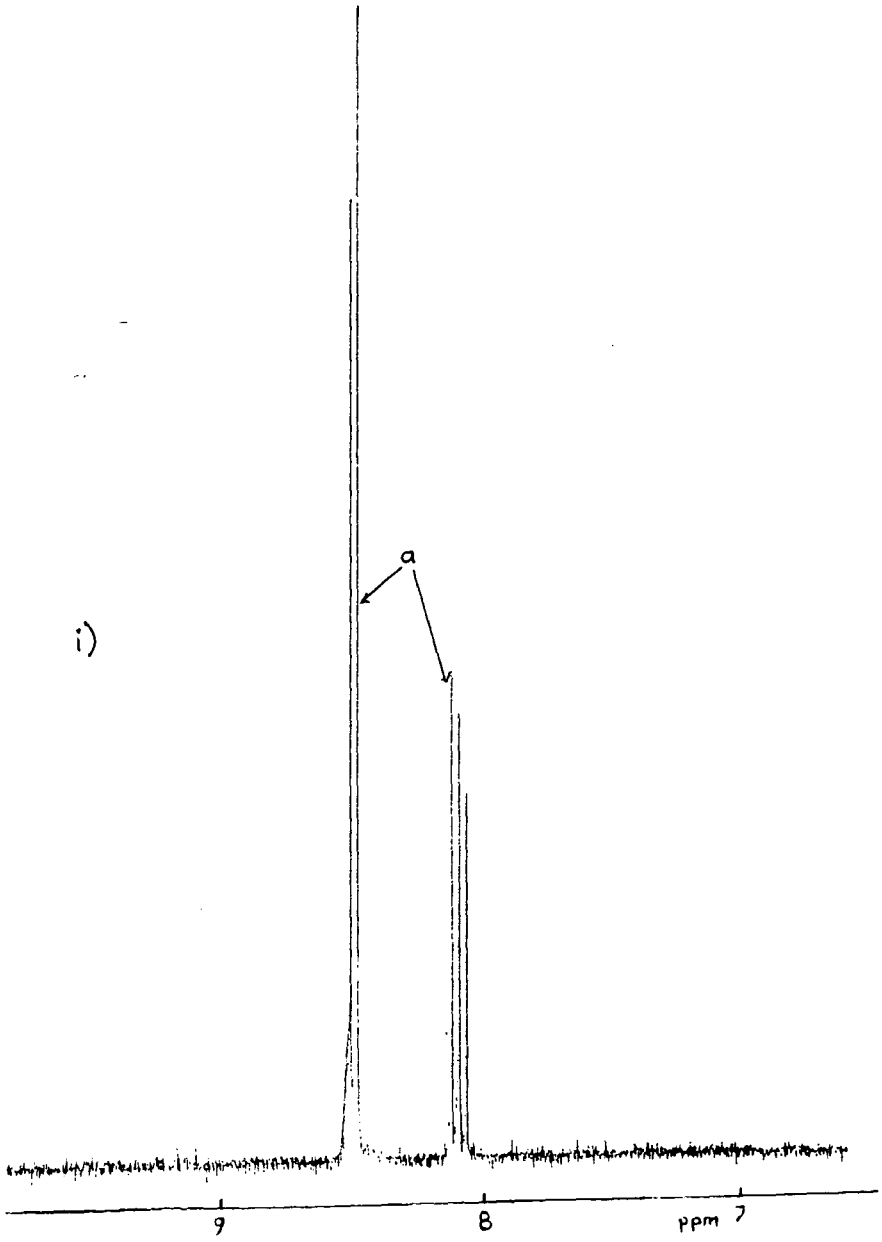
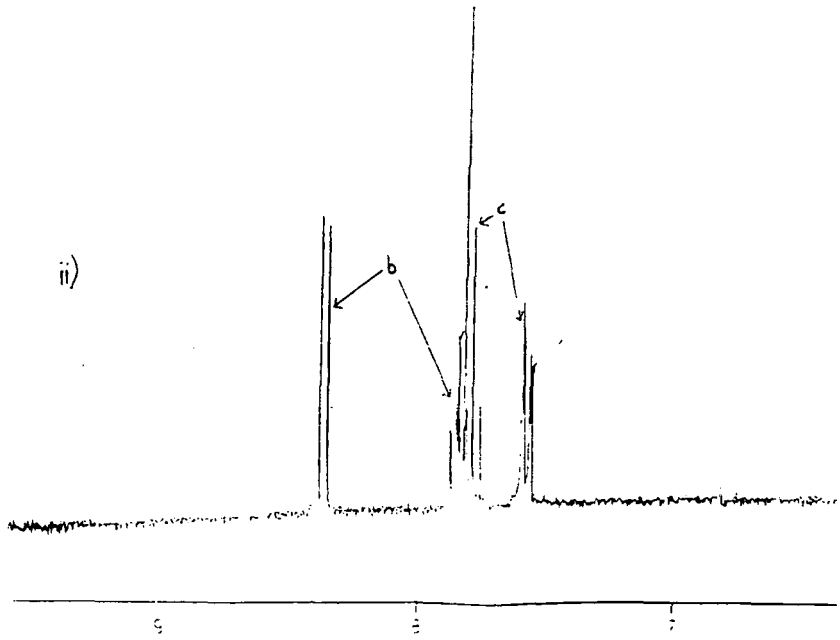


Figure 4.9

^{1}H NMR spectra of 1CN26DNB in CD_3OD i) in the absence of methoxide; ii) at completion of the fast reactions with methoxide and iii) at completion of slow reaction with methoxide. Bands labelled "a" are due to parent, "b" are due to solvate (4.9), "c" are due to 1CN2MeO6NB (4.10) and "d" are due to 1CN26DMB (4.11).




ii)
b
c
9
8
7

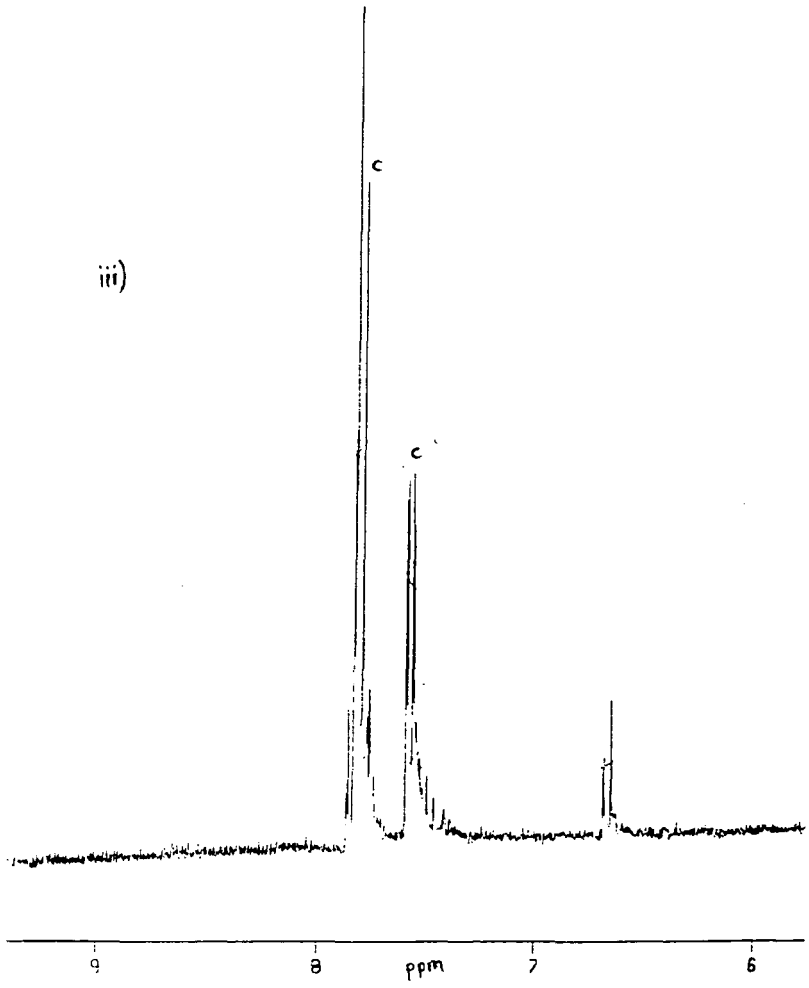
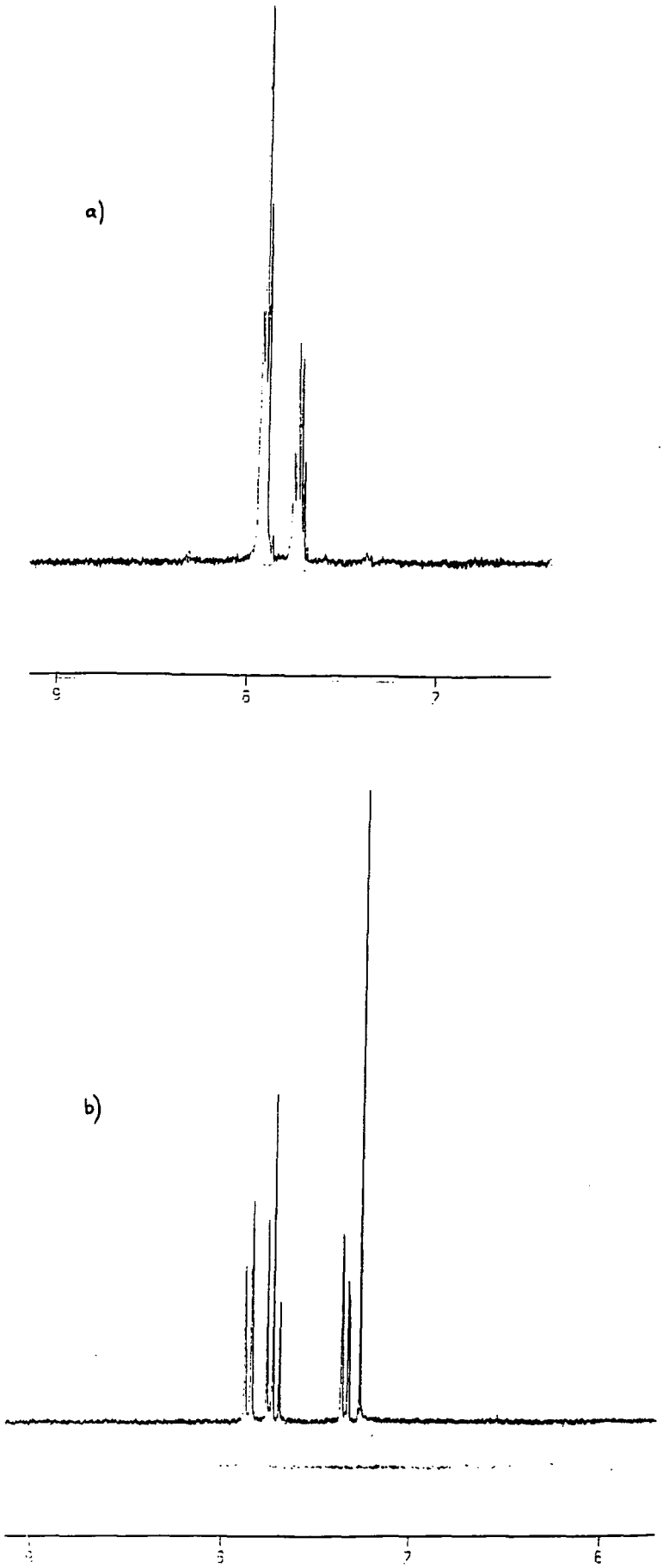
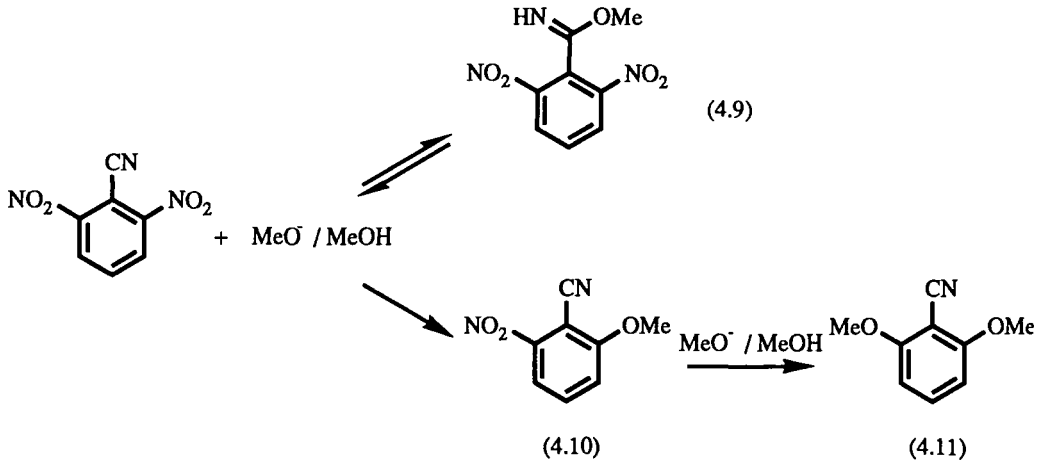

iii)
c
c
9
8
ppm
7
6

Figure 4.10

^{1}H NMR spectra of 1CN2MeO6NB (4.10) in a) d_6-DMSO and b) $CDCl_3$.



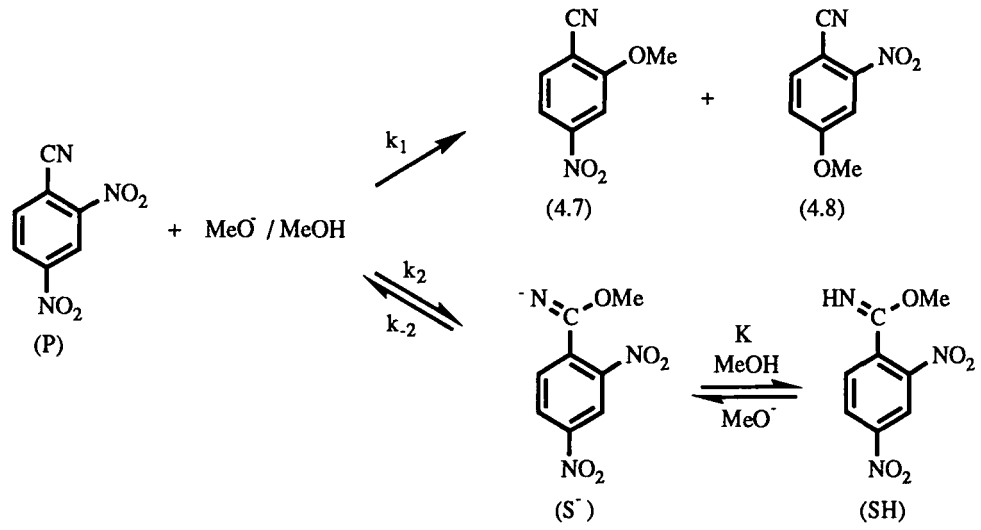
Scheme 4.2



4.2.2 Kinetic Analysis.

The results for 1CN24DNB can be interpreted in terms of scheme 4.3 and calculation 4.1; an analogous analysis can be used for 1CN26DNB.

Scheme 4.3



(S^-) will be a fairly strong base so will be predominantly in the form of the solvate (SH). The fast reaction is the initial disappearance of the parent (P). From the rate expression for this fast reaction (eqn.4.5) a value for the sum of ($k_1 + k_2$) can be calculated using a graph of k_f against methoxide concentration (figs.4.5 & 4.7). The expression for the gradients of the k_s against methoxide concentration graphs (figs.4.4 & 4.6) is given by eqn.4.6. These two equations, together with the average values for the ratios of k_1 to the sum ($k_1 + k_2$) shown in tables 4.4 and 4.5, allow calculations of values for k_1, k_2 and the ratio (k_{-2}/K). From these values the equilibrium constants for the solvolysis of the parent dinitrobenzonitriles (K_i) (eqn.4.7) can be calculated (calc.4.1); and compared with those found for other substituted benzonitriles (table 4.8).

Calculation 4.1

For the fast reaction: $k_f = (k_1 + k_2)\,[MeO^-]$ Eqn.4.5

For the slow reaction: Assume (S^-) and (SH) are in rapid equilibrium:

$$K = \frac{[SH]\,[OMe^-]}{[S^-]}$$

Assume (P) is a steady-state intermediate:

$$\frac{d[P]}{dt} = k_{-2}\,[S^-] - (k_1 + k_2)\,[MeO^-]\,[P] = 0$$

therefore

$$[P] = \frac{k_{-2}\,[S^-]}{(k_1 + k_2)\,[MeO^-]}$$

$$[P] = \frac{k_{-2}\,[SH]}{K\,(k_1 + k_2)}$$

but

$$\frac{d[(4.7)+(4.8)]}{dt} = \frac{-d[SH]}{dt} = k_1\,[P]\,[OMe^-]$$

$$\frac{-d[SH]}{dt} = \frac{k_1\,k_{-2}\,[SH]\,[OMe^-]}{K\,(k_1 + k_2)}$$

but

$$\frac{-d[SH]}{dt} = k_s\,[SH]$$

so

$$k_s = \frac{k_1\,k_{-2}\,[OMe^-]}{K\,(k_1 + k_2)}$$ Eqn.4.6

For solvolysis: $K_{imidate}$ (K_i):

$$(P) \overset{K_i}{\underset{MeOH}{\rightleftharpoons}} (SH)$$ Eqn.4.7

$$K_i = \frac{(SH)}{(P)}$$

therefore

$$K_i = K_2.K = \frac{k_2\,K}{k_{-2}}$$

Table 4.8

Calculated values of k_1, k_2 and K_i.

	k_1 [a]	k_2 [a]	log 10^2K_i
C_6H_5CN [b]	——	——	1.40
pClC$_6$H$_4$CN [b]	——	——	1.91
pNO$_2$C$_6$H$_4$CN [b]	——	——	2.69
mNO$_2$C$_6$H$_4$CN [b]	——	——	2.78
1CN24DNB [c]	0.080	0.070	2.81
1CN26DNB [c]	0.077	0.058	2.69

a) units of $dm^3 mol^{-1} s^{-1}$
b) ref 8.
c) this work.

4.2.3 In DMSO.

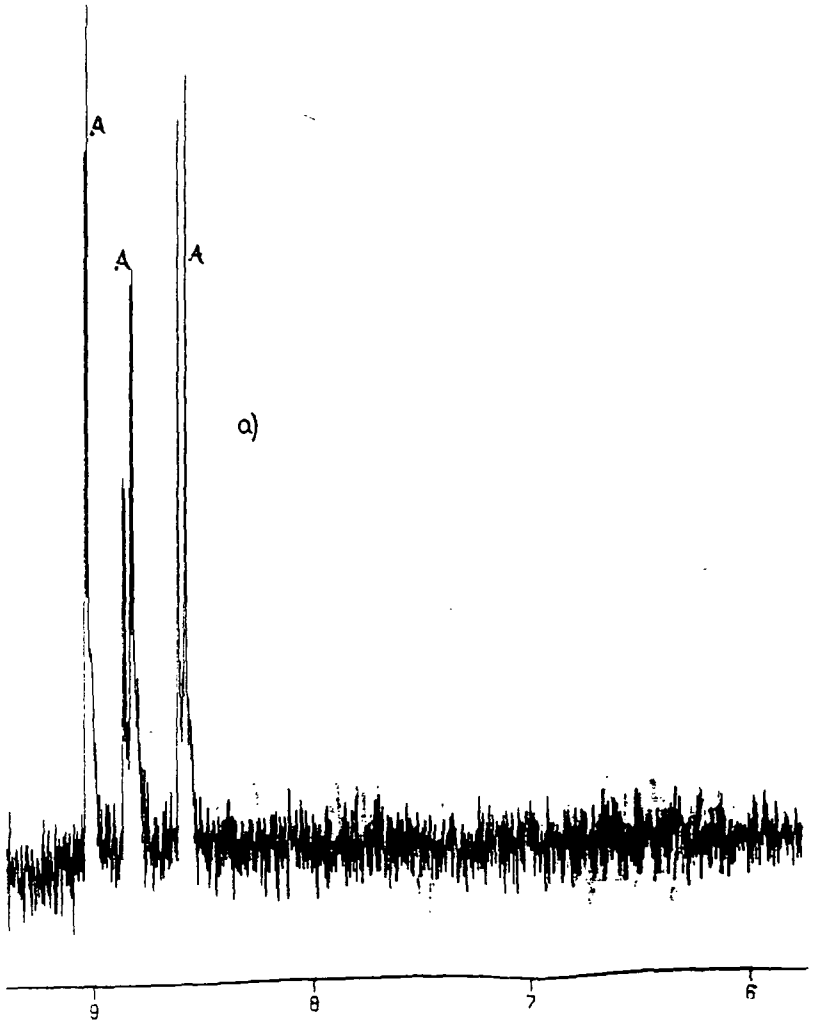
In DMSO there are also two processes involved. There is a rapid equilibrium involving the formation of the respective methoxy-sigma complex; and slower, irreversible replacement of a nitro group by a methoxy group. In turn this is followed in excess methoxide by the replacement of the remaining nitro group to yield the final product, the dimethoxybenzonitrile.

The NMR spectrum of 1CN24DNB in DMSO-d_6 shows three coupled signals of the ring protons (table 4.5) (fig.4.11a) at 8.93, 8.74 and 8.50ppm. In the presence of a three times excess of methoxide in DMSO-d_6 the initial spectrum (fig.4.11b) shows the signals of the sigma complex (4.12) (δ_{ppm}: 8.46(s)(H^3), 6.38(s)(H^6), 5.42(s)(H^5), J_{56}=5.95Hz; λ_{max} 495nm) (fig.4.12), but these fade over an hour to leave the signals (table 4.6) of a mixture of (4.7), (4.8) and 2,4-dimethoxybenzonitrile (1CN24DMB) (4.13) (fig.4.11c) (scheme 4.4). After seven days (4.13) is the predominant species (scheme 4.4).

The NMR spectrum of 1CN26DNB in DMSO-d_6 shows two coupled signals of the three ring protons at 8.67 and 8.19ppm (fig.4.13a) (table 4.7). On mixing with a three times excess of methoxide a crimson/purple colour (λ_{max} 544nm) is initially observed by uv/vis spectroscopy (fig 4.14) due to the sigma complex (4.12), but this fades too quickly for NMR analysis. The first species observed by NMR are 1CN2MeO6NB (4.10) and 1CN26DMB (4.11) (table 4.7) (fig.4.13b). After an hour (4.11) is the predominant species (scheme 4.5).

Figure 4.11

^{1}H NMR spectra of 1CN24DNB in d_6-DMSO a) in the absence of methoxide; b) initially after mixing with methoxide and c) at completion of slow reactions with methoxide.



Bands labelled: A - 2,4-dinitrobenzonitrile, B - sigma-complex (4.12), C - 2-methoxy-4-nitrobenzonitrile, D - 4-methoxy-2-nitrobenzonitrile, E - 2,4-dimethoxybenzonitrile.

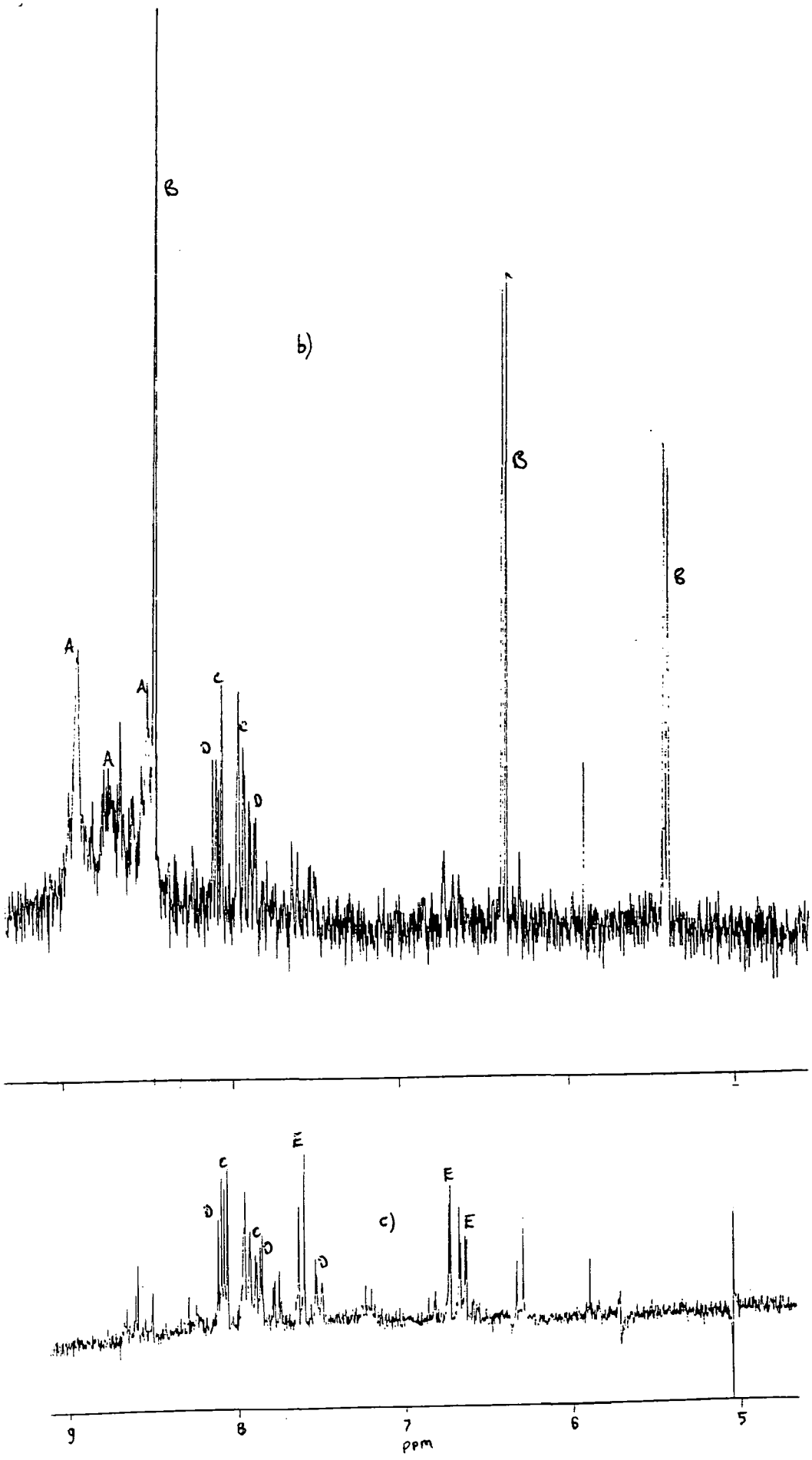

B
b)
B
B
A
A
A
C
C
D
D
D
E
C
D
C
D
D
c)
E
E
9
8
7
6
5
ppm

Figure 4.12

UV/Vis spectra of 1) 1CN24DNB($1x10^{-4}$M) /DMSO,
2) 1CN24DNB($1x10^{-4}$M) + MeO^-(0.0011M) /DMSO (int. = 3min)
and 3) after 40mins.

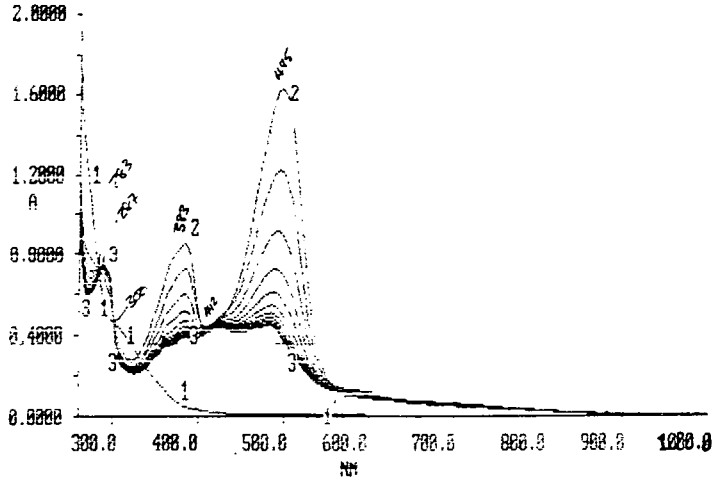


Figure 4.14

UV/Vis spectra of 1) 1CN26DNB($1x10^{-4}$M) /DMSO,
2) 1CN26DNB($1x10^{-4}$M) + MeO^-(0.0011M) /DMSO,
3) after 30sec (int. = 30sec) and 4) after 4mins.

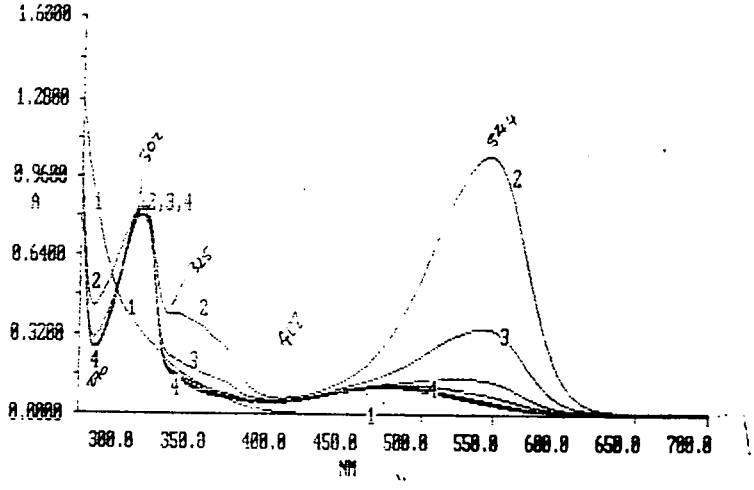
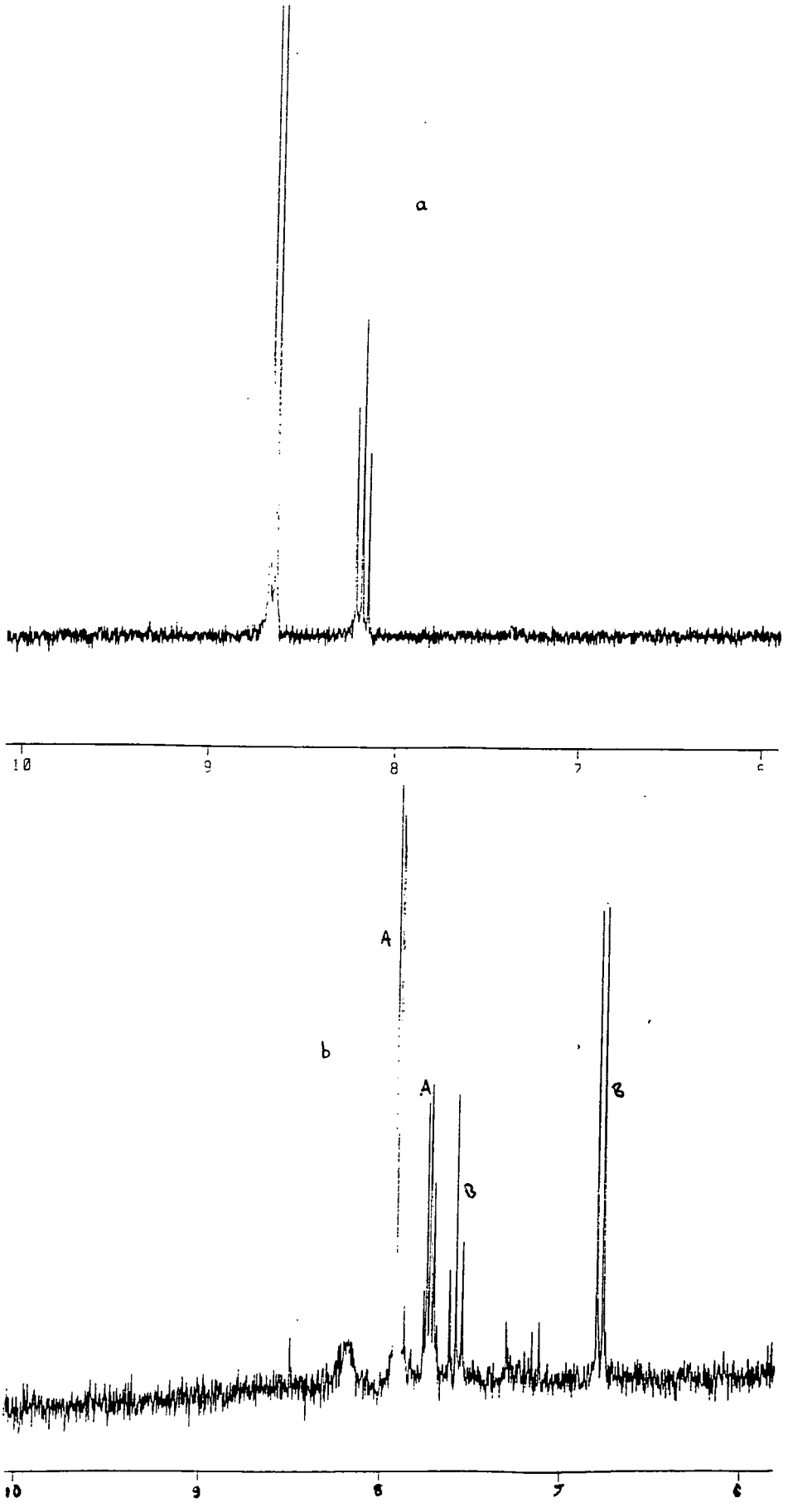


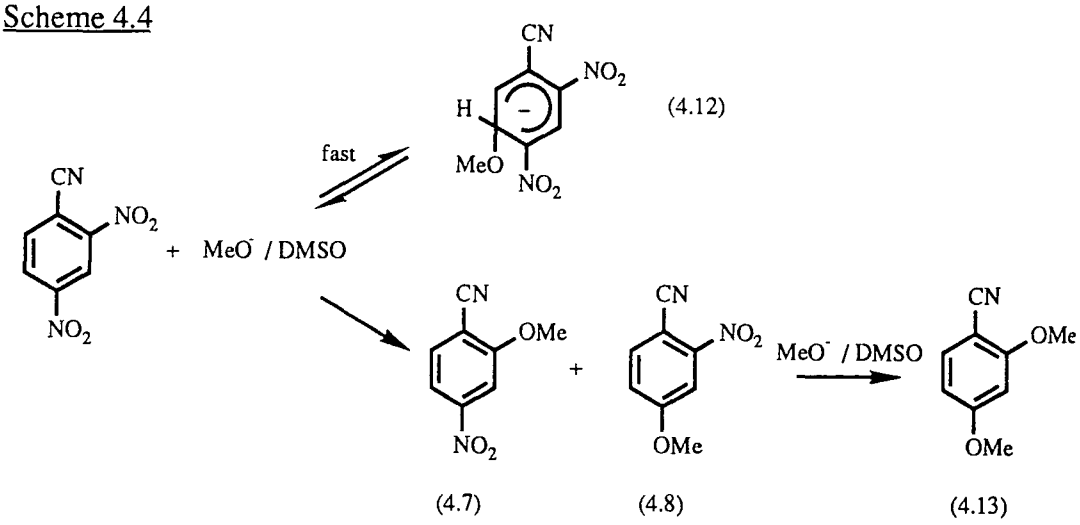
Figure 4.13

^{1}H NMR spectra of 1CN26DNB in d_6-DMSO a) in the absence of methoxide and b) 2mins after mixing with methoxide.

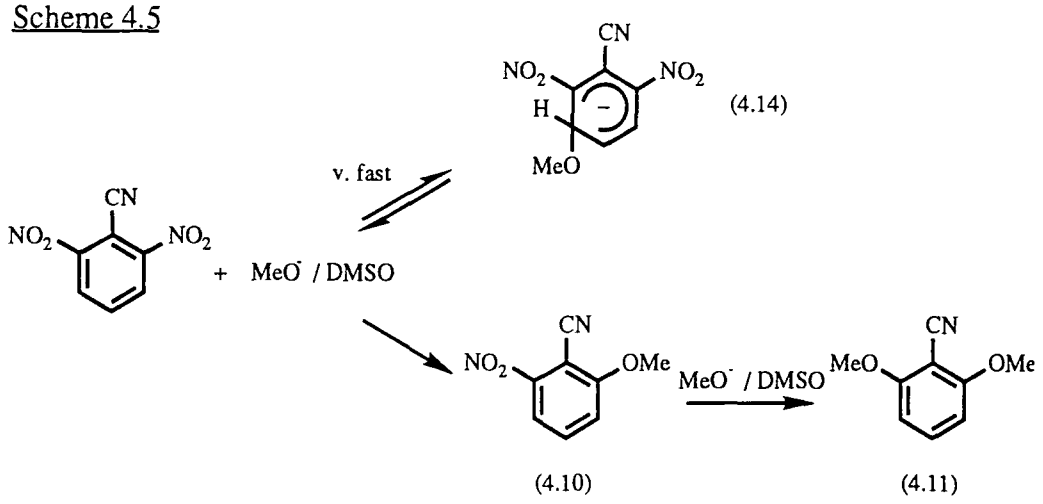
Bands labelled: A - 2-methoxy-6-nitrobenzonitrile, B - 2,6-dimethoxybenzonitrile.



Scheme 4.4



Scheme 4.5



4.2.4 The Solvent Effect.

In methanol there is competition between attack at ring-carbons carrying a nitro group and at the carbon of the cyano group. There is no evidence of detectable concentrations of sigma-complex intermediates because the equilibrium constants for their formation are too low in this medium.

Solutions of methoxide in DMSO are many orders of magnitude more basic than solutions in methanol. Hence we initially observe rapid formation of sigma complexes. A slower reaction involves attack at ring-carbons carrying nitro groups, which in excess methoxide can lead to replacement of both nitro groups.

In DMSO there is no evidence for methanol addition to the cyano group. This reaction involves methanol as a reactant, and in this media, where the activity of methanol is low, the reaction will be disfavoured.

4.3 THE REACTIONS OF SUBSTITUTED-*META*-DINITROBENZENES WITH CYANIDE IN METHANOL.

Russell and Tebbens [1] produced 2-methoxy-6-nitrobenzonitrile in their synthesis of 2,6-dimethoxybenzonitrile from *meta*-dinitrobenzene and potassium cyanide in methanol. This reaction has been repeated on a smaller preparative scale and on the NMR scale with *meta*-dinitrobenzene and 2,4- and 2,6-dinitrobenzonitrile. Different products to those originally recorded have been examined, and the effect of pH has been studied.

4.3.1 *Meta*-dinitrobenzene.

A solution of potassium cyanide (11.5g) (0.18 moles) in water (20ml) was added to a solution of *meta*-dinitrobenzene (25g) (0.15 moles) in methanol (375ml) at 40°C with stirring. The resulting dark purple mixture was stirred for 2hrs and then allowed to stand at room temperature for 2-3 days. A black precipitate was collected by filtration and allowed to dry in the air. The filtrate was diluted with 3l of water and allowed to stand overnight. A further brown precipitate was collected by filtration and allowed to dry in the air. The combined precipitates were refluxed for 30mins with successive 30, 25 and 25ml aliquots of chloroform. The chloroform extracts were filtered while hot and the red filtrates combined and concentrated to 25ml. Addition of petroleum ether (b.p. 60-80°C) (50ml) causes a suspension to separate.

Filtration and drying yields a red powder which contains a mixture of products (16% yield, m.pt. 169-70°C, lit.[1] 148-57°C). Analysis by HPLC gave the ratio of 1CN2MeO6NB(r_t = 7.4min) to 1CN2MeO4NB(r_t = 10.7min) as 10:1, also evident are traces of 1CN4MeO2NB(r_t = 9.2min)and 1CN26DMB(r_t = 7.9min). Mass spectrometry shows the molecular ion of 178mu., consistent with a nitro-methoxy-substituted benzonitrile. The observed elemental analysis: 15.8% N, 54.5% C, 3.5% H, agrees well for that calculated for a nitro-methoxy-substituted benzonitrile (15.7% N, 53.9% C, 3.4% H). UV/Vis spectrophotometry and proton NMR confirm that the major product is 2-methoxy-6-nitrobenzonitrile (tables 4.1 and 4.7).

The experiment was repeated, but with acid added in an effort to control the pH and limit the concentration of methoxide ions (13DNB 25g, KCN 17.25g 0.265 moles, HCl (11.6M) 7.7ml 0.09 moles). Since hydrochloric acid quantitatively converts potassium cyanide to hydrogen cyanide, the amounts used leave the same ratio of free cyanide to substrate as in the original experiment. The pH of the reaction mixture was monitored during the reaction (table 4.9).

An orange brown powder was produced (1.81g, 7.2% yield by mass; m.pt. 106-8°C). Two molecular ions are shown in the mass spectrum, 178 and 181mu. NMR (fig.4.15) shows the coupled signals of 1CN2MeO6NB (table 4.7) and other significant signals at 7.00ppm (d) J = 9.18Hz and 6.85ppm (s). In experiments with 2,4- and 2,6-dinitrobenzonitrile described below (sections 4.3.3 and 4.3.2 respectively) the doublet at 7.00ppm is associated with a doublet at 7.85ppm, and the singlet at 6.85ppm is associated with a singlet at 7.94ppm. In fig.4.15 these further signals are obscured by those of 1CN2MeO6NB. In sections 4.3.2 and 4.3.3 below these signals are ascribed to the isomeric dicyano-dimethoxy-benzenes (4.16) and (4.17). HPLC (fig 4.15) shows two major products, one of which is 1CN2MeO6NB; no 1CN26DMB, 1CN2MeO4NB or 1CN4MeO2NB are observed. The peaks r_t = 8.0 and 9.0min are assigned below to (4.16) and (4.17) respectively.

Table 4.9

The pH of the buffered reaction mixture of 13DNB and KCN in methanol.

Time /min	0	10	60	90	120
pH	10.9	10.7	11.4	11.8	12.4

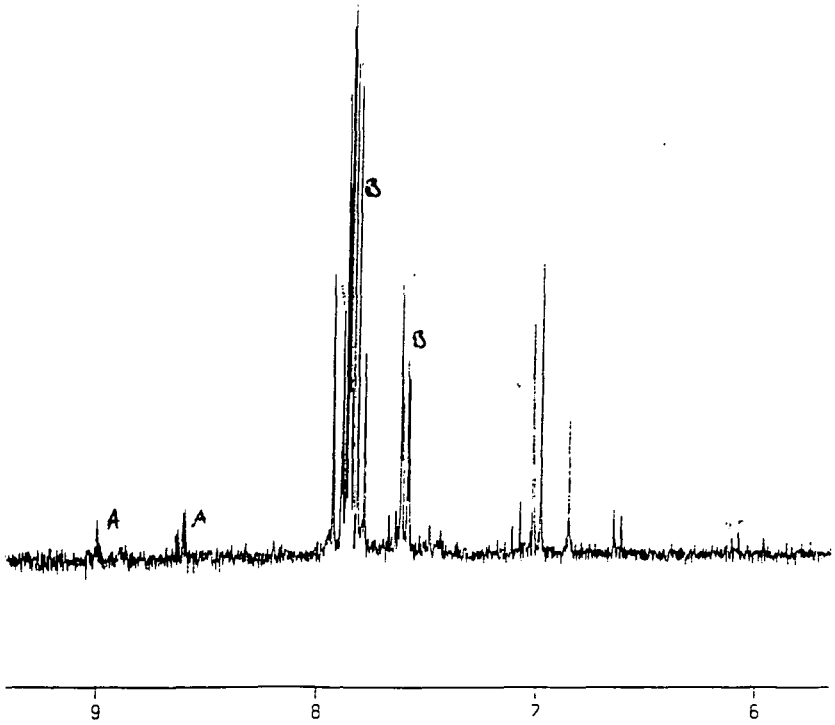
The Russell-Tebbens reaction has been simulated on an NMR scale using deuterated solvents (molar ratio 13DNB:KCN 1:1.2, 5.3% D_2O v/v in CD_3OD).The mixture was kept at 40°C at all times except when spectra were being acquired (when it was at room temperature), and was shaken regularly. The spectrum recorded after two hours is shown in figure 4.17a; major bands seen are due to 13DNB and 1CN2MeO6NB but other minor species are also present. At the end of reaction the major signals observed (fig.4.17b) are due to 13DNB, 1CN2MeO6NB and 1CN26DMB.

In an attempt to produce 2,6-dinitrobenzonitrile from 13DNB the Russell-Tebbens reaction was carried out in *iso*-propanol instead of methanol. It has been reported [9] that alcoholysis of the cyanide ion occurs less readily in *iso*-propanol than in methanol.

13DNB (1.68g in 30ml *iso*-propanol) was mixed with KCN (0.92g in 1.6ml water) and the usual Russell-Tebbens procedure carried out. This yielded a small amount of solid which gave the NMR spectrum shown (fig.4.18a). This spectrum is consistent with 6-*iso*-propoxy-2-nitrobenzonitrile (4.15). The aromatic protons give a complex ABX pattern (c.f. 1CN2MeO6NB). The coupled signals at 4.93 and 1.35ppm are due to the *iso*-propoxy group. The coupling constant within the alkoxy group is 6.00Hz. The signal at 2.50ppm is due to incomplete deuteration of the solvent (DMSO); that at 3.31ppm may be due to water in the solvent.

Figure 4.15

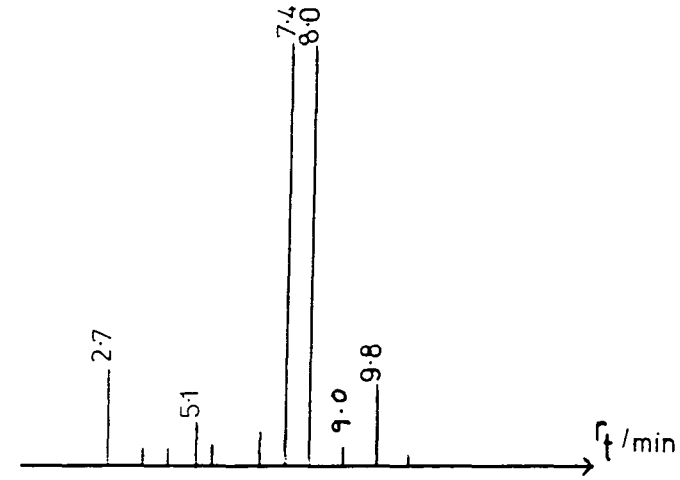
^{1}H NMR spectra of the product of the reaction between 13DNB and KCN in methanol in the presence of acid.



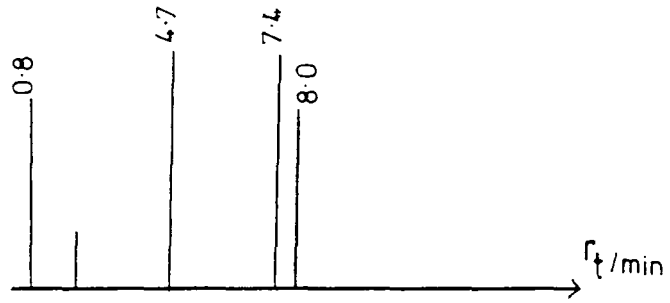
Bands labelled: A - *meta*-dinitrobenzene, B - 2-methoxy-6-nitrobenzonitrile.

Figure 4.16

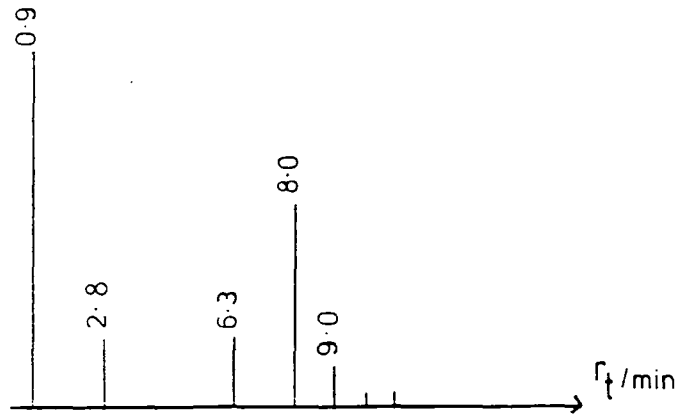
HPLC analysis of final product mixtures.



13DNB + KCN (controlled pH)



1CN26DNB + KCN



1CN24DNB + KCN

Figure 4.17

^{1}H NMR spectra of the reaction between 13DNB and KCN in CD_3OD after a) 2hrs and b) 24hrs.

Bands labelled: A - *meta*-dinitrobenzene, B - 2-methoxy-6-nitrobenzonitrile, C - 2,6-dimethoxybenzonitrile.

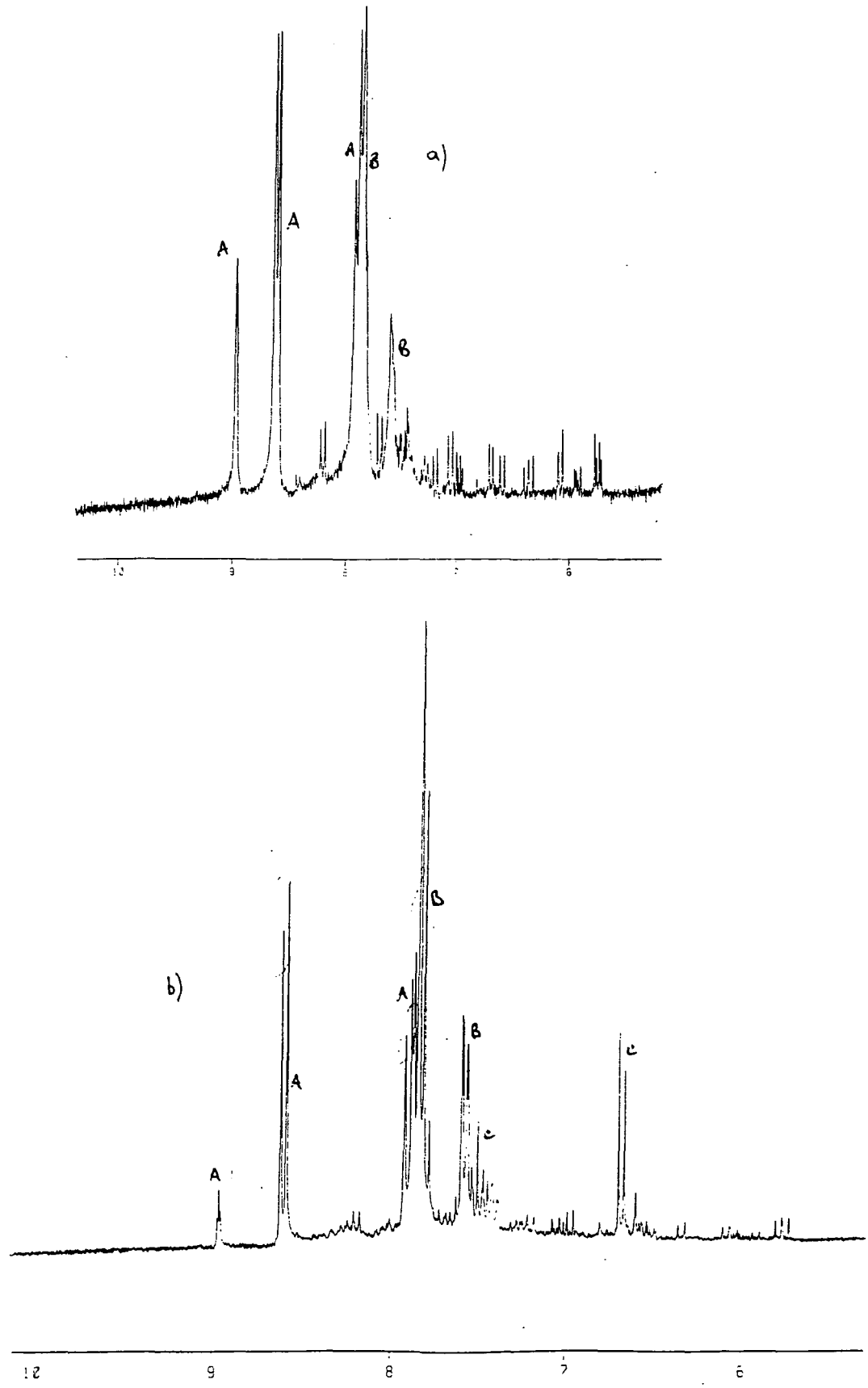
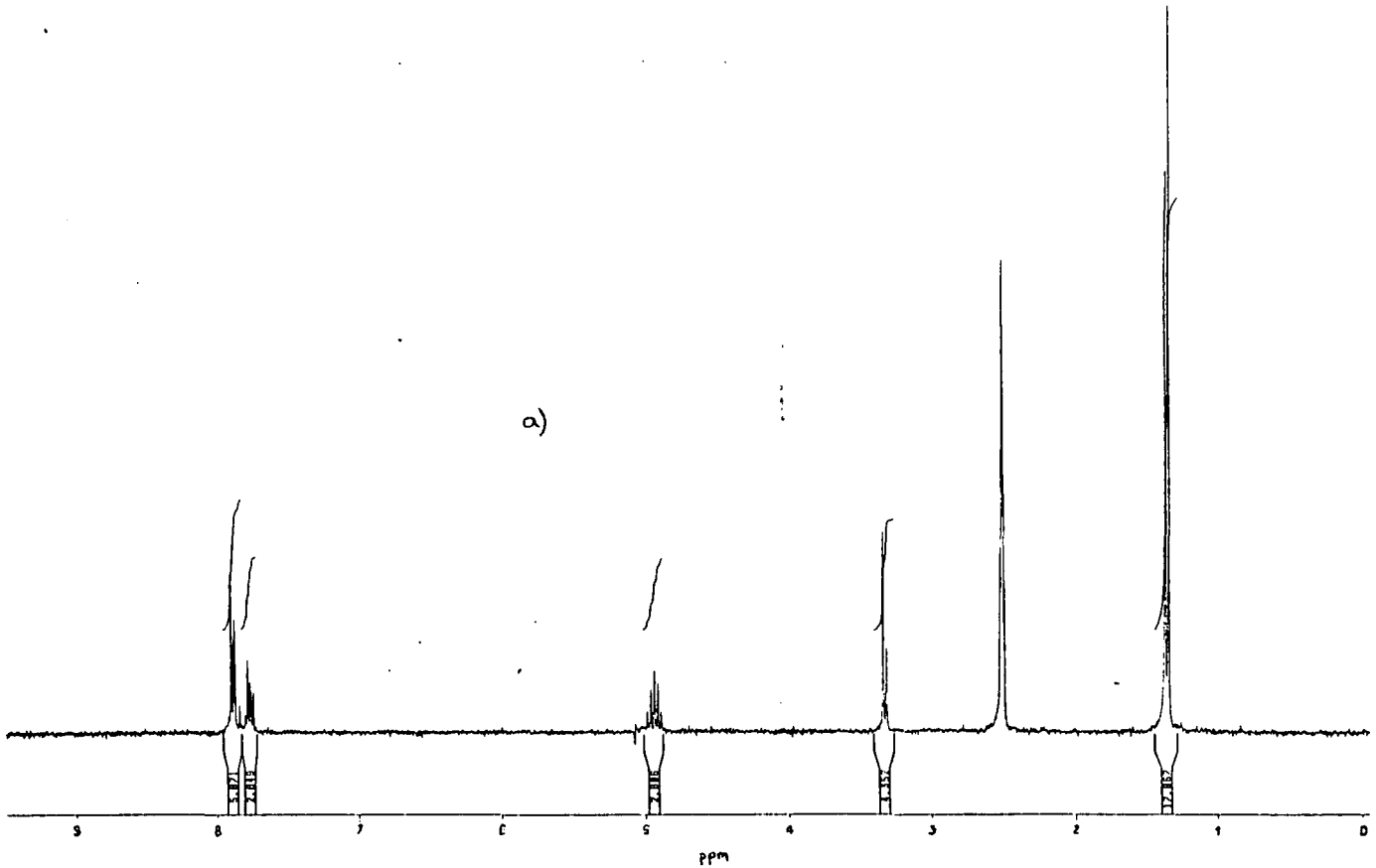
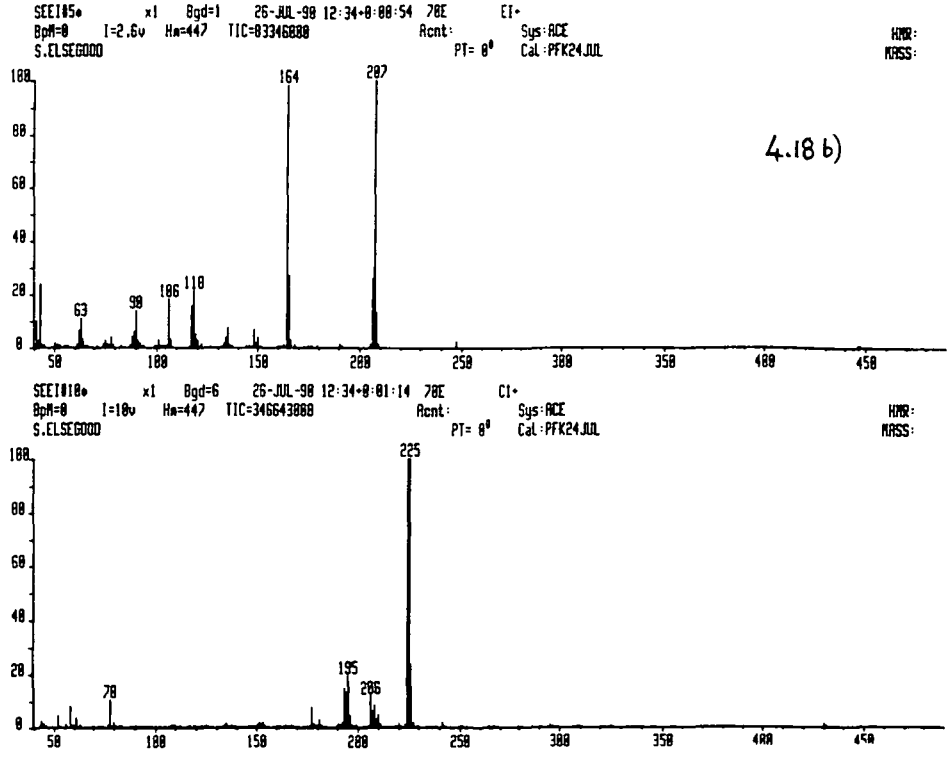


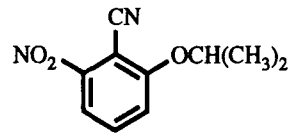
Figure 4.18

The product of the reaction between 13DNB and KCN in *iso*-propanol:
a) ^{1}H NMR spectrum and b) mass spectra.




SEE#85◆ x1 Bgd=1 26-JUL-98 12:34+0:00:54 78E EI+
BpM=0 I=2.6v Hm=447 TIC=83346888 Acnt: Sys:ACE HMR:
S.ELSEGOOD PT= 0° Cal:PFK24.JUL MASS:
100
80
60
40
20
0
164
207
63
98
106
110
50
100
150
200
250
300
350
400
450
4.18 b)
SEE#18◆ x1 Bgd=6 26-JUL-98 12:34+0:01:14 78E EI+
BpM=0 I=10v Hm=447 TIC=346643888 Acnt: Sys:ACE HMR:
S.ELSEGOOD PT= 0° Cal:PFK24.JUL MASS:
100
80
60
40
20
0
225
195
206
78
50
100
150
200
250
300
350
400
450

The electron ionisation (E.I.) mass spectrum (fig.4.18b) shows a molecular ion peak at 207mu. The relative molecular mass of 6-*iso*-propoxy-2-nitrobenzonitrile is 206. The signal at 207mu. is indicative of self-protonation in the ion chamber, probably caused by the labile proton in the *iso*-propoxy group. The strong (M-43) peak (164mu.) is due to the loss of the C_3H_7 fragment.



(4.15)

4.3.2 2,6-Dinitrobenzonitrile.

The reaction of 1CN26DNB with cyanide under Russell-Tebbens conditions has been studied on the NMR and preparative scale.

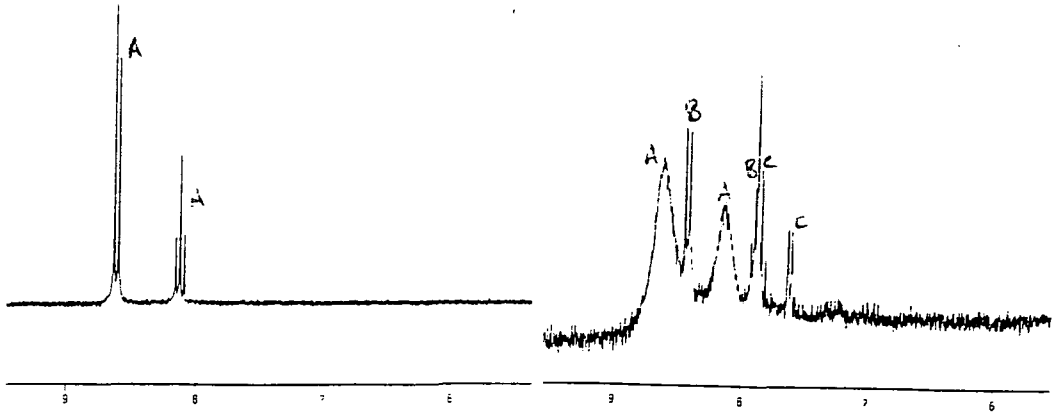
The NMR spectrum of 1CN26DNB in methanol-d_4 shows the two coupled signals of the ring protons (table 4.7). 10 minutes after mixing with cyanide broad bands are observed due to the parent and sharp bands assigned to the imidate (4.9) and 1CN2MeO6NB (4.10) (fig.4.19). After an hour the small resonances of the parent are sharp; bands due to (4.9) and (4.10) are still present. There are three unassigned doublets: 7.10ppm (d) J = 9.45Hz, 7.00ppm (d) J = 9.20Hz and 6.64ppm (d) J = 8.70Hz. With time the doublet at 7.00ppm increases in intensity to become a major peak in the final spectrum. Experiments with 2,4-dinitrobenzonitrile, described below (4.3.3), in which a product is isolated show that this doublet is associated with one of equal intensity at 7.85ppm. These peaks are attributed to 1,3-dicyano-2,4-dimethoxybenzene (4.16). The doublets at 7.10 and 6.64ppm gradually decay and are replaced by doublets at 7.31 and 6.55ppm, J = 8.8Hz. The latter pairs of doublets have not been unambiguously assigned but might be due to solvate of the eventual product or to phenolic products. HPLC of the final product mixture (fig.4.16) reveals the presence of several species. The band at r_t 7.4min is assigned to 1CN2MeO6NB, that at r_t 8.0min is assigned to 1,3-dicyano-2,4-dimethoxy-benzene. The other bands remain unassigned, but it is suspected that those species with a very short retention time may be phenolic products.

A Russell-Tebbens type preparation with 1CN26DNB (2g in 30ml methanol) and KCN (0.92g in 1.6ml water) yielded a pale brown solid: 15.59% N, 58.41% C, 3.80% H. The ^1H NMR spectrum in CD_3OD gave the signals expected for 1CN2MeO6NB (table 4.7) together with bands at 7.85(d) J=9.20Hz, 7.00(d), J=9.20Hz, 4.24(s) and4.02(s) (fig.4.20). It is proposed that the doublets at 7.85 and 7.00ppm are

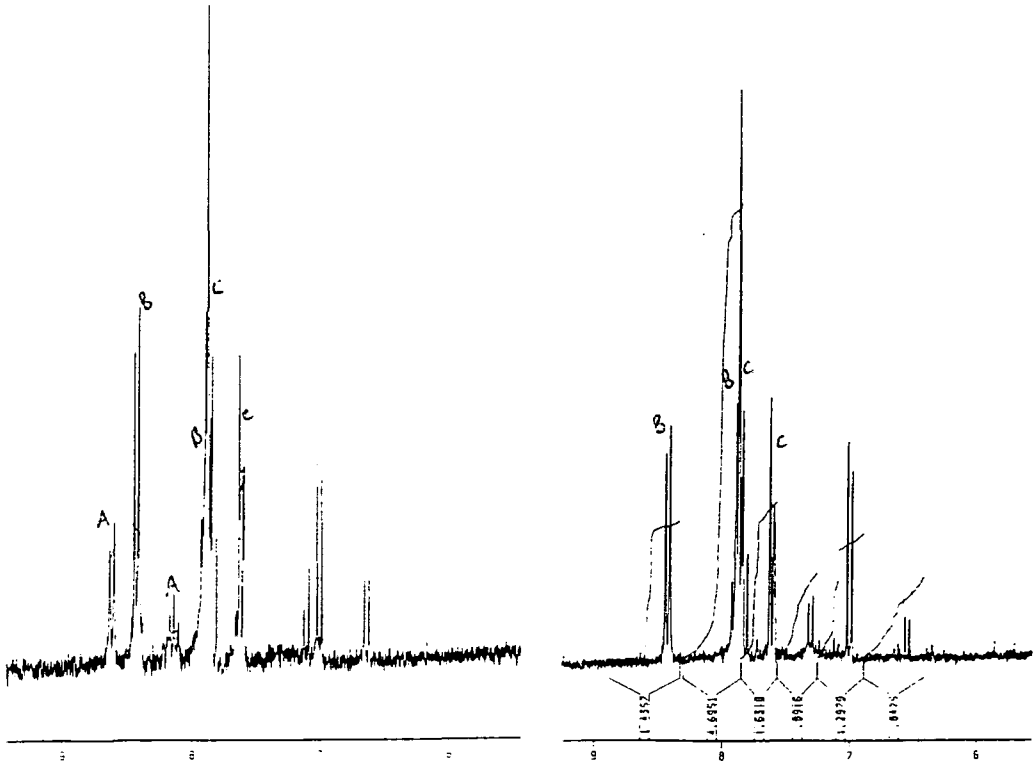
Figure 4.19

^{1}H NMR spectra of 1CN26DNB in CD_3OD a) in the absence of cyanide, b) 10mins and c) 1hr after mixing with cyanide, and d) the final product.

Bands labelled: A - 2,6-dinitrobenzonitrile, B - imidate (4.9), C - 2-methoxy-6-nitrobenzonitrile.



substrate 10 min

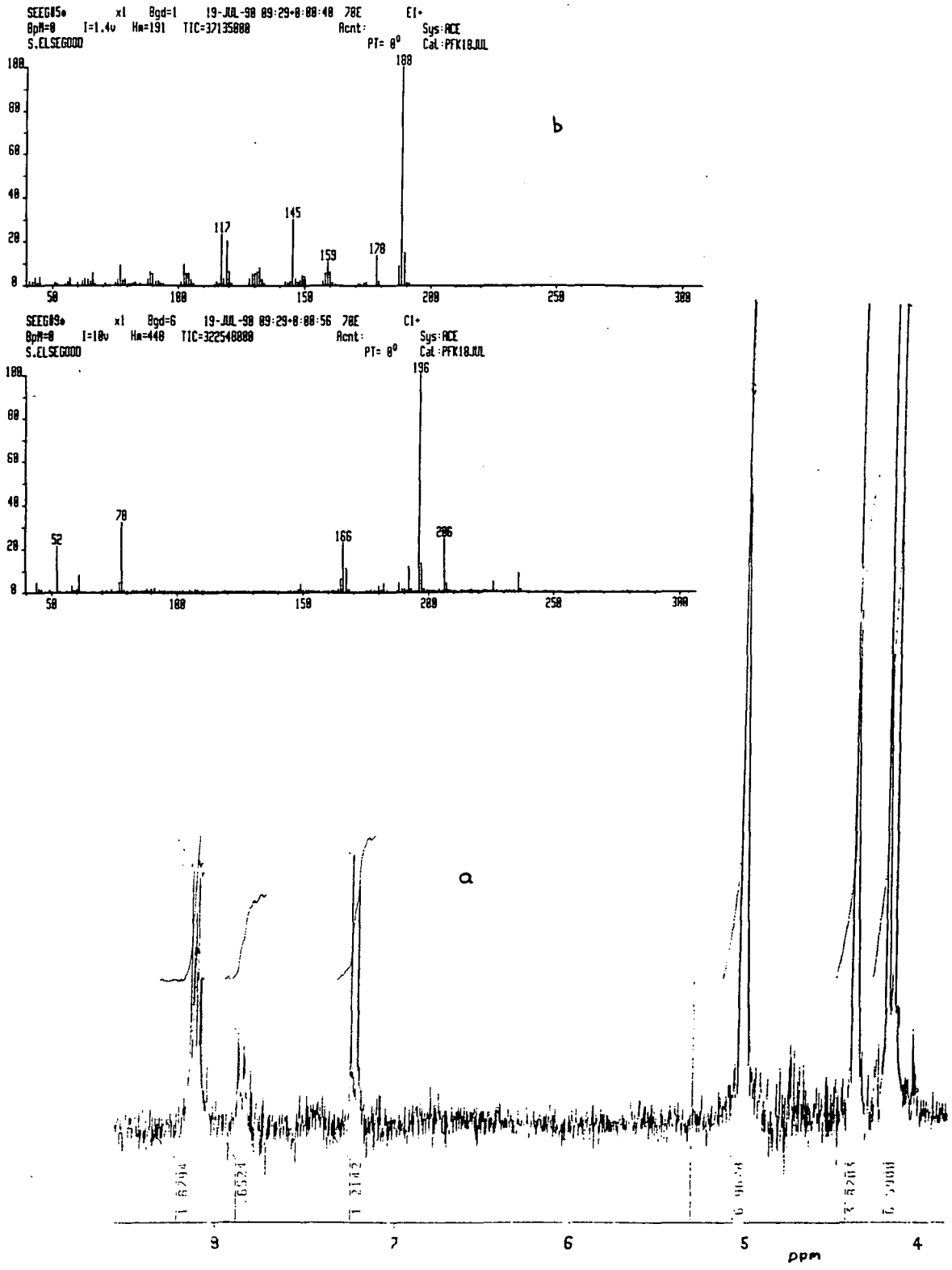


1hr final product

Figure 4.20

The product of the reaction between 1CN26DNB and KCN in methanol:

a) ^{1}H NMR spectrum and b) mass spectra.



due to he ring protons at the 6-position and 5-position respectively of 1,3-dicyano-2,4-dimethoxybenzene (4.16). The signal of the proton in the 6-position, *ortho* and *para* to the two electron-withdrawing cyano groups, will appear down field of the proton in the 5-position, *ortho* and *para* to the two methoxy groups. The electron ionisation (E.I.) mass spectrum (fig.4.20b) shows the molecular ion peak of 1CN2MeO6NB (178mu.) together with a peak at 188mu., consistent with a dicyano-dimethoxybenzene. The peak at 159mu. is due to loss of a CHO (19mu.) fragment from the molecular ion (188mu.), loss of such a fragment is frequently observed [10] in anisoles. The peak observed at 145mu. is due to loss of N (14mu.) from the fragment (159mu.). The chemical ionisation (C.I.) mass spectrum shows the (M+18) peaks of 1CN2MeO6NB (196mu.) and 206mu., consistent with a dicyano-dimethoxybenzene. The carrier gas is ammonia, and consequently ionisation is frequently caused by the ammonium ion (18mu.). The peak at 166mu. is due to loss of NO (30mu.) from 1CN2MeO6NB, loss of such a fragment is common for nitroaromatics.

4.3.3 2,4-Dinitrobenzonitrile.

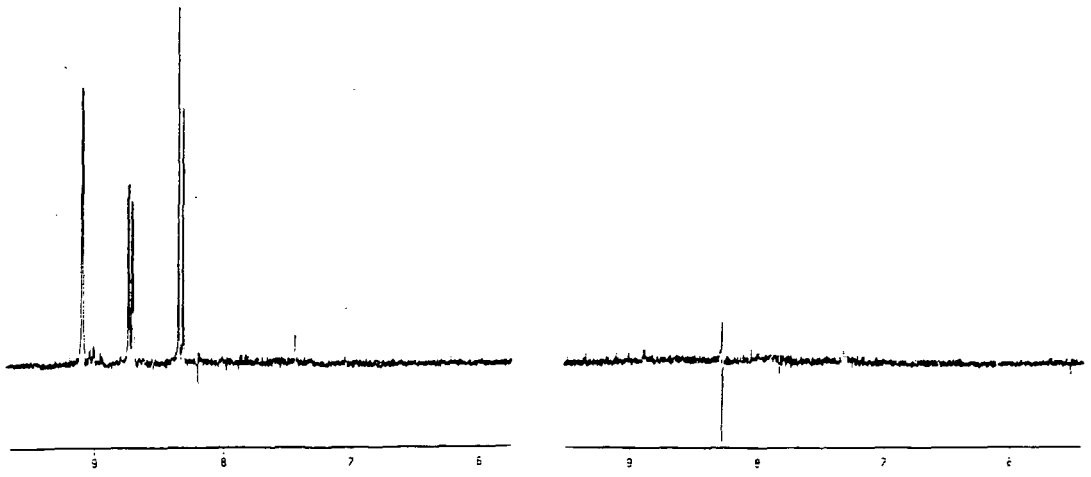
The reaction of 1CN24DNB with cyanide under Russell-Tebbens conditions has been studied on the NMR and preparative scale.

The NMR spectrum of 1CN24DNB in methanol-d_4 shows the three coupled signals of the ring protons (table 4.6) (fig.4.21). Addition of cyanide produces no NMR signals in the aromatic region for the first ten minutes of the reaction (fig.4.21). This could possibly be due to the presence of radical species. After ten minutes signals are evident and sharpen over an hour to reveal the spectrum of the final product mixture: ^{1}H NMR δ_{CD3OD} /ppm: 7.94(s), 7.85(d) and 7.00(d) J = 9.20Hz, 6.84(s). HPLC (fig.4.15) reveals five major species present: 1,3-dicyano-2,4-dimethoxybenzene (4.16) (r_t = 8.0min.) and possibly 1,5-dicyano-2,4-dimethoxybenzene (4.17) (r_t = 9.0min.); the remaining peaks have yet to be assigned, but there appears to be no 1CN2MeO4NB (r_t = 10.7min.) or 1CN4MeO2NB (r_t = 9.2min.) present. The two ring protons of 1,5-dicyano-2,4-dimethoxybenzene would give rise to two singlets of equal intensity in proton NMR, and such signals are observed in the spectrum of the product mixture at 7.94 and 6.84ppm. The proton in the 6-position between the two cyano groups would be expected to appear down field of the proton in the 3-position between the two methoxy groups.

A Russell-Tebbens type preparation was carried out with 1CN24DNB (2g in 30ml methanol) and KCN(0.92g in 1.6ml water). Recrystallisation from ethanol of the crude product yielded a small amount of solid: 17.8% N, 57.43% C, 3.8% H (calculated for a dicyano-dimethoxybenzene: 14.9% N, 63.8% C, 4.26% H); i.r. spectrum (nujol

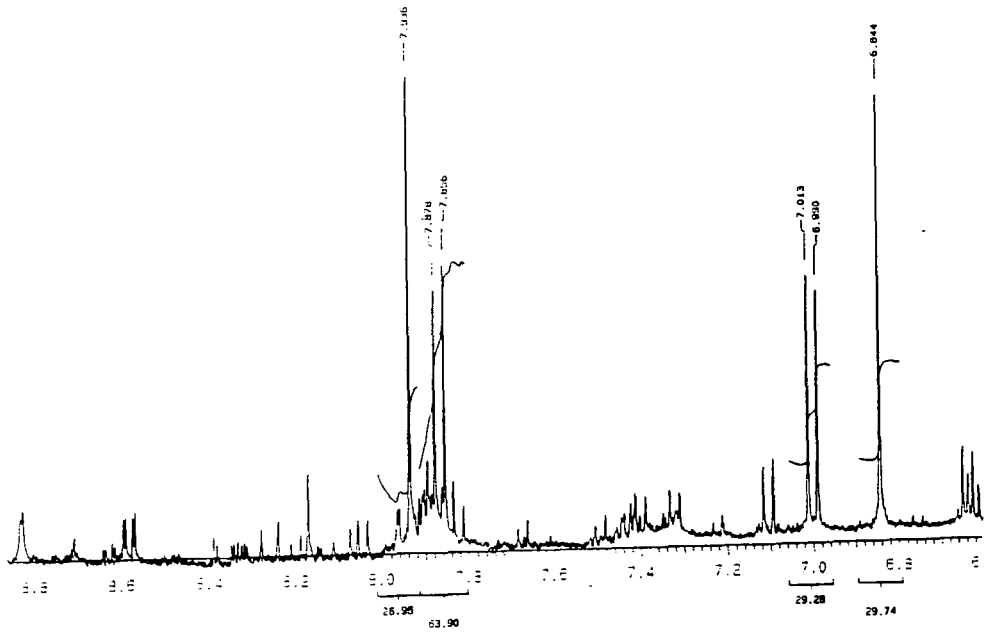
Figure 4.21

^{1}H NMR spectra of 1CN24DNB in CD_3OD a) in the absence of cyanide, b) 3mins after mixing with cyanide and c) the final product.



substrate

3min

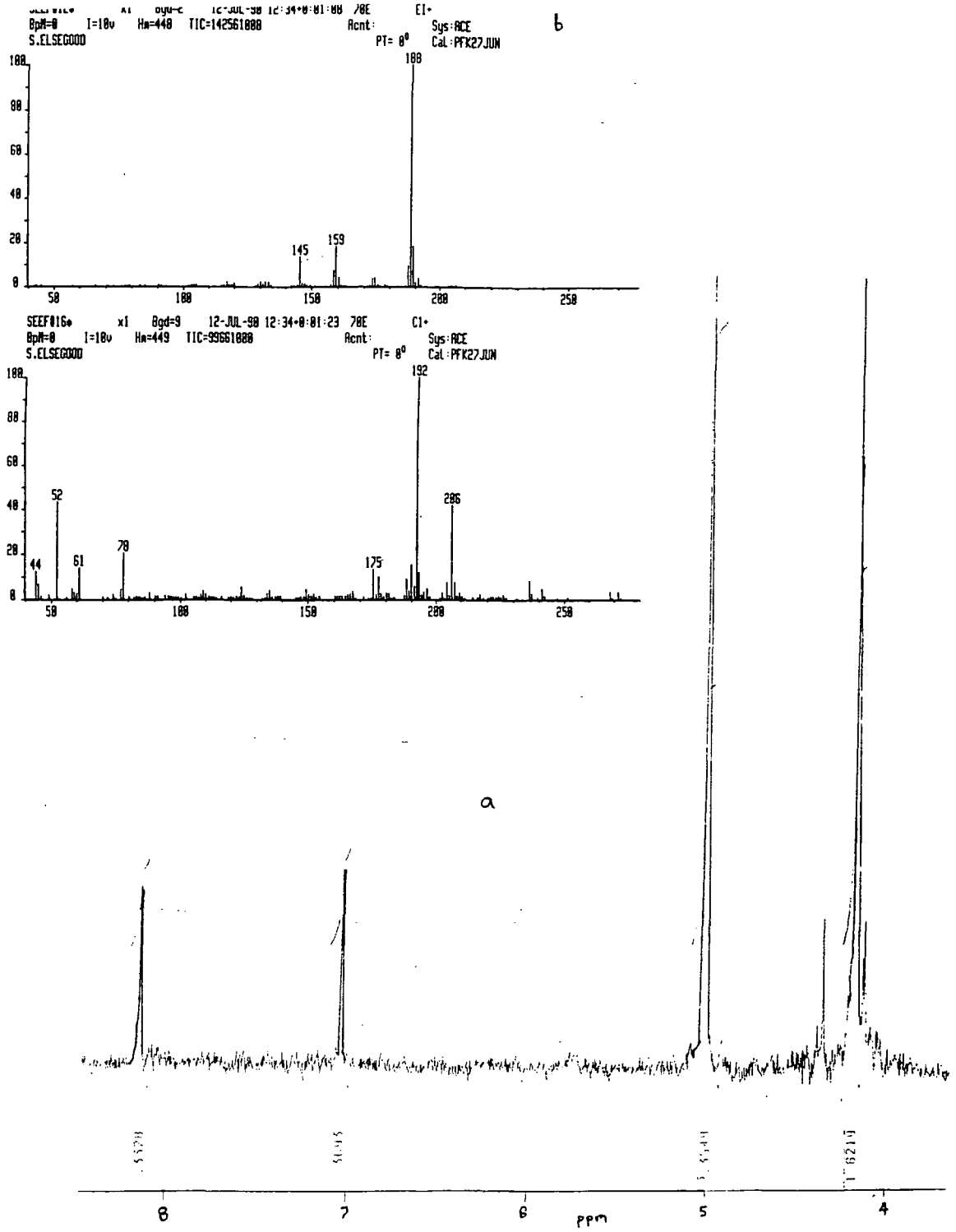


final product

Figure 4.22

The product of the reaction between 1CN24DNB and KCN in methanol:

a) ^{1}H NMR spectrum and b) mass spectra.



mull): 2240cm^{-1} (CN stretch), 1620cm^{-1} (aromatic CC stretch), 1230cm^{-1} (C-OMe stretch); ^{1}H NMR δ_{CD3OD} /ppm 7.94(s)(H^6), 6.85(s)(H^3), 4.06(s)(OMe) (fig.4.22a). The electron ionisation (E.I.) mass spectrum (fig.4.22b) shows the molecular ion peak of 1,5-dicyano-2,4-dimethoxybenzene (4.17) (188mu.). The peak at 159mu. is due to loss of a CHO (19mu.) fragment from the molecular ion of 1,5-dicyano-2,4-dimethoxybenzene (4.17). The peak observed at 145mu. is due to loss of N (14mu.) from the fragment (159mu.). The chemical ionisation (C.I.) mass spectrum shows the (M+18) peak of 1,5-dicyano-2,4-dimethoxybenzene (206mu.). Loss of N (14mu.) yields the fragment (192mu.). Loss of a methoxy fragment (31mu.) from the molecular ion yields the fragment (175mu.).

4.3.4 Discussion.

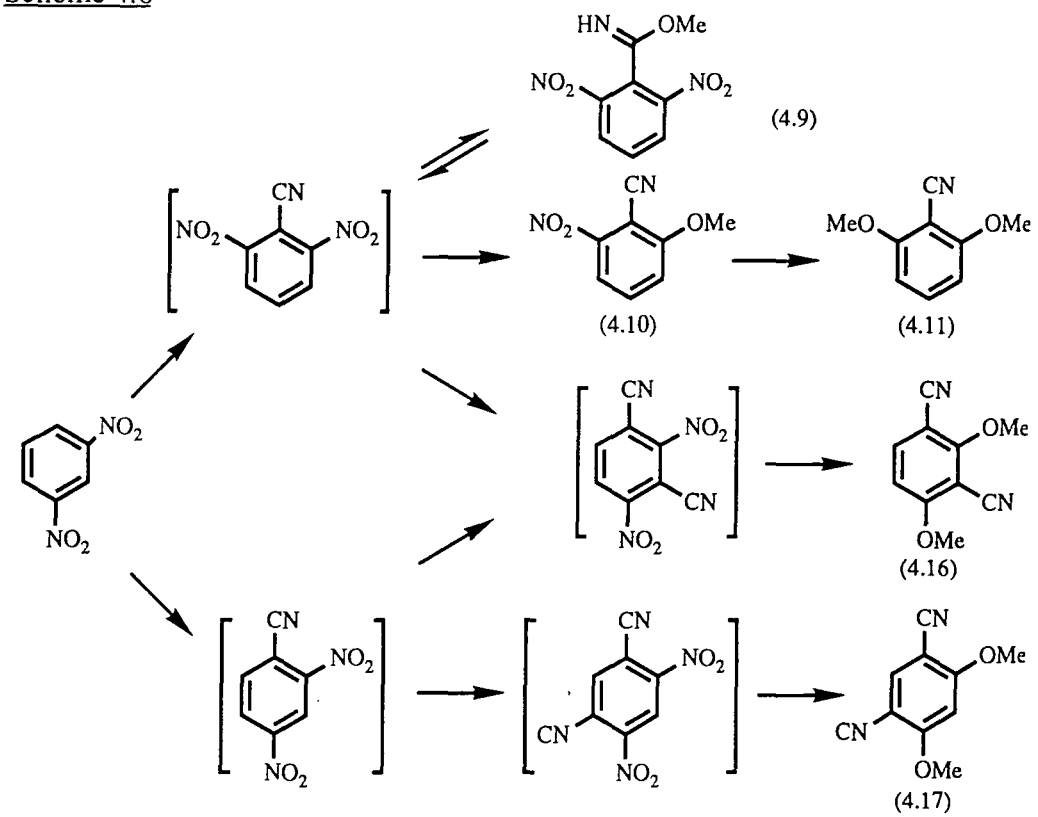
The results of this study of Russell-Tebbens reaction are summarised by scheme 4.6. Under the normal Russell-Tebbens conditions of a slight excess of potassium cyanide in 5.3% v/v water in methanol, *meta*-dinitrobenzene produced 2-methoxy-6-nitrobenzonitrile (4.10) and small amounts of 2-methoxy-4-nitrobenzonitrile (4.7), 4-methoxy-2-nitrobenzonitrile (4.8) and 2,6-dimethoxybenzonitrile (4.11). 2,4- and 2,6-dinitrobenzonitrile were not detected in the system, but these are presumably intermediates along the reaction pathway. When the reaction mixture was buffered with acid production of (4.10) was observed, together with other species which, on the basis of NMR and HPLC evidence, appear to be common to the reaction products of the dinitro-benzonitriles. No dinitrobenzonitriles or dicyano-dinitrobenzenes were detected. Under the usual Russell-Tebbens conditions 2,6-dinitrobenzonitrile initially produced the imidate (4.9) and the usual product (4.10). The final products of the reaction were (4.10) and 1,3-dicyano-2,4-dimethoxybenzene (4.16). Under indentical conditions 2,4-dinitrobenzonitrile appeared to produce mainly (4.16) and 1,5-dicyano-2,4-dimethoxy-benzene (4.17), no methoxy-nitrobenzonitrile products were observed.

When *meta*-dinitrobenzene is the starting substrate and the pH is not controlled the production of the expected product (4.10) is observed. However, when the ratio of cyanide (or cyano groups) to methoxide is increased, either by regulating the pH or starting with a benzonitrile substrate, the formation of dicyano-dimethoxybenzene products (4.16-7) is observed.

There is evidence (chapter 3) that alcoholysis of cyanide ions in methanol produces a significant concentration of methoxide ions. It is well known (section 1.4) that an *ortho*-cyano group promotes the substitution of a nitro group by methoxide ions in DMSO. Consequently it is not surprising that we are unable to detect or isolate any

dinitrobenzonitriles or dicyano-dinitrobenzenes in these systems since they are ideally activated for methoxydenitration.

Scheme 4.6



The methanolysis constant for cyanide ions in methanol, K_{Meth}, has been calculated to be $4x10^{-4}moldm^{-3}$ (section 3.2.3), and also the second order rate constants for the reaction of dinitrobenzonitriles with methoxide in methanol at 25°C have been determined (section 4.2.2) to be approximately $0.08dm^3mol^{-1}s^{-1}$.

Calculation 4.2

The cyanide concentration is *c.a.* 0.4moldm^{-3}

$$CN^- + MeOH \underset{}{\overset{K_{Meth}}{\rightleftharpoons}} HCN + MeO^-$$

$$[MeO^-] = (K_{Meth}[CN^-])^{1/2}$$

$$= (0.4 \times 4x10^{-4})^{1/2}$$

$$= \underline{0.012moldm^{-3}}$$

$$k_{second\ order} = 0.08dm^3mol^{-1}s^{-1}$$

therefore $k_{first\ order} = (0.08 \times 0.012)s^{-1}$

$$= 1x10^{-3}s^{-1}$$

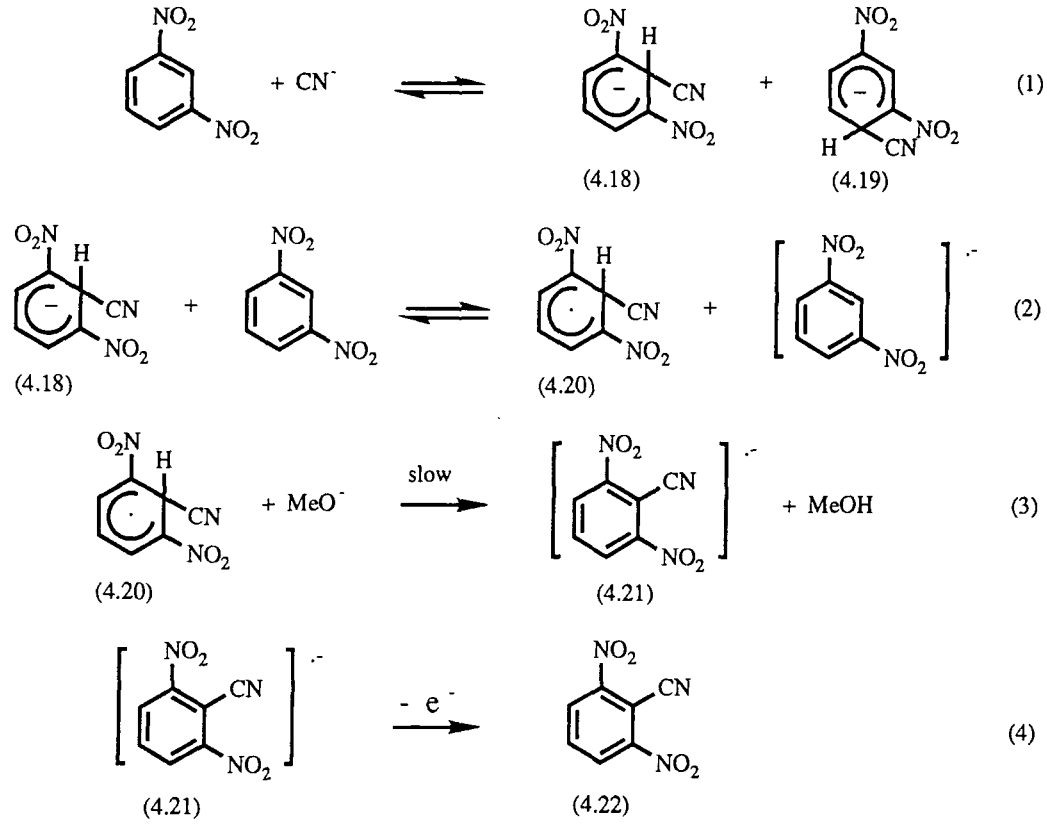
therefore $t_{1/2} = 10min$ at 25°C

and hence $= c.a.$ 2min at 40°C

These values may be used to calculate a value of 2mins for the half-life of dinitrobenzonitriles under the conditions of the Russell-Tebbens reaction (calculation 4.2). Thus the half-life for dinitrobenzonitriles would be approximately two minutes for the methoxydenitration reaction.

The results for the reaction of *meta*-dinitrobenzene and the isomeric dinitrobenzonitriles with cyanide in methanol are interpretable in terms of ring-cyanation followed by methoxydenitration. However, there is no conclusive proof for this pathway. It is of interest to speculate how ring-cyanation might occur, and a possible mechanism is outlined below (scheme 4.7) for *meta*-dinitrobenzene.

Scheme 4.7

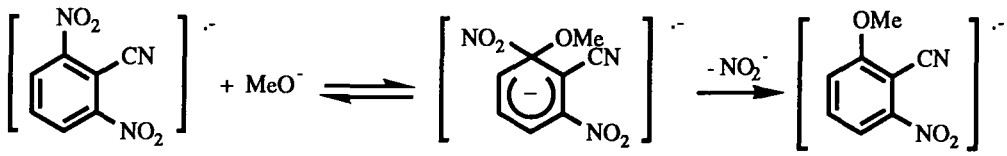


The first step (step 1) involves sigma-adduct formation by cyanide attack at the 2-position to give (4.18) or at the 4-position to give (4.19). Normally sigma-adducts formed by nucleophilic attack at the 4-position of dinitrobenzenes have higher thermodynamic stabilities than their isomers.[11-13] However, the products isolated from the Russel-Tebbens reaction appear to be mainly derived from attack at the 2-position.

The second step (step 2) involves rapid electron transfer to give the radical (4.20) which is acidic due to the presence of the electron withdrawing groups, and transfers a proton to base to give the radical anion (4.21) (step 3). It seems probable that this step (step 3) will be rate-determining and this might give a rationalisation for the predominant formation of the 2-substituted product rather than the 4-substituted product. It is known that in *meta*-dinitrobenzene itself the hydrogen at the 2-position is considerably more "acidic" than that at the 4-position so that deuterium exchange and tritium exchange occur rapidly at the 2-position.[14-20] Hence by analogy rate of proton loss from (4.20) might be expected to be much more rapid than proton loss from the radical derived from (4.19).

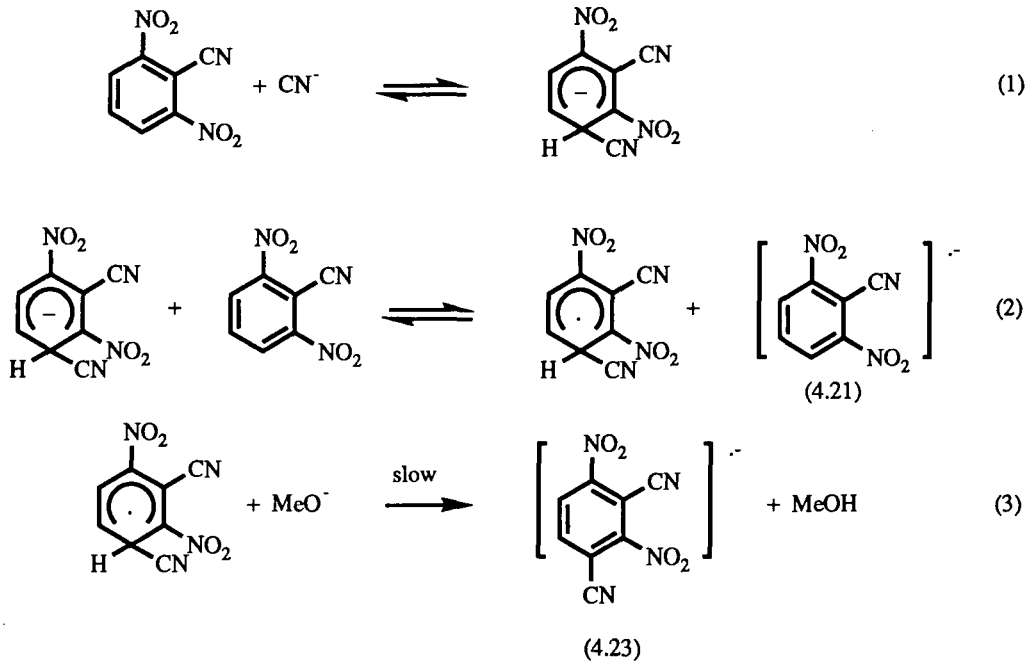
Step (4) involves electron transfer to give 2,6-dinitrobenzonitrile (4.22) which may rapidly undergo methoxydenitration to give the observed product 2-methoxy-6-nitrobenzonitrile (4.10). An alternative possibility is that methoxydenitration may occur in the radical anion (4.21) rather than in the neutral species. This would yield the

radical anion of the substitution product (4.10) (eqn.4.8) which should readily lose an electron to give the neutral product. A similar mechanism of substitution in the radical anion of 1-chloro-2,4-dinitrobenzene has been postulated previously.[21] One piece of evidence favouring substitution in the radical anion is that NMR spectra observed during the reaction of *meta*-dinitrobenzene with cyanide ions under the Russell-Tebbens conditions do not show any bands attributable to the solvate (4.9) of 1CN26DNB (4.22) which would be expected in these conditions.



(4.21) Eqn.4.8

Scheme 4.8



(4.23)

Starting from 2,6-dinitrobenzonitrile and cyanide ions in methanol there is evidence for initial formation of the solvate (4.9) and the substitution product (4.10). The dicyano-dimethoxybenzene formed as a major product might be derived by successive methoxydenitrations of 1,3-dicyano-2,4-dinitrobenzene or by methoxy-denitration of the radical anion (4.23) itself (scheme 4.8).

The reaction of 2,4-dinitrobenzonitrile with cyanide under Russell-Tebbens conditions, when followed by NMR spectroscopy, was found to produce the dimethoxy-dicyanobenzene isomers (4.16) and (4.17), in rather similar yields. These might be formed by initial cyanide attack at the 5- or at the 3-position. Again, methoxy-denitration might occur in the neutral dicyano-dinitrobenzenes or in their radical anions.

In the preparative experiment only the 1,5-dicyano-2,4-dimethoxybenzene (4.17) was separated. This might be due to slightly different reaction conditions or to loss of the second isomer in work-up.

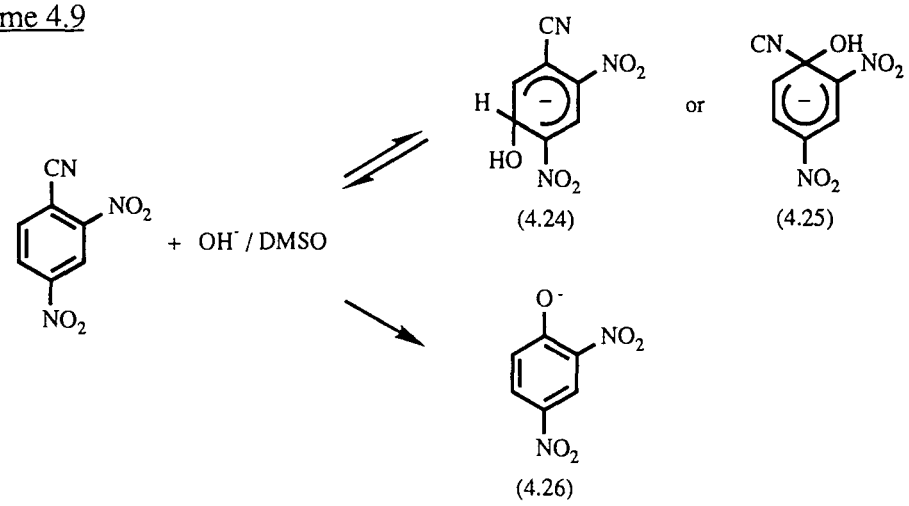
4.4 THE REACTIONS OF 2,4- AND 2,6-DINITROBENZONITRILE WITH HYDROXIDE IN DMSO.

The reactions between 2,4- and 2,6-dinitrobenzonitrile with hydroxide ions in DMSO have been studied by uv/vis spectroscopy and NMR, and the results compared with those for methoxide in DMSO (section 4.2.3).

4.4.1 2,4-Dinitrobenzonitrile.

The uv/vis spectrum of 1CN24DNB in DMSO shows absorbance upto 400nm (table 4.1). In the presence of a large excess of sodium hydroxide (0.01M) in DMSO the uv/vis spectrum of 1CN24DNB ($1x10^{-4}$M) initially shows absorbance bands at 500 and 385nm (fig.4.23). Over 24hrs these bands fade leaving bands at 375 and 430nm. The spectrum of 2,4-dinitrophenol in basic DMSO solution (fig.4.24) shows two absorbance bands at 375 and 428nm, both $\varepsilon = 8x10^{-3}dm^3mol^{-1}cm^{-1}$. In d_6-DMSO the NMR spectrum of 1CN24DNB shows the three coupled signals of the aromatic hydrogens (table 4.6). After 5mins in the presence of a slight excess of sodium hydroxide (0.1M) in 5%/95% v/v D_2O/d_6-DMSO the coupled signals of the parent remain the only significant resonances (fig 4.25a). After 1hr the signals of the parent have disappeared; and new coupled signals are apparent at 8.54, 7.73, 7.27, 6.66 and 6.26ppm. These are the significant signals of the spectrum of the final product mixture (after 6 days) (fig 4.24b).

Scheme 4.9



The results are interpreted in terms of scheme 4.9. It is known [13b] that complexes of the type (4.24) and (4.25) are produced in basic solutions of 1-substituted-2,4-dinitrobenzenes in DMSO, and that they have absorbance bands at approximately

350 and 500nm. Hence it is proposed that there is rapid reversible production of the complex (4.24) or (4.25), which is competing with slower irreversible formation of the nucleophilic substitution product 2,4-dinitrophenol, which in these basic conditions exists as 2,4-dinitrophenoxide (4.26).

There is evidence from the proton NMR spectra that 2,4-dinitrophenoxide (4.26) is the major product. Thus the bands at 8.54, 7.73 and 6.26ppm are attributable to protons at the 3-, 5- and 6-positions respectively (table 4.6). The low intensity of the band at 8.54ppm may be caused by hydrogen-deuterium exchange of the proton at the 3-position with deuterium in the solvent. This exchange probably occurs in the parent before reaction. There is evidence in the literature [14-20] for such exchange in basic media. Because the atom at the 3-position is largely deuterium the proton spin-coupling between the 3- and 5-positions is largely lost, so that the resonances due to H-5 becomes a doublet. The remaining bands in the NMR are unassigned although it is possible that these may be derived from cyano-nitro-phenols produced by hydroxydenitration (section 1.4).

4.4.2 2,6-Dinitrobenzonitrile.

In DMSO the uv/vis spectrum of 1CN26DNB (table 4.1) shows absorbance upto 400nm. In the presence of a large excess of hydroxide (0.01M) in DMSO, 1CN26DNB ($1x10^{-4}$M) rapidly forms a species λ_{max} 345 and 545nm (fig.4.26). A narrow band is also present at 300nm. Over the next 10mins the bands at 345 and 545nm fade, leaving a weak broad band at 470nm and the band at 300nm.. In d_6-DMSO the NMR spectrum of 1CN26DNB shows the two coupled signals of the aromatic hydrogens (table 4.7). After 5mins in the presence of a slight excess of sodium hydroxide (0.1M) in 5%/95% v/v D_2O/d_6-DMSO the spectrum shows no resonances of the parent. Coupled signals are observed at 7.80, 7.11, 6.78, 6.62 and 6.03ppm. A similar spectrum is observed after 1hr and after one week (fig.4.27).

The NMR spectra of 2,6-dinitrophenoxide in d_6-DMSO (table 4.7) shows two coupled signals at 7.80 and 6.03ppm. Consequently it is reasonable to conclude that 2,6-dinitrophenoxide is a product of the reaction above. The remaining bands are a triplet at 7.11ppm and two doublets at 6.78 and 6.62ppm. Each of these multiplets are of equal intensity. Hence the presence of a 1,2,3-trisubstituted-benzene is indicated. The chemical shifts are consistent with the formation of 2-cyano-3-nitrophenoxide resulting from displacement of a nitro group by hydroxide.

Figure 4.23

UV/Vis spectra of 1CN24DNB in DMSO 1) in the absence of hydroxide, 2) with hydroxide initially and after 3) 3mins, 4) 5hrs and 5) 24hrs.

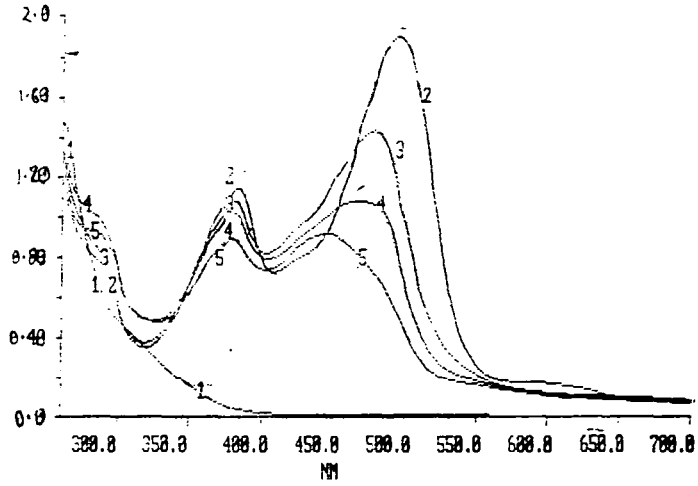


Figure 4.24

UV/Vis spectra in DMSO of 2,4-dinitrophenol 1) in the absence of added hydroxide and 2) in the presence of a large excess of hydroxide.

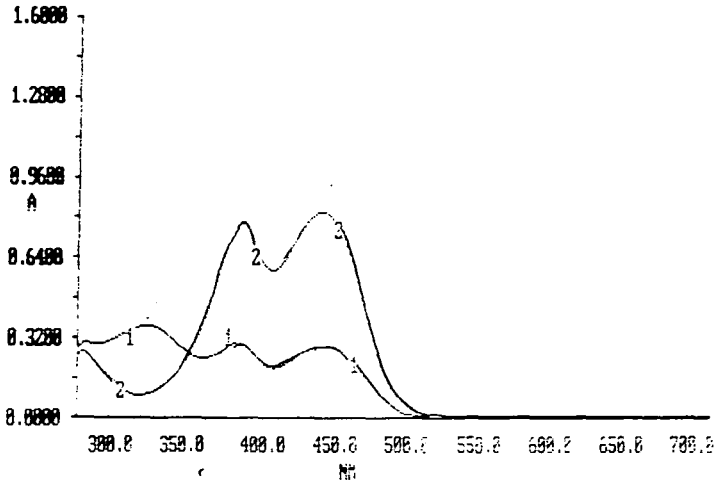
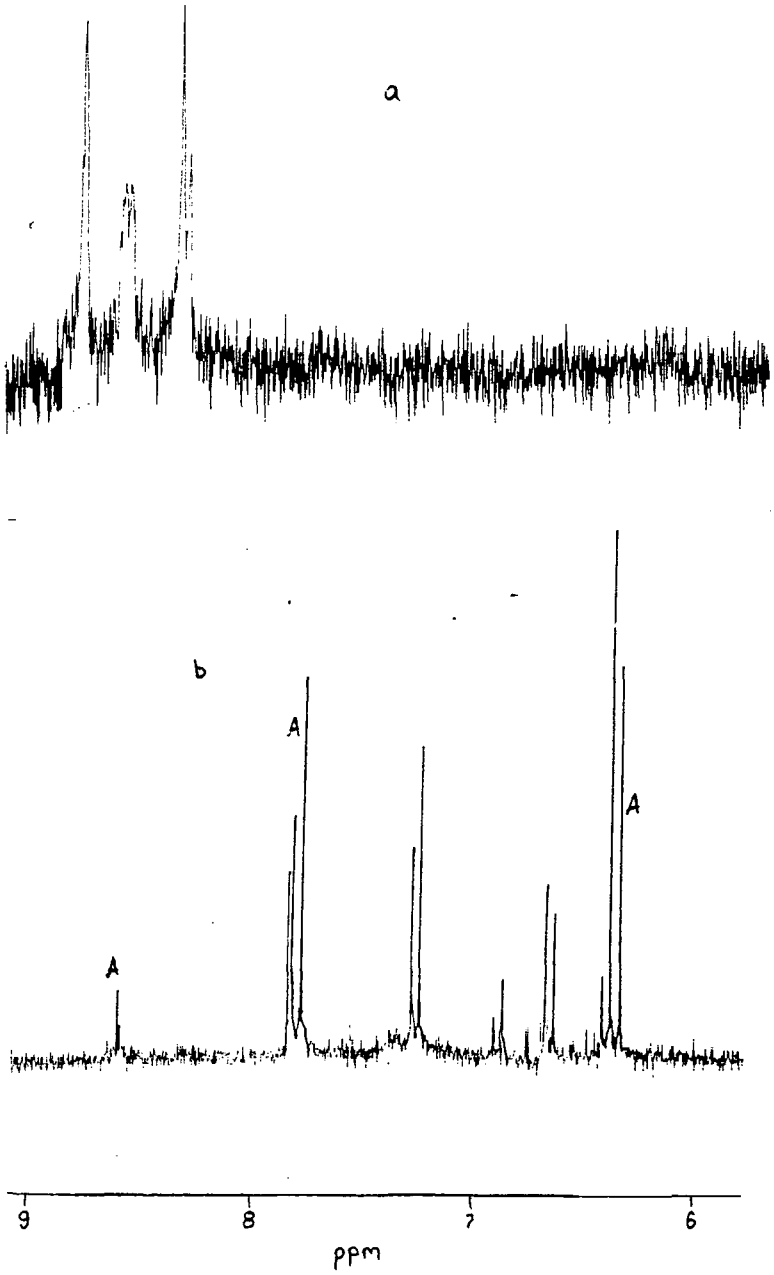


Figure 4.25

^{1}H NMR spectra of 1CN24DNB and NaOH in d_6-DMSO

a) 5mins after mixing and b) at completion.



Bands labelled: A - 2,4-dinitrophenoxide.

Figure 4.26

UV/Vis spectra of 1CN26DNB in DMSO 1) in the absence of hydroxide, 2) with hydroxide (int. = 5mins) and 3) 30min.

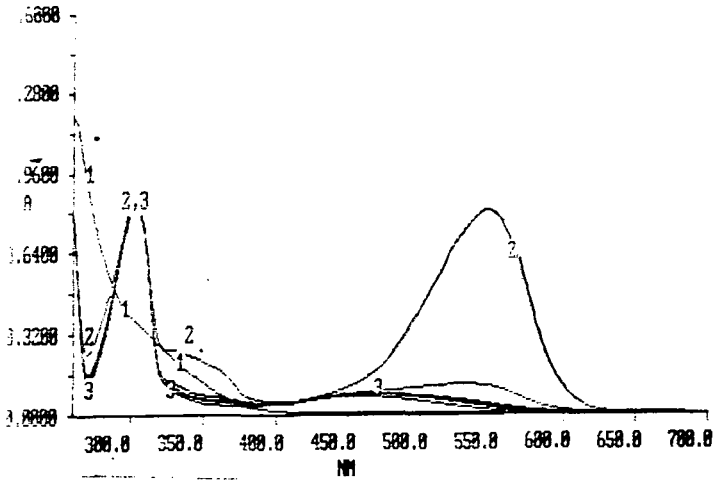
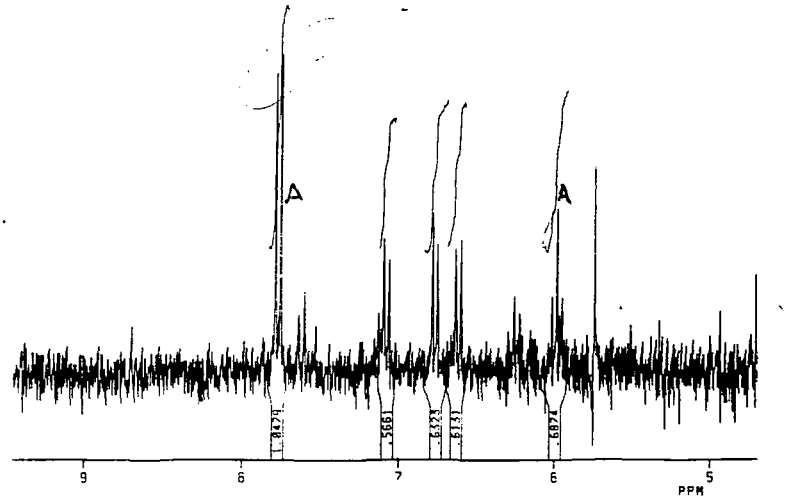


Figure 4.27

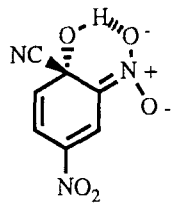
^{1}H NMR spectra of 1CN26DNB and NaOH in d_6-DMSO at completion.



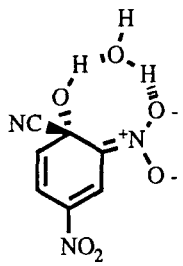
Bands labelled: A - 2,6-dinitrophenoxide.

4.4.3 Discussion

The visible spectra provide evidence for the initial rapid formation of sigma adducts by hydroxide attack on both the 2,4- and 2,6-dinitrobenzonitrile. These spectra were obtained with parent concentrations of 10^{-4}M with hydroxide in large excess in DMSO containing very little water. The NMR spectra did not show the presence of appreciable concentrations of sigma-adducts probably because of the smaller excess of hydroxide and because the medium contains more water (D_2O). It is known [22] that the basicity of hydroxide solutions increase dramatically with increasing proportion of DMSO in DMSO-water mixtures.



(4.27)



(4.28)

The results for hydroxide attack indicate that nucleophilic substitution of the cyano group occurs to give dinitrophenols and there is also evidence for competitive attack at ring-carbons carrying nitro groups to give nitro-cyano-phenols. This behaviour differs from that observed with methoxide ions where methoxydenitration was the only substitution reaction observed (section 4.2). The reasons for this difference are unclear. It is possible that the intermediate in hydroxydenitration, and the transition state leading to it, may be stabilised by intramolecular hydrogen bonding with an *ortho*-nitro group. Structures (4.27) and (4.28) show this involving, respectively, direct hydrogen-bonding and hydrogen-bonding involving a water molecule.

The reactions of the dinitrobenzonitriles with hydroxide were not investigated further since they do not constitute processes central to the theme of this project.

4.5 REFERENCES

1 A.Russell & W.G.Tebbens, *Org. Synth., Coll. Vols.*, (1955), **3**, 293.

2 E.J.Fendler, J.H.Fendler, N.L.Arthur & C.E.Griffin, *J. Org. Chem.*, (1972), **37**, 812.

3 T.Abe, *Bull. Chem. Soc. Jpn.*, (1983), **56**, 1206.

4 F.Bazzano, P.Mencarelli & F.Stegel, *J. Org. Chem.*, (1984), **49**, 2375.

5 N.Kornblum, L.Cheng, R.C.Kerber, M.M.Kestner, B.N.Newton, H.W.Pinnick, R.G.Smith & P.A.Wade, *J. Org. Chem.*, (1976), **41**, 1560

6 I.R.Bellobono, A.Gamba, G.Sala & M.Tampieri, *J. Am. Chem. Soc.*, (1972), **94**, 5781.

7 I.R.Bellobono, P.Govoni & F.Zavattarelli, *J. Chem. Soc., Perkin Trans. II*, (1974), 981.

8 F.C.Schaefer & G.A.Peters, *J. Org. Chem.*, (1960), **26**, 412.

9 L.H.Gan & A.R.Norris, *Can. J. Chem.*, (1974), **52**, 1.

10 D.H.Williams and I.Fleming, *"Spectroscopic Methods in Organic Chemistry"*, 3rd edn.,McGraw-Hill, London, (1980), 173.

11 C.A.Fyfe, *"Chemistry of the Hydroxyl Group"*, Wiley-Intersciece, New York, (1971), 93.

12 M.R.Crampton & V.Gold, *J. Chem. Soc.(B)*, (1966), 498.

13 a) Y.Hasegawa & T.Abe, *Chem. Letters (Tokyo)*, (1972), 985; b) Y.Hasegawa, *Bull. Chem. Soc. Jpn.*, (1974), **47**, 2186.

14 E.Buncel & E.A.Symons, *J. Org. Chem.*, (1973), **38**, 1201.

15 E.A.Symons & E.Buncel, *Can. J. Chem.*, (1972), **50**, 1729.

16 E.Buncel & A.W.Zabel, *Can. J. Chem.*, (1981), **59**, 3168 & 3177.

17 A.J.Parker, *Chem. Revs.*, (1969), **69**, 1.

18 C.Reichardt, *"Solvent Effects in Organic Chemistry"*, Verlag Chemie, Weinheim, (1979); *Agnew. Chem. Int. Ed. Engl.*, (1979), **18**, 98.

19 E.Buncel & H.Wilson, *Adv. Phys. Org. Chem.*, (1977), **14**, 133; *Acc. Chem. Res.*, (1979), **12**, 42.

20 E.Buncel & E.A.Symons, *"Advances in Solution Chemistry"*, eds: I.Bertini, L.Lunazzi & A.Dei, Plenum Press, New York, (1981).

21 L.A.Blyumenfel'd, L.V.Bryukhovetskaya, G.V.Formin & S.M.Shein, *Russ. J. Phys. Chem.*, (1970), **44**, 518.

22 A.J.Parker, *Quart. Rev.*, (1962), 163.

CHAPTER 5

THE REACTIONS OF *META*-DINITROBENZENE, 2,4- AND 2,6-DINITRO-BENZONITRILE WITH CYANIDE IONS IN DMSO-RICH MEDIA.

It was thought to be of interest to compare the reactions of the isomeric dinitrobenzonitriles with cyanide in DMSO with the reactions in methanol. Measurements were made by uv/vis spectroscopy and by proton NMR spectroscopy. Because of the likelihood of the formation of radical species in these systems it was decided to examine their e.s.r. spectra. Some polarographic measurements were made of neutral compounds and also of reaction mixtures containing cyanide.

5.1 2,4- AND 2,6-DINITROBENZONITRILE WITH CYANIDE IONS IN DMSO AND 25%/75% v/v METHANOL/DMSO.

5.1.1 UV/Vis Spectra.

The uv/vis spectra of the reactions between 2,4- and 2,6-dinitrobenzonitrile with cyanide in DMSO or 25%/75% v/v MeOH/DMSO have been recorded.

The uv/vis spectrum of 2,4-dinitrobenzonitrile (1CN24DNB) in 25%/75% v/v MeOH/DMSO shows a shoulder at 300nm which extends to 400nm (table 4.1). In the presence of a large excess of potassium cyanide (0.015M) in 25%/75% v/v MeOH/DMSO 1CN24DNB ($1x10^{-4}$M) initially produces a species λ_{max} 645nm, which decays over the next 2min (fig.5.1). A species λ_{max} 550nm is produced slightly more slowly which reaches a maximum absorbance after a minute, and then fades over the next 5min. The spectrum after 7min shows a broad band λ_{max} 420nm. Isosbestic points are observed at 290 and 405nm.

The results in DMSO are rather similar to those in the mixed solvent. Thus the uv/vis spectrum of 1CN24DNB in DMSO is similar to that described above. In the presence of a large excess of potassium cyanide (0.01M) in DMSO 1CN24DNB ($1x10^{-4}$M) initially produces a species λ_{max} 670nm, which fades over 30sec (fig.5.2). A species λ_{max} 555nm fades over 4min. The spectrum after 5min shows a band λ_{max} 440nm. In the presence of a smaller excess of potassium cyanide (0.001M) in DMSO 1CN24DNB ($1x10^{-4}$M) shows a similar spectrum, but with considerably less absorbance at 550nm (fig 5.3).

The uv/vis spectrum of 2,6-dinitrobenzonitrile (1CN26DNB) in DMSO shows a tail extending down to 400nm (table 4.1) without a distinct peak or shoulder. In the presence of a large excess of potassium cyanide (0.01M) in DMSO the uv/vis spectrum of 1CN26DNB ($1x10^{-4}$M) (fig.5.4) shows a broad absorbance with a shoulder at 450nm. After 1min a sharp peak is discernible at 550nm and absorbance has increased at 450nm. The peak at 550nm fades over the next few minutes while the absorbance at 450nm remains steady. In the presence of a smaller excess of potassium cyanide (0.001M) in DMSO 1CN24DNB ($1x10^{-4}$M) initially produces a species λ_{max} 580nm, which fades over the next few minutes (fig.5.5). A species λ_{max} 455nm is produced more slowly and reaches a maximum intensity after 8min.

5.1.2 NMR Spectra.

The reactions between 1CN24DNB and 1CN26DNB and a slight excess of cyanide in d_6-DMSO have been studied using proton NMR.

The NMR spectrum of 1CN24DNB in d_6-DMSO shows the three coupled signals of the ring protons (table 4.6). The spectrum recorded initially after adding a slight excess of sodium cyanide (0.04M) to 1CN24DNB (0.02M) showed no signals above 6ppm (c.f. fig.4.21). After 7 days the spectrum of the reaction mixture (fig.5.6) shows two singlets at 8.12 and 7.82ppm and two doublets at 7.58 and 6.66ppm (J = 8.28Hz).

The NMR spectrum of 1CN26DNB in d_6-DMSO shows the two coupled signals of the ring protons (table 4.7). In the presence of a slight excess of sodium cyanide (0.06M) the spectrum of 1CN26DNB (0.02M) shows (fig.5.7a) only two doublets at 7.58 and 6.66ppm (J = 8.28Hz). No signals of the parent can be observed; an identical spectrum is observed after 24hr. When the day-old reaction mix is neutralised with [^{2}H]-HCl the two doublets shift downfield to 8.09 and 7.57ppm (J = 8.78Hz) (fig.5.7b).

5.1.3 Discussion.

On the basis of the NMR spectra it is possible to make some tentative assignments as to the probable reaction products in these systems. The shift downfield on acidification of the proton NMR sample strongly suggests the presence of phenoxides which are protonated in acid solution (eqn.5.1).

The spectrum of the product from 2,4-dinitrobenzonitrile shows two singlets of equal intensity, strongly suggesting a 1,2,4,5-tetrasubstituted benzene. The common

Figure 5.1

UV/Vis spectra of 1CN24DNB ($1x10^{-4}M$) + KCN (0.015M) /25%/75% v/v MeOH/DMSO (int. = 40sec).

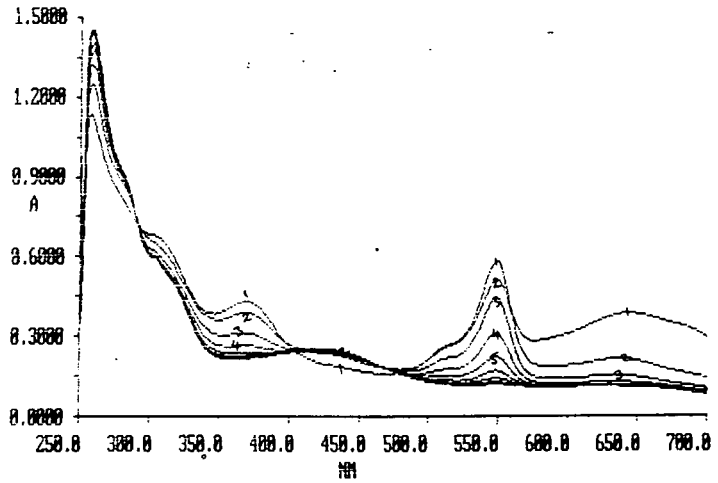


Figure 5.2

UV/Vis spectra of 1CN24DNB ($1x10^{-4}M$) + KCN (0.01M) /DMSO (int. = 45sec).

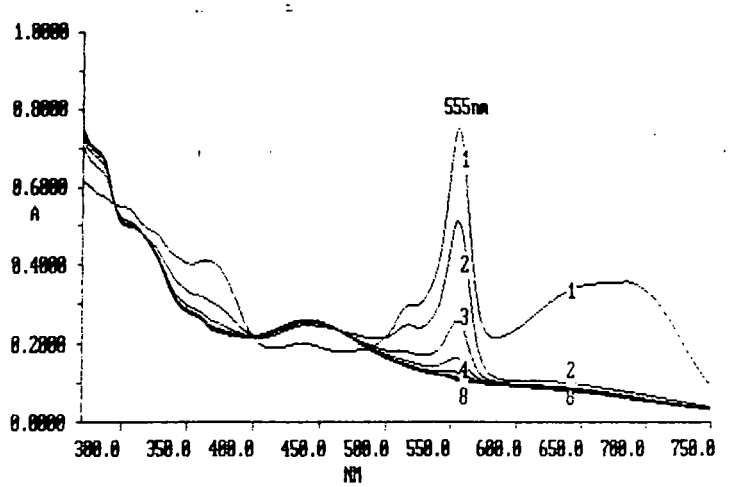


Figure 5.3

UV/Vis spectra of 1CN24DNB ($1x10^{-4}$M) + KCN (0.001M) /DMSO (int. = 60sec).

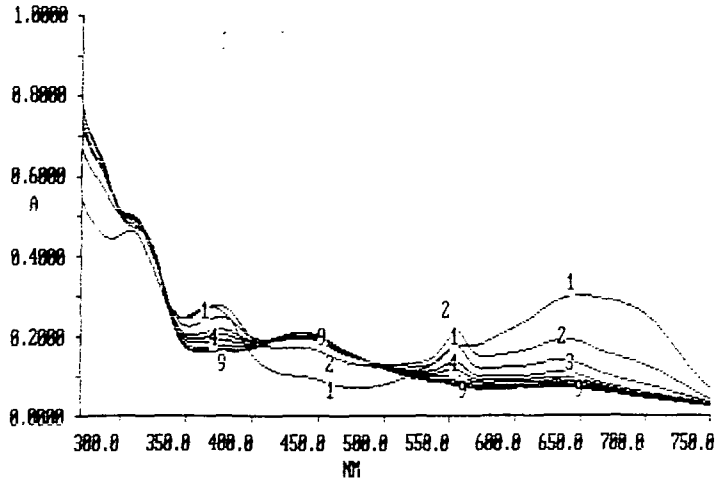


Figure 5.4

UV/Vis spectra of 1CN26DNB ($1x10^{-4}$M) + KCN (0.01M) /DMSO (int. = 60sec).

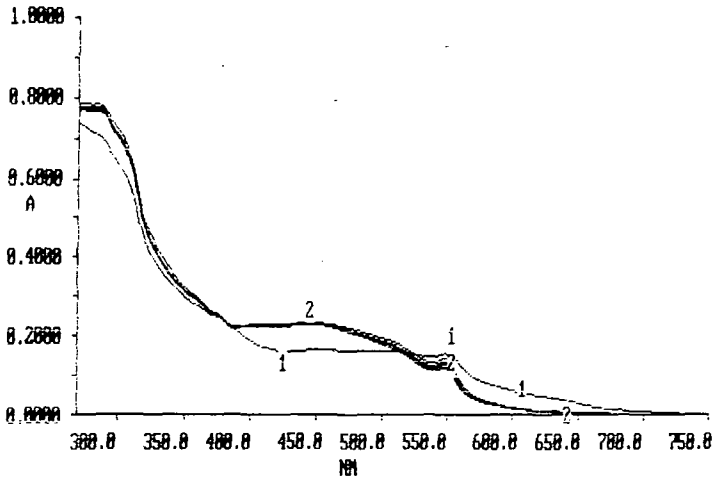


Figure 5.5

UV/Vis spectra of 1CN26DNB ($1x10^{-4}$M) + KCN (0.001M) /DMSO (int. = 60sec).

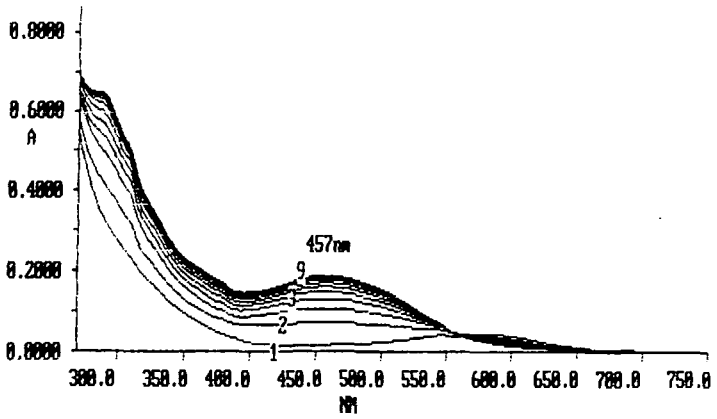


Figure 5.6

Proton NMR spectrum of 1CN24DNB (0.02M) + NaCN (0.04M) /d_6-DMSO after 7 days.

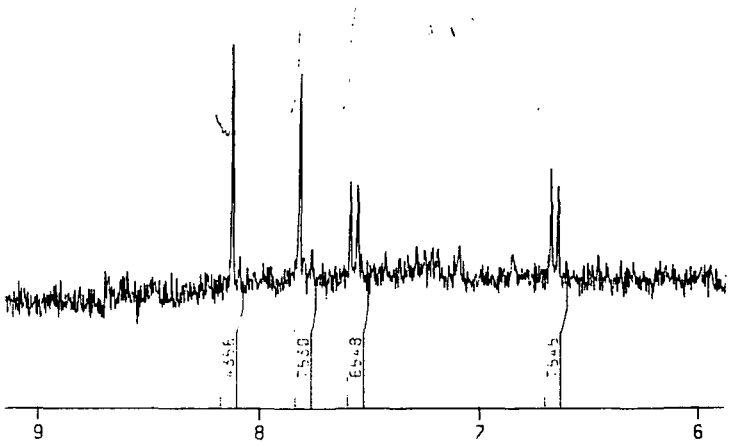


Figure 5.7

Proton NMR spectra of 1CN26DNB (0.02M) + NaCN (0.06M) a) /d_6-DMSO, b) /d_6-DMSO + [^{2}H]-HCl.

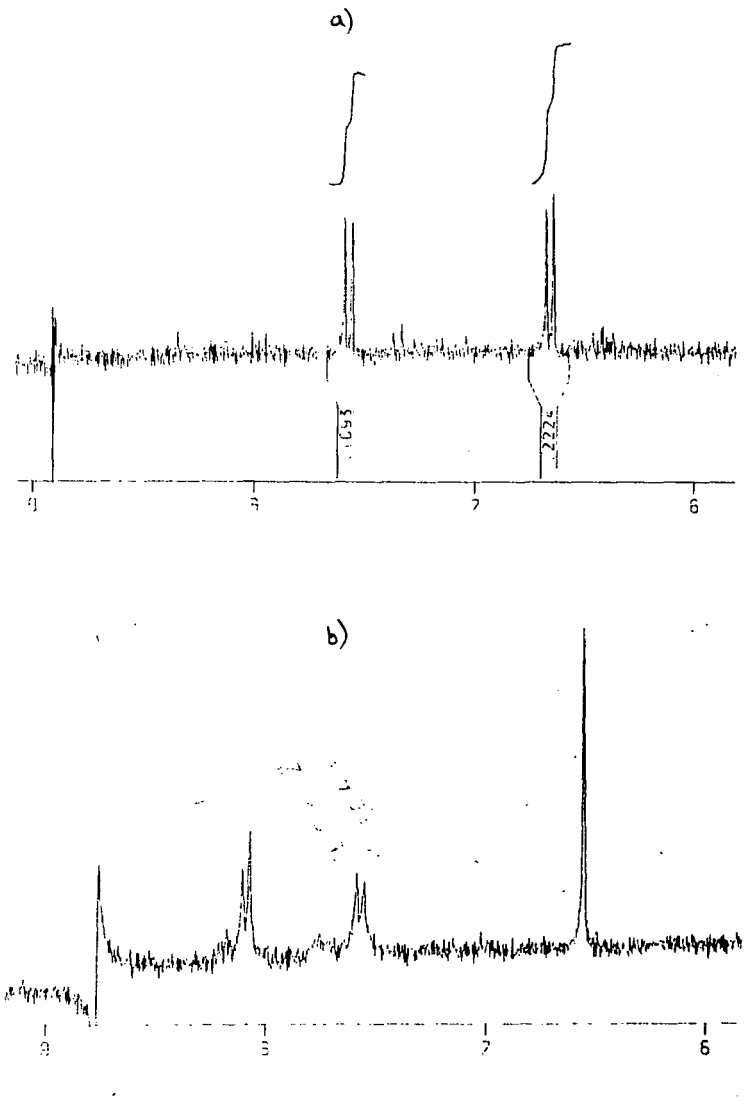
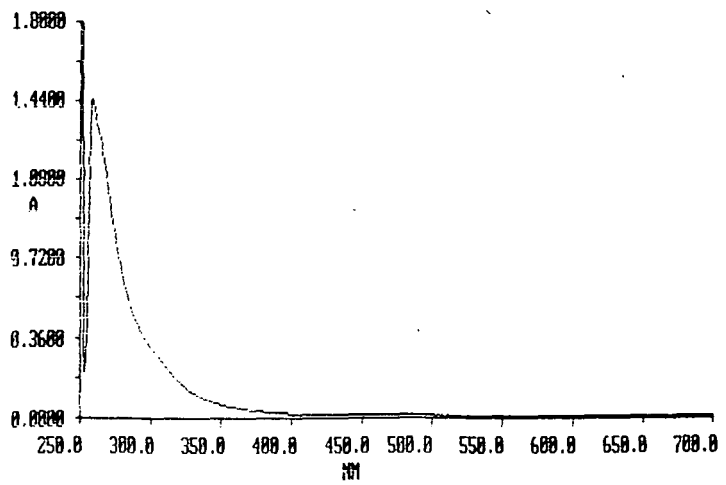
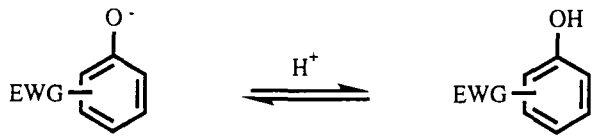


Figure 5.8

UV/Vis spectrum of 13DNB (1x10^{-4}M) /DMSO.

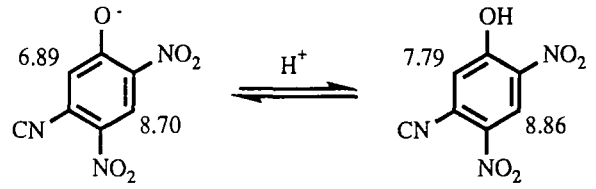


species, showing a pair of doublets with a typical *ortho*-coupling (8.3Hz), produced from both substrates is most likely to be a 1,2,3,4-tetrasubstituted benzene.



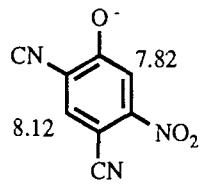
Eqn.5.1

Comparison with known data suggests that the chemical shifts of the species produced are in accord with the formation of dicyanonitrophenols. For comparison it is shown in chapter 6 that the chemical shifts of 5-cyano-2,4-dinitrophenol and its phenoxide are as shown (eqn.5.2).

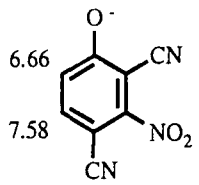


Eqn.5.2

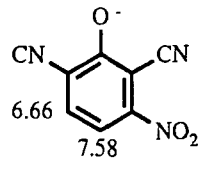
The chemical shifts of the dicyanonitrophenols are expected to be smaller than those of the dinitrocyanobenzenes so that likely structures are (5.1-3). It is possible to distinguish between (5.2) and (5.3) by comparing the shifts of the phenols with simulated spectra. The spectra were simulated using a computer programme which calculates additively the effects of the various functional groups at *ortho*, *meta* or *para* positions. Clearly the spectrum simulated for (5.2) agrees better with the observed data than that simulated for (5.3).



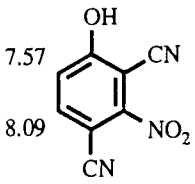
(5.1)



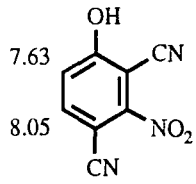
(5.2)



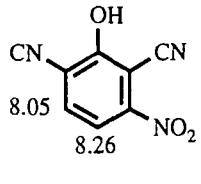
(5.3)



observed



simulated

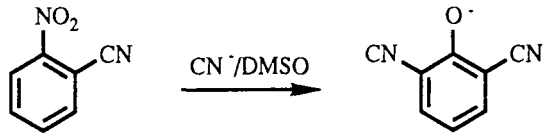


simulated

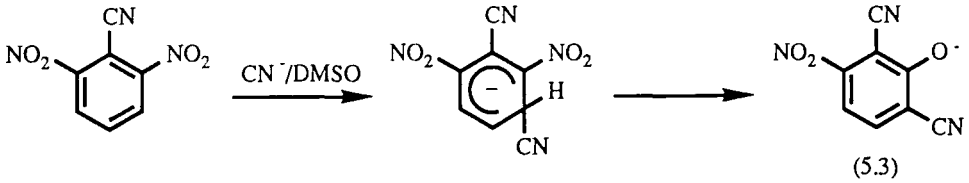
Hence the NMR data indicates the formation of (5.2) from 2,6-dinitrobenzonitrile and a mixture of (5.1) and (5.2) from 2,4-dinitrobenzonitrile. These

highly activated phenols would be expected to absorb strongly in the visible spectrum so that the absorbances observed at *c.a.* 450nm after completion of the reactions (figs.5.1-5) support the structures proposed.

There are at least three possible mechanisms for the production of nitro-dicyanophenols from dinitrobenzonitriles and cyanide. The first possibility is a Nef-type reaction, discussed in chapter 1 (section 1.4.2). This mechanism (scheme 1.20) was postulated [1] without any real evidence for the transformation of 2-nitrobenzonitrile into 2,6-dicyanophenol (eqn.5.3). The Nef reaction requires that a nitro group is replaced *ortho* to the added cyanide and would require the formation of (5.3) rather than (5.2) from 2,6-dinitrobenzonitrile (*i.e.* eqn.5.4). The fact that the NMR evidence supports the formation of (5.2) argues against this mechanism, as does the fact that no gas evolution was observed experimentally. The Nef reaction involves the formation of nitrous oxide gas (scheme 1.18).



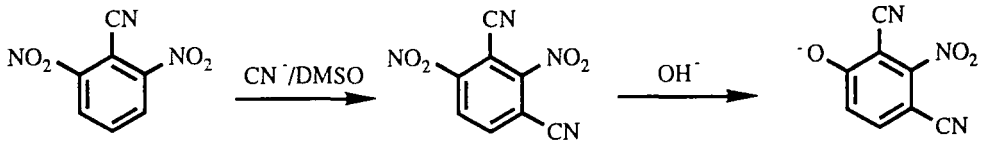
Eqn.5.3



Eqn.5.4

(5.3)

The second possibility is that neutral dicyano-dinitrobenzenes are produced as intermediates and that these produce phenols by hydroxydenitration (eqn.5.5). The hydroxide necessary might be produced by hydrolysis of cyanide ions by adventitious water in the solvent. NMR spectroscopy was performed using fresh ampoules of d_6-DMSO in which the water content was at a low level. Nevertheless spectra showed a band due to water absorbed by the solvent.



Eqn.5.5

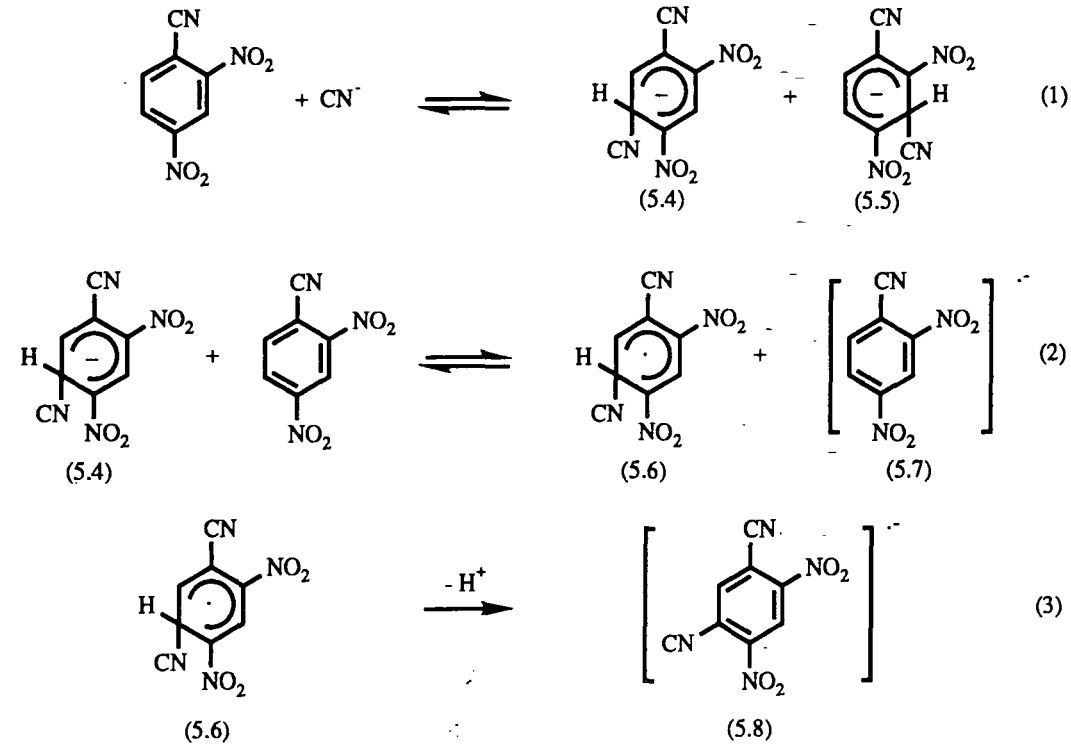
(5.2)

There is some evidence from recent synthetic work [2] that suggests that *ortho*-nitrobenzonitriles may exist as neutral species in the reaction between activated nitro-compounds and cyanide ions in DMSO (section 1.4.2). When substitution occurs in these compounds it is the nitro group *ortho* to cyano groups which are most readily displaced. Hence formation of (5.3) might be expected rather than (5.2) which is

observed. There is also evidence [3] from the literature and the present work (section 4.4) that reaction of dinitrobenzonitriles with hydroxide in DMSO results in the displacement of the cyano group rather than the nitro group. Hence it is thought to be unlikely that this second possibility is the actual mechanism.

A third possibility is a mechanism involving addition of cyanide followed by proton transfer to give the radical anions of the respective dicyano-dinitrobenzenes (*e.g.* 5.8). Fragmentation of these radical anions would be expected to produce radicals that would lead to phenol production. Evidence from e.s.r. spectroscopy for these radical anions as reaction intermediates is given below (section 5.3). An outline of the possible mechanism for reaction of 2,4-dinitrobenzonitrile with cyanide in DMSO is given in scheme 5.1. The NMR suggests that both phenols (5.1) and (5.2) are produced from 2,4-dinitrobenzonitrile, indicating that products derived from both of the sigma-complexes (5.4) and (5.5) are observed.

Scheme 5.1



The first step (1) is rapid reversible formation of either the C-3 (5.5) or the C-5 (5.4) sigma-complex. This species is observed by uv/vis spectroscopy in media rich in DMSO as an absorbance band *c.a.* 650nm (figs. 5.1-5). It is known [4] that C-5 sigma-adducts from nucleophilic attack on 1-halo-2,4-dinitrobenzenes are more thermodynamically stable than their C-3 counter-parts, so structure (5.4) is more likely than (5.5).

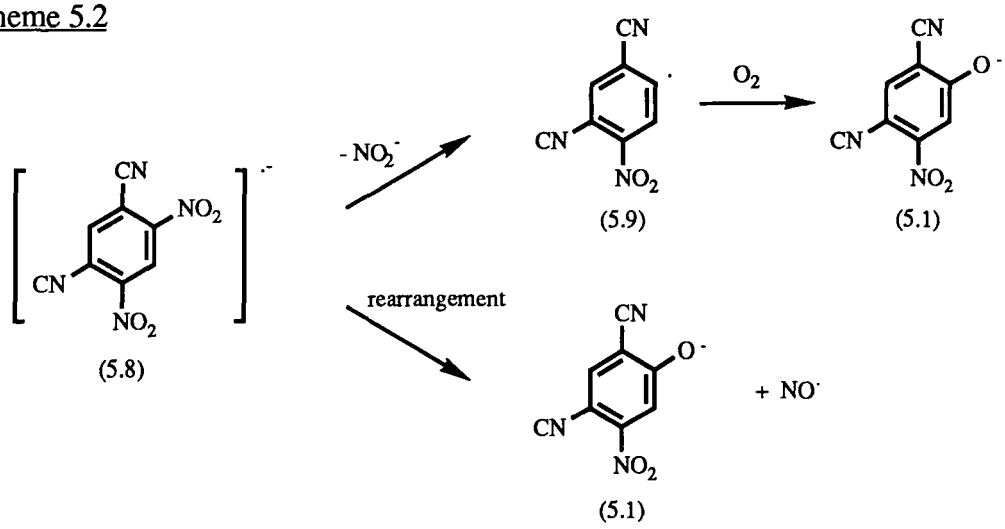
The second step (2) is an electron transfer from the sigma-complex (*e.g.* 5.4 and 5.5) to the parent, yielding a sigma-aryl radical (5.6) and the anion radical of the parent

(5.7). There are precedents for this type of electron transfer in the literature.[5] This step is further discussed in chapter 6.

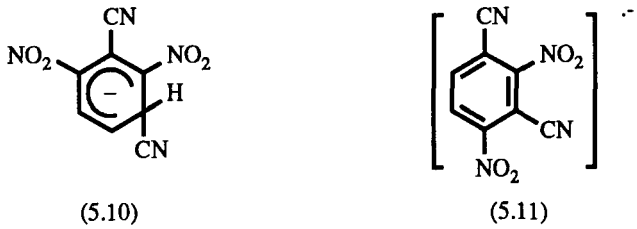
The *ipso* proton of (5.6) will be acidic due to the neighbouring electron withdrawing groups, and its removal should be facile in the basic media employed in this reaction (step 3). Elsewhere in this work (section 5.2) there is also evidence for replacement of a ring hydrogen by cyanide. The anion radicals of dicyano-dinitrobenzenes (*e.g.* 5.8) are likely to be relatively stable due to the four electron withdrawing groups on the ring. There is also no obvious nucleofuge from (5.8). Evidence is discussed below (section 5.3) for the existence of species such as (5.8) in these systems and others (sections 5.2 and 6.3).

There are two possibilities for the introduction of oxygen onto the ring of (5.8) to form the observed phenoxide products. The most likely nucleofuge from (5.8) is the nitrite ion (NO_2^-), which would produce the radical (5.9). It is then possible that (5.9) could react with dissolved oxygen in the solvent to produce a phenoxide species (5.1) (scheme 5.2). Another possibility is that (5.8) rearranges internally to an oxiridine (1.71) isomer and then expels the nitric oxide radical (scheme 1.20), leaving an oxygen bonded to the ring (scheme 5.2).

Scheme 5.2



If the starting substrate is 1CN26DNB the only likely sigma-complex is (5.10). This would go on to form the radical anion (5.11) *via* scheme 5.1, and from there to the observed phenoxide products.

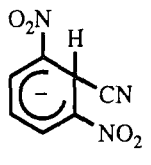


This mechanism (scheme 5.1) should be compared with that (scheme 6.4) for 1-chloro-2,4-dinitrobenzene with cyanide in DMSO rich media (section 6.4.4) in which the radical anion (6.17) is proposed as a key intermediate. This species is unlikely to be as stable as (5.8) since it has an obvious nucleofuge, the chloride ion. This allows the nitro groups to remain bound to the ring and consequently yields a cyano-dinitrophenoxide product.

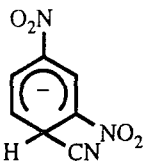
5.2 THE REACTION OF *META*-DINITROBENZENE WITH CYANIDE IN DMSO-RICH MEDIA.

The reactions of *meta*-dinitrobenzene (13DNB) and excess cyanide in DMSO and methanol-DMSO mixtures have been studied by uv/vis spectrophotometry and proton NMR.

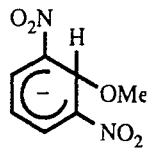
The uv/vis spectrum of 13DNB ($1x10^{-4}M$) in DMSO (fig.5.8) shows absorbance tailing to 400nm, but with no definite absorbance maximum above 300nm. In the presence of KCN (0.02M) in 25%/75% v/v MeOH/DMSO the uv/vis spectrum of 13DNB ($5x10^{-3}M$) initially shows two broad absorbance bands at 665 and 550nm (fig.5.9). Both of these peaks increase in intensity over the next few minutes, the latter more than the former. There is also an increase in absorbance below 500nm. After 5min the predominant feature in the visible region is a fairly sharp band at 550nm with a shoulder at 520nm. Because the parent concentration is high in these spectra, the extent of conversion to the absorbing species is probably fairly low. A similar sharp band has been observed in the reactions of 2,4-dinitrobenzonitrile (section 5.1) and 1-fluoro-2,4-dinitrobenzene (section 6.3) with cyanide in DMSO rich media. The nature of the species giving rise to this band is discussed below (section 5.5). It is likely that the species causing the band at 665nm is either (5.12) or (5.13).



(5.12)



(5.13)



(5.14)

In the presence of a slight deficit of KCN ($2x10^{-3}M$) in 25%/75% v/v MeOH/DMSO the uv/vis spectrum of 13DNB ($5x10^{-3}M$) shows a broad absorbance band at 550nm (fig.5.10). No other absorbance bands are observed. There is evidence from other parts of this work (chapter 3) to suggest that, especially at lower concentrations, there is a significant amount of methoxide ions produced by methanolysis of cyanide in methanolic solutions. Consequently it is possible that the broad absorbance at 550nm is due to the sigma-complex (5.14).[6]

The uv/vis spectrum of 13DNB ($5x10^{-4}M$) plus KCN (0.01M) in DMSO initially shows three bands λ_{max} : 665, 555 and 495nm (fig.5.11). Band λ_{max} 665nm fades over the next few minutes. The sharp band λ_{max} 555nm develops over the next 10min to a steady absorbance in the final product. Band λ_{max} 495nm develops over the next 2min, but then fades slightly. The spectrum of the final product is shown (fig.5.11).

It is possible that, similar to the reaction in 25%/75% v/v MeOH/DMSO, the species causing the band at 665nm is (5.12) or (5.13). It is known [4] that in substituted *meta*-dinitrobenzenes that attack of the nucleophile at the carbon inbetween the nitro groups is faster than attack at a position *para* to one of the nitro groups. However, the sigma-complex from the attack at the latter position is more thermodynamically stable than that formed by attack at the former position. It has also been shown [7] that 2,6-dinitrocyclohexadienyl anions (*e.g.* 5.12 and 5.14) absorb at longer wavelengths than the 2,4-dinitrocyclohexadienyl anions (*e.g.* 5.13). Consequently it is likely that in DMSO the band λ_{max} 665nm is due to (5.12), and band λ_{max} 495nm is due to (5.13). The nature of the final product is discussed later in this section.

The reaction of 13DNB with a slight excess of sodium cyanide has been studied in d_6-DMSO by proton NMR. The spectrum of 13DNB in d_6-DMSO (fig.5.12) shows the three coupled signals of the aromatic ring protons (table 4.7) at 8.85, 8.67 and 7.97ppm. In the presence of a slight excess of NaCN (0.04M) in d_6-DMSO the spectrum of 13DNB (0.02M) is initially blank downfield of 6ppm. This is probably due to the presence of radicals in the solution. After one week the spectrum is clear, and is shown in fig.5.13. Amongst other signals which remain to be assigned it is significant that two doublets of equal intensity are observed at 7.58 and 6.66ppm (J = 8.28Hz). These signals, together with a uv/vis spectrum λ_{max} 430nm, are common to the reactions of 2,4- and 2,6-dinitrobenzonitrile with cyanide under similar conditions (section 5.1), and have been assigned to 3-nitro-2,4-dicyanophenoxide (5.2).

Figure 5.9

UV/Vis spectra of 13DNB ($5x10^{-3}$M) + KCN (0.02M) /25%/75% v/v MeOH/DMSO (int. = 30sec).

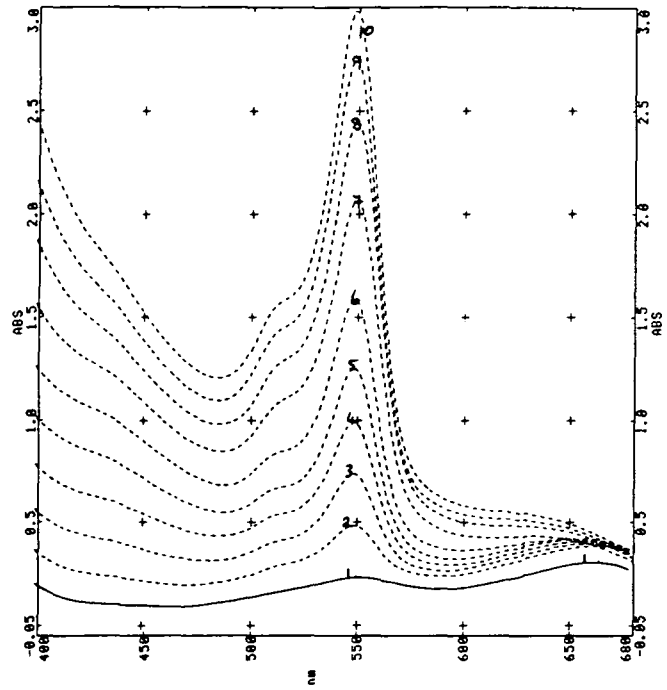


Figure 5.10

UV/Vis spectrum of 13DNB ($5x10^{-3}$M) + KCN ($2x10^{-3}$M) /25%/75% v/v MeOH/DMSO.

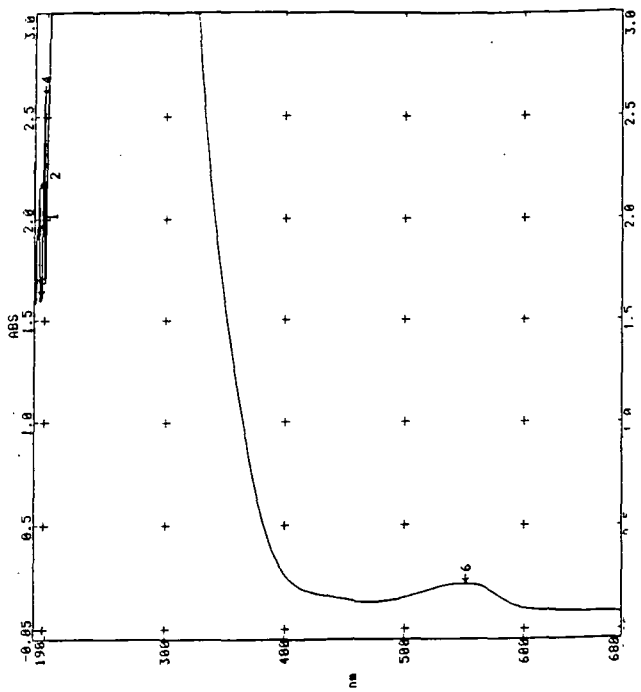


Figure 5.11

UV/Vis spectra of 13DNB ($5x10^{-4}$M) + KCN (0.01M) /DMSO a) (int. = 30sec), b) final product (30min).

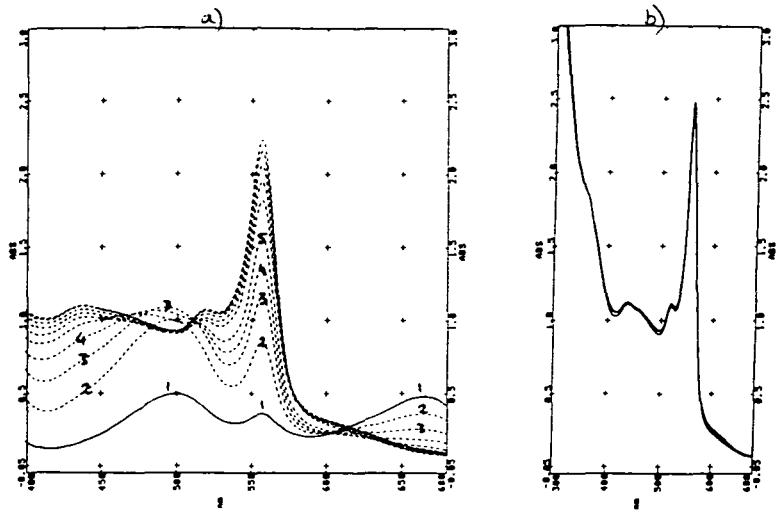


Figure 5.12

Proton NMR spectrum of 13DNB /d_6-DMSO.

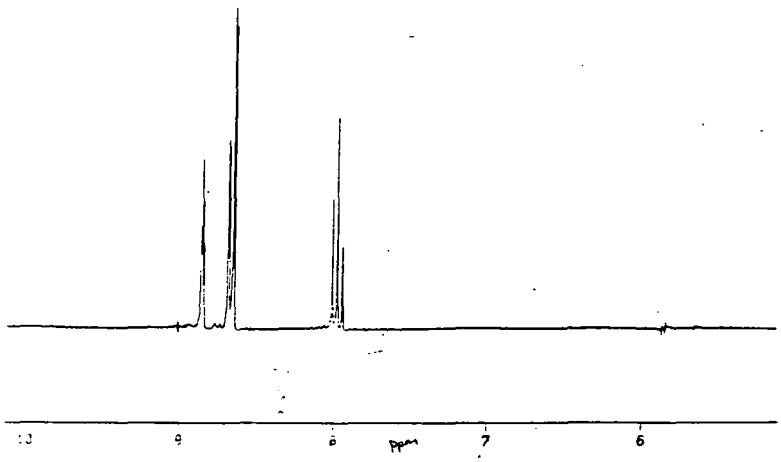
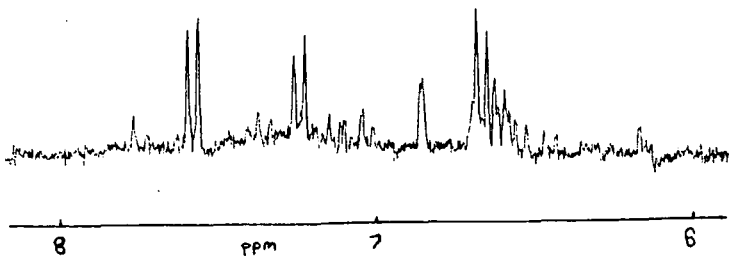


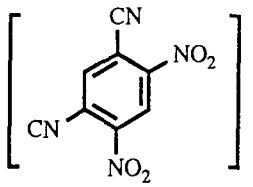
Figure 5.13

Proton NMR spectrum of 13DNB (0.02M) + NaCN (0.04M) /d_6-DMSO.

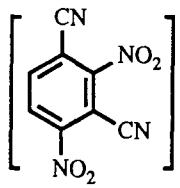


5.3 E.S.R. MEASUREMENTS.

In an attempt to find evidence for the existence of radical anions such as (5.8) and (5.11) in the systems described above some e.s.r. spectrometric studies have been undertaken. Thanks are due to Prof. B.C.Gilbert and Dr. A.C.Whitwood of the University of York for running these spectra. The author has studied the reactions of *meta*-dinitrobenzene, 1-fluoro-2,4-dinitrobenzene, 2,4- and 2,6-dinitrobenzonitrile with potassium cyanide in DMSO and in methanol-DMSO mixtures.



(5.8)



(5.11)

5.3.1 Results.

After mixing 13DNB ($3x10^{-3}M$) with an excess of KCN (0.02M) in 25%/75% v/v MeOH/DMSO there is a steady build-up of an e.s.r. signal over 20min. The spectrum of the mixture after 8min is shown (fig.5.14). Initially after mixing the mixture is a faint violet colour, but a stronger orange/brown colour soon develops. When 13DNB ($3x10^{-3}M$) is mixed with an excess of KCN (0.01M) in 3%/97% v/v MeOH/DMSO there is a steady build-up of an e.s.r. signal of approximately the same intensity as (fig.5.14) over the first 5min; this signal subsequently decays. The spectrum after 5min is shown (fig.5.15). When 13DNB ($3x10^{-4}M$) is added to a large excess of KCN (0.01M) in DMSO there was a build-up of a weak signal over the first 5min, which then subsequently faded. The spectrum of this mixture after 5min is shown (fig.5.16).

After mixing 1-fluoro-2,4-dinitrobenzene (1F24DNB) ($2.5x10^{-4}M$) with an excess of KCN (0.02M) in 25%/75% v/v MeOH/DMSO there is a broad e.s.r. signal initially present after 1min (fig.5.17), which fades continuously over 5min. Initially after mixing the reaction mixture is a blue colour, which rapidly becomes violet. Gradually the solution becomes an orange/brown colour. When 1F24DNB ($1x10^{-3}M$) is mixed with an excess of KCN (0.01M) in DMSO there is an initial steady build-up of a strong e.s.r. signal over the first 5min; which then subsequently fades. The spectrum after 4min is shown (fig.5.18). The reaction mixture is initially a blue colour, but quickly becomes orange/brown. When 1F24DNB (0.025M) was added to a deficiency

Figure 5.14

E.S.R. spectrum of 13DNB ($3x10^{-3}M$) + KCN (0.02M)
/25%/75% v/v MeOH/DMSO (8min).

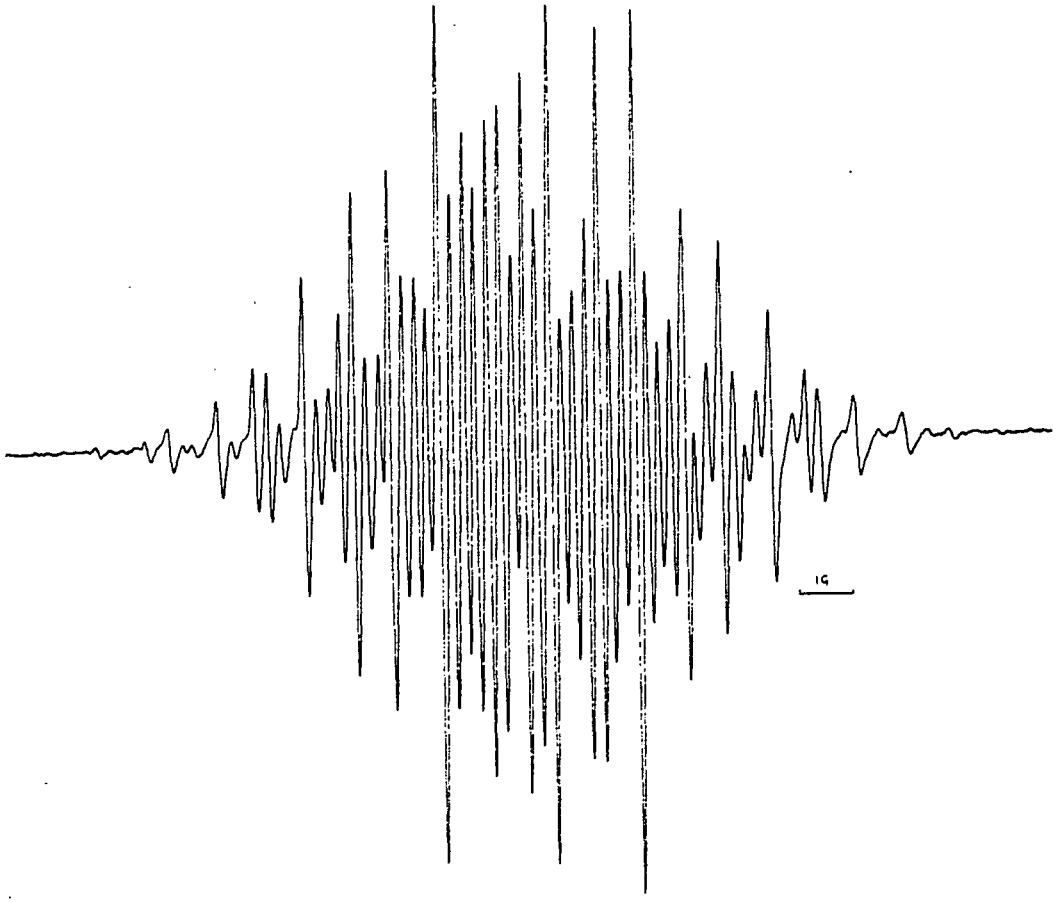


Figure 5.15

E.S.R. spectrum of 13DNB ($3x10^{-3}M$) + KCN (0.01M)
/3%/97% v/v MeOH/DMSO (5min).

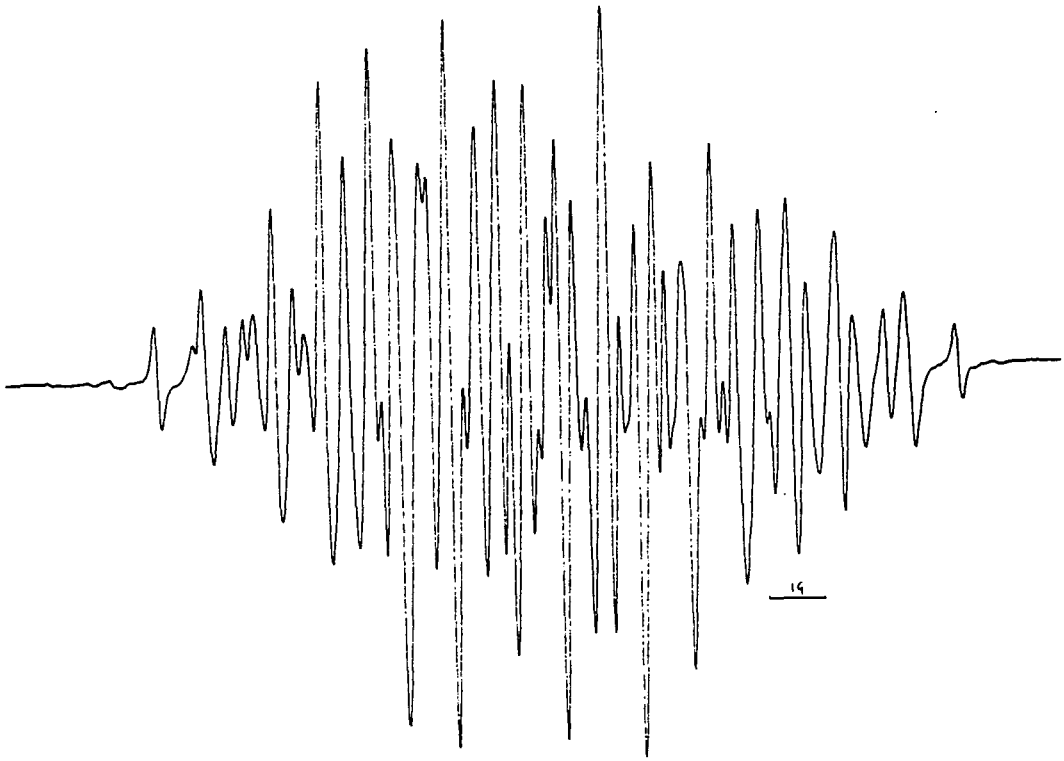


Figure 5.16

E.S.R. spectrum of 13DNB ($3x10^{-4}M$) + KCN (0.01M) /DMSO (5min).

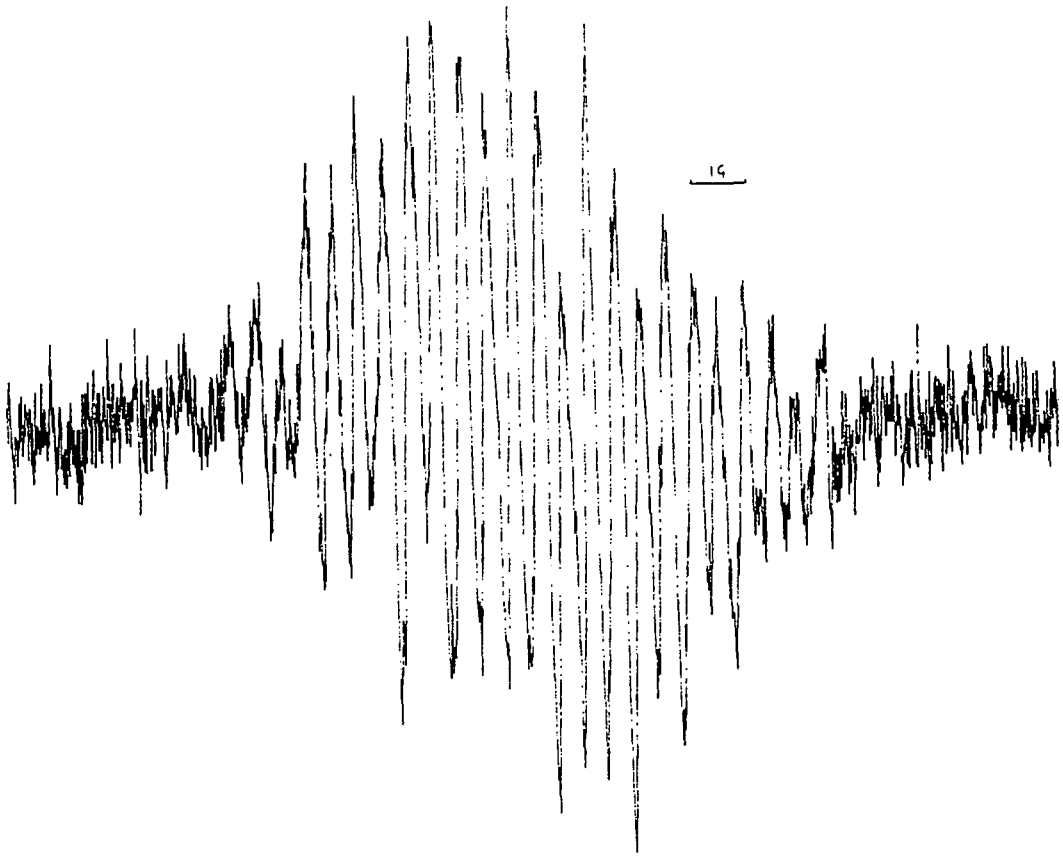


Figure 5.17

E.S.R. spectrum of 1F24DNB ($2.5x10^{-4}M$) + KCN (0.02M) /25%/75% v/v MeOH/DMSO (1min).

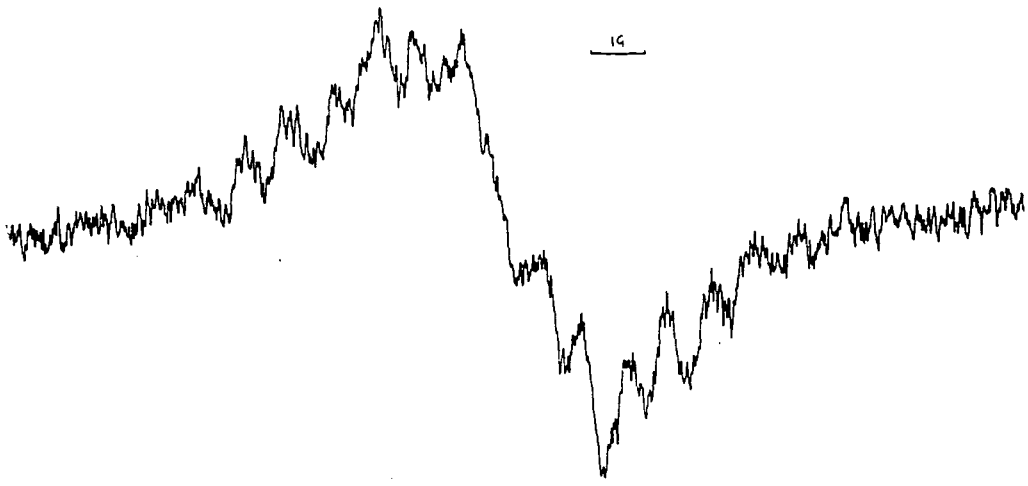


Figure 5.18

E.S.R. spectrum of 1F24DNB ($1x10^{-3}M$) + KCN (0.01M) /DMSO (4min).

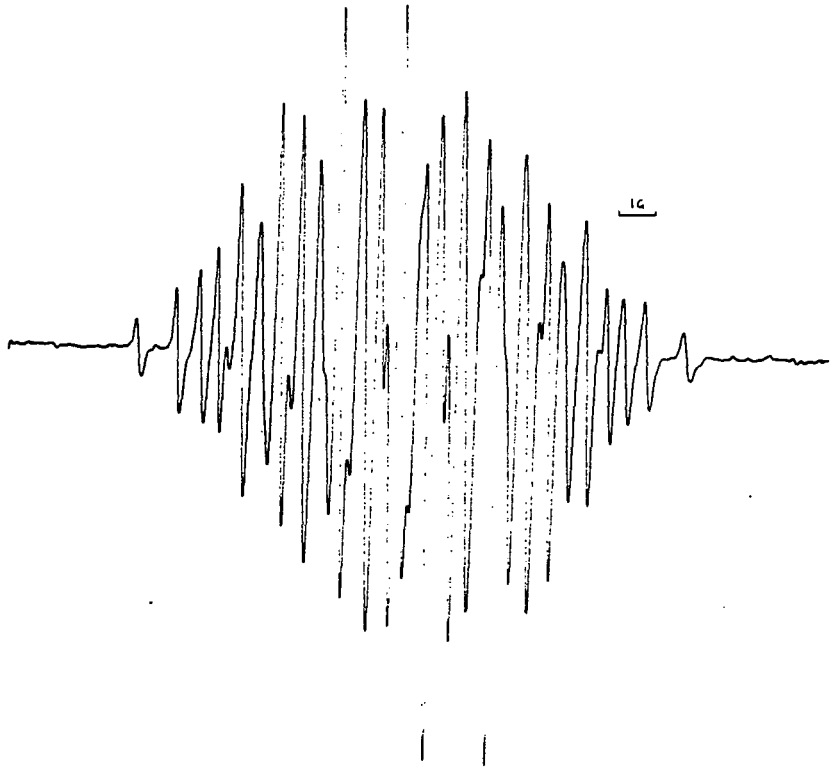


Figure 5.20

E.S.R. spectrum of 1CN26DNB ($1x10^{-3}M$) + KCN (0.01M) /DMSO (10min).

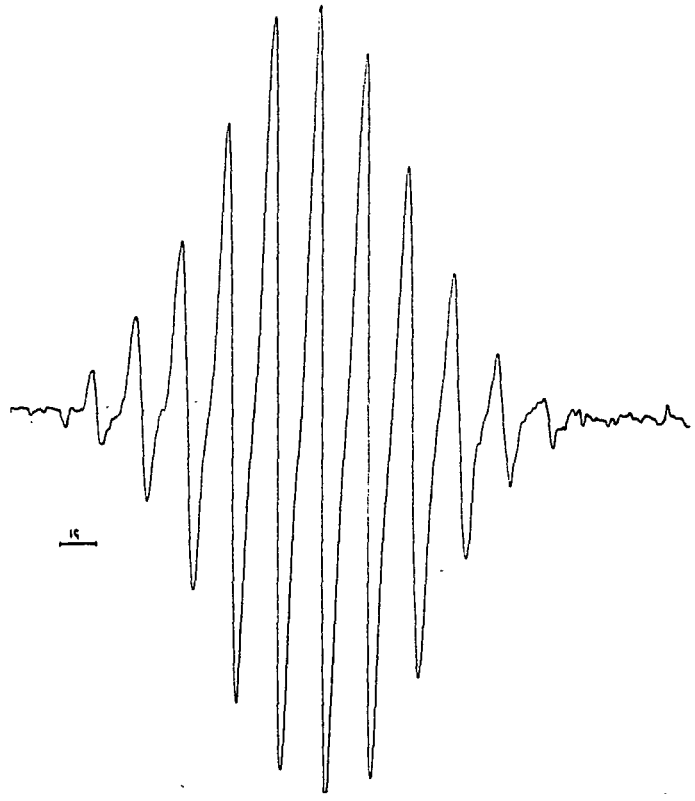


Figure 5.19

E.S.R. spectrum of 1CN24DNB ($1x10^{-3}$M) + KCN (0.01M) /DMSO (initially).

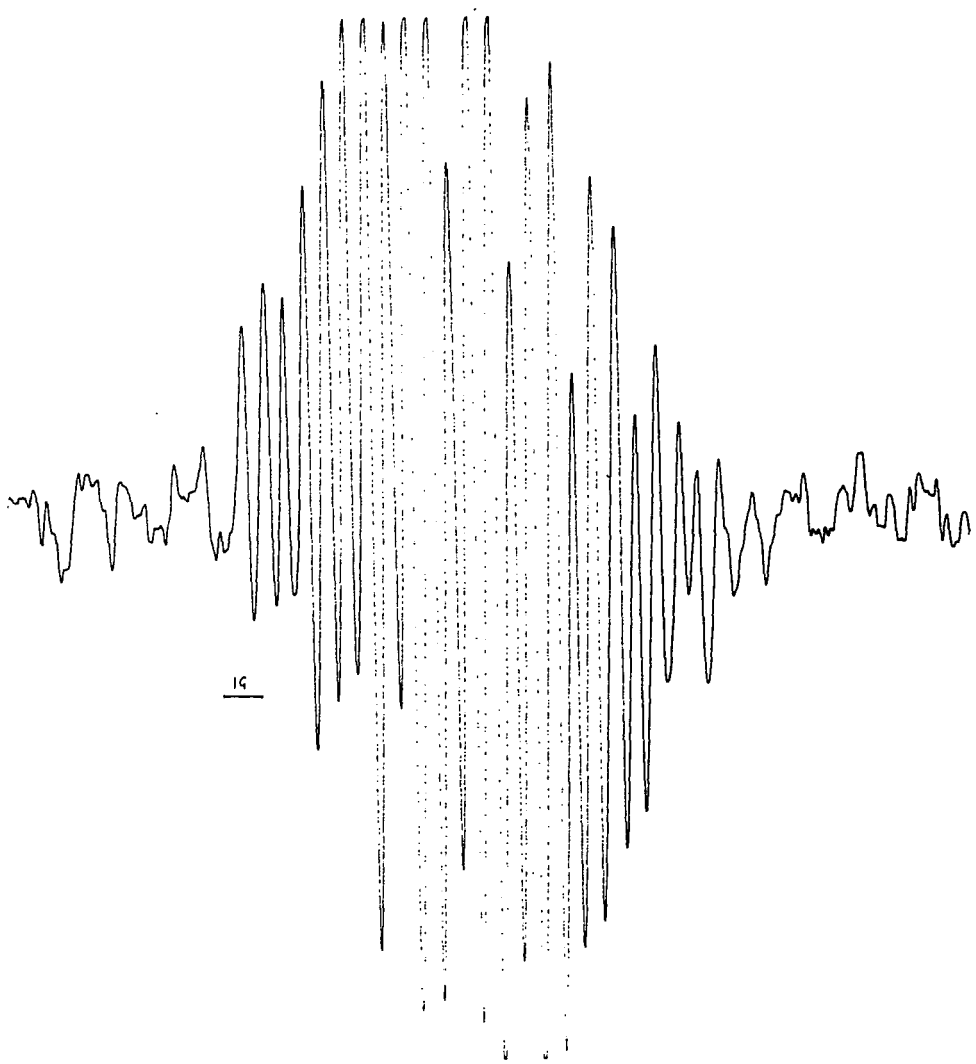


Figure 5.21

Simulated e.s.r. spectrum for $2a_N = 1.80G$, $2a_N = 1.15G$, $a_H = 2.30G$, $a_H = 1.80G$.

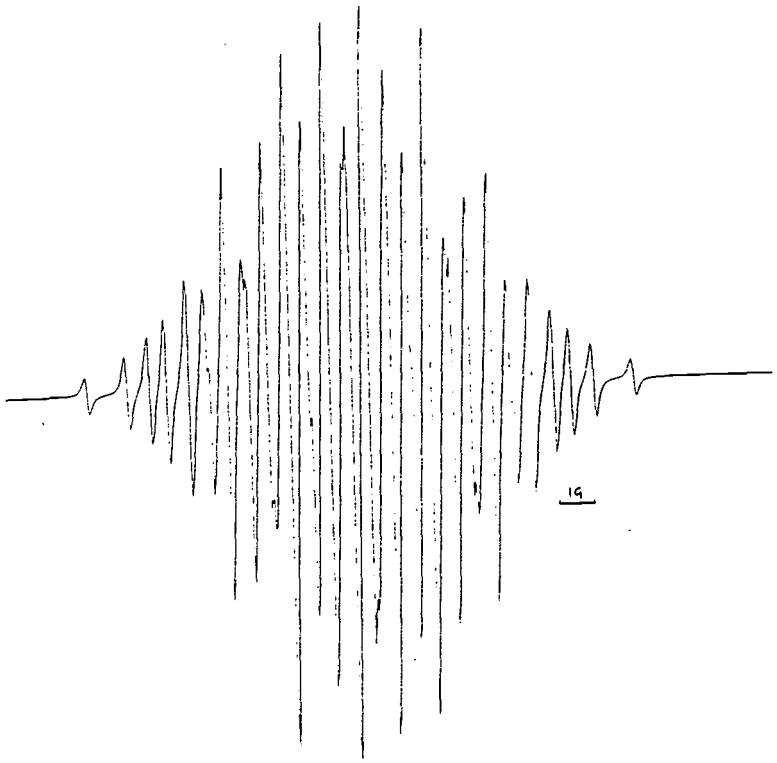
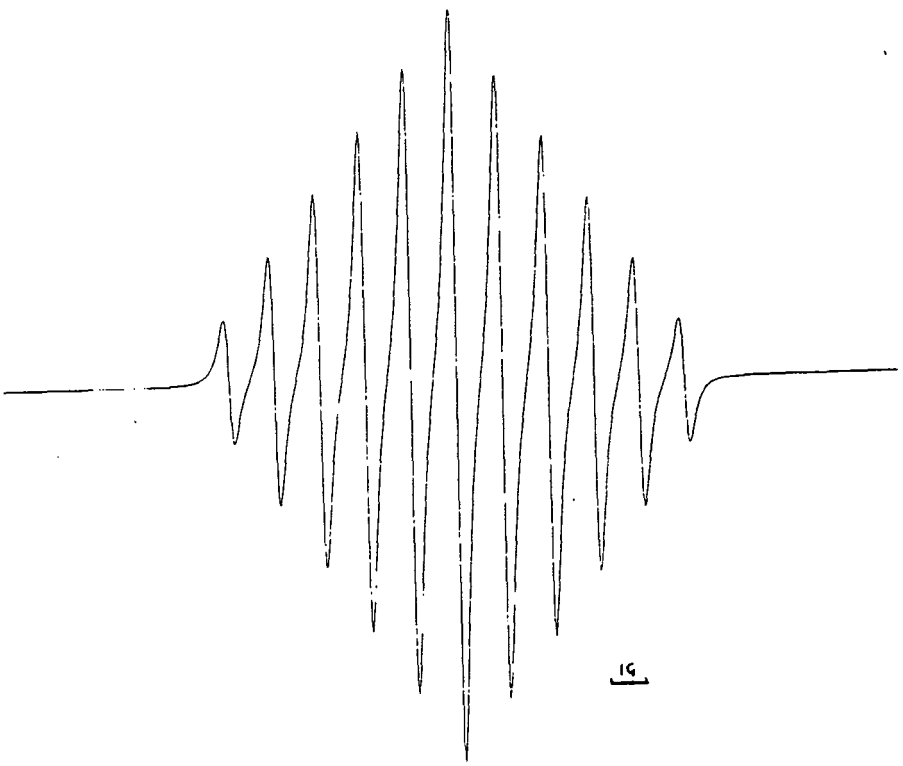


Figure 5.22

Simulated e.s.r. spectrum for $2a_N = 2.65G$, $2a_H = 1.32G$.



of KCN ($1.5x10^{-3}M$) in 25%/75% v/v MeOH/DMSO only a very weak e.s.r. signal is observed (radical concentration of approximately $10^{-7}M$) which fades with time.

On mixing 1CN24DNB ($1x10^{-3}M$) with an excess of KCN (0.01M) in DMSO a strong e.s.r. signal is observed initially, but this gradually fades over the next few minutes. The initial spectrum is shown (fig.5.19). When the same concentration of substrate is added to a larger excess of KCN (0.02M) in 12%/88% v/v MeOH/DMSO a similar spectrum is initially obtained, but this rapidly fades. No significant e.s.r. signal can be observed when 1CN24DNB ($1x10^{-3}M$) is mixed with NaOMe (0.05M) in DMSO. Initially after mixing 1CN26DNB ($1x10^{-3}M$) with an excess of KCN (0.01M) in DMSO a strong, relatively simple e.s.r. signal is observed, which subsequently fades over the next few minutes. The spectrum after 10min is shown (fig.5.20). The e.s.r. spectra of the radical anions of 1CN24DNB and 1CN26DNB were measured. The coupling constants are given in table 5.1.

Table 5.1

E.S.R. data for the radical anions of some dinitrobenzonitriles.

	coupling constants (a) /G			
	$2a_N^{(NO2)}$	$2a_H$	a_H	$a_N^{(CN)}$
1CN26DNB [a]	3.3	2.9	0.9	0.3
1CN24DNB [a]	3.2	3.2	0.5	0.5
1CN35DNB [b]	3.0	5.0	2.8	—

a) This work.
b) 3,5-Dinitrobenzonitrile; from electochemical reduction in DMF.[8]

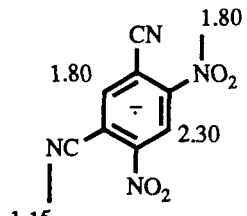
5.3.2 Discussion.

The rate at which the e.s.r. signal during the reactions between *meta*-dinitrobenzene, 1-fluoro-2,4-dinitrobenzene and 2,4-dinitrobenzonitrile with excess potassium cyanide in DMSO or methanol-DMSO develops and fades appears to follow that of the sharp band at 550nm in the uv/vis spectra of these reactions. It is therefore possible that the same species gives rise to both.

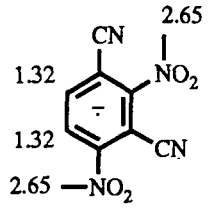
The e.s.r. spectra of the reaction of 1-fluoro-2,4-dinitrobenzene and 2,4-dinitrobenzonitrile with cyanide in DMSO (figs.5.18 and 5.19) appear to be very similar; both have 26 lines and a total spectrum width of 15G. In each spectrum the peaks at each end are separated by 1.1G from the neighbouring peaks. The e.s.r. spectra obtained from *meta*-dinitrobenzene contain all the lines observed in the above spectrum together

with additional lines. Hence it is likely that a common species is produced in these reactions, with a second radical being present in the dinitrobenzene reaction.

A similar spectrum to that obtained from 1-fluoro-2,4-dinitrobenzene and 2,4-dinitrobenzonitrile with cyanide can be computed using the model coupling constants: $2a_N$ = 1.80G, $2a_N$ = 1.15G, a_H = 2.30G and a_H = 1.80G (fig.5.21). These coupling constants could be caused by a species with two pairs of nitrogens in different environments, and two hydrogens in different environments. It is possible that the radical anion (5.8) would give an e.s.r. spectrum with these coupling constants. The radical anion of 2,4-dinitrobenzonitrile does not give a similar e.s.r. spectrum to that observed experimentally.



(5.8)



(5.11)

A relatively simple e.s.r. spectrum is observed on mixing 2,6-dinitrobenzonitrile with excess cyanide in DMSO (fig.5.20). Each line is separated from the others by approximately 1.3G. There are 11 lines, with a total spectrum width of approximately 12.4G. A similar spectrum (fig.5.22) can be calculated using the coupling constants: $2a_N$ = 2.65G and $2a_H$ = 1.32G. These coupling constants could be due to a species with a pair of nitrogens and a pair of hydrogens coupling with the unpaired electron. It is possible that the radical anion (5.11) would give an e.s.r. spectrum with these coupling constants. If this were the case then the coupling between the unpaired electron and the cyano-nitrogens would be slight (<0.5G). Again, the radical anion of 2,6-dinitrobenzonitrile does not give a similar spectrum to that observed experimentally.

However, this is not conclusive proof of the existence of either (5.8) or (5.11) in these reaction systems. It is possible that the e.s.r. spectra observed arise from species different to (5.8) and (5.11), but which have similar coupling constants. More conclusive evidence would be gained from recording the e.s.r. spectra of the anion radicals from neutral species that are known to be the respective dicyano-dinitro-benzenes in the solvents used above.

5.3.3 Features of E.S.R. Spectroscopy.

It has been shown [9] that in aromatic anion radicals the coupling constant for a nitrogen of a nitro group is much larger than that for a cyano group nitrogen; *e.g.* for the

radical anion of *para*-nitrobenzonitrile formed by electrochemical reduction in DMF, $a_N^{(CN)}$ = 0.76G and $a_N^{(NO2)}$ = 6.24G. This effect arises because the nitrogen of the nitro group is directly bound to the aromatic ring, and consequently has a greater spin population than the nitrogen of the cyano group, which is not directly bound to the ring.

A difference in spin density also effects the coupling constants of the ring protons. The coupling constants of protons *meta*, *ortho* and *para* to an electron withdrawing group increases in that order; *e.g.* for the radical anion of benzonitrile [9] prepared by electrolytic reduction in DMF $a_{H meta}$ = 0.03G, $a_{H ortho}$ = 3.63G and $a_{H para}$ = 8.42G.

A solvent effect has been observed [10] in the e.s.r. spectra of substituted *meta*-dinitrobenzene radical anions when changing from protic solvents (water or alcohols) to aprotic solvents (*e.g.* DMF). Any solvent that favours charge localisation (protic solvents) causes the spin density of the radical anion to gather on one of the two nitrogens. Consequently the nitrogens of the nitro groups are no longer equivalent and different coupling constants are observed. With the two nitrogens now non-equivalent, the fluctuation between the two possible structures causes a certain degree of line broadening.[11] In aprotic solvents, which do not favour charge localisation, line broadening is not as pronounced since both nitrogens are equivalent.

The dependence of coupling constants on solvent is exemplified by the anion radical of 3,5-dinitrobenzonitrile. In DMF the e.s.r. spectrum shows [8] two identical nitro group nitrogen couplings (3.00G), two identical proton couplings (2.84G) and a single proton coupling (5.00G). The cyano group nitrogen coupling is not observed (<0.3G). The single large proton coupling is due to the hydrogen in the 4-position; the smaller twin proton couplings are due to the hydrogens in the 2- and 6-positions. However, in 20%/80% v/v MeOH/DMSO, the e.s.r.spectra shows only one nitro group nitrogen coupling (9.62G). There still remains a twin proton coupling of 2.98G. Note that now these proton couplings are similar, there is little difference in spin densities on the aromatic hydrogens because the main spin population is now centred on the one nitro group. The author has not observed any similar solvent effects in this work.

Association of radical anions with alkali metal cations is also possible.[12] In the case of such an association, there is an overlap between the M.O. of the unpaired π-electron in the radical anion and the orbitals of the gegenion, so that the unpaired electron can delocalise into the gegenion orbitals. The spin population thus donated to the gegenion is generally small. However, in the case of alkali metal cations as gegenions, such an effect can be observed by e.s.r. because the s-character of the spin population at the cation gives rise to a sufficiently high spin density, and the magnetic moments of the abundant isotopes ^{7}Li, ^{23}Na and ^{39}K are all non-zero (I=3/2).

This effect has been demonstrated [13] using *meta*-dinitrobenzene. At room temperature in DME (dimethoxyethane) the e.s.r. spectrum of the sodium and potassium

salts of the radical anion show two distinct nitrogen couplings, one vary large (9.85G for Na salt and 9.00G for K) and one vary small (0.29 and 0.22G respectively). However, with the cesium salt, twin nitrogen couplings are observed (4.66G). In the case of the sodium and potassium salts the metal cation spends sufficient time close to one of the nitro groups to allow association with it. In the case of cesium, cation motion is faster and consequently the cation can be said to associate with each nitro group equally. The author has not observed association in this work. This failure to observe association with cations is expected since measurements were made in DMSO or in media rich in DMSO. In such systems the cations and anions will be well solvated so that interaction between them is unlikely.

5.4 POLAROGRAPHIC MEASUREMENTS.

5.4.1 Reduction Potentials of Some Neutral Substrates.

Table 5.2

Reduction potentials (V) of some neutral substrates.

Substrate	Solvent	
	$^{n}Bu_4N.Br$ (0.0078M) /DMSO [g]	$KClO_4$ (0.2M) /DMSO [h]
TNB [a]	-1.24	-0.47, -0.99
13DNB [b]	-0.82, -1.27	-0.76, -1.08
24DNA [c]	-0.95, -1.34	-0.90, -1.16
1F24DNB	-0.81, -1.23	-0.76, -1.05
1Cl24DNB [d]	-1.38	-0.72, -1.16
1Br24DNB	-1.21, -1.30	-0.73, -1.07
1I24DNB	-1.10, -1.23	-0.75, -1.13
15DF24DNB [e]	-1.15	-0.75, -0.99
1CN2MeO4NB	-0.98, -1.56	-0.68
1CN4MeO2NB	-1.80	-0.69
1CN2MeO6NB	-1.70	-0.70
1CN24DMB	-2.53	<-1.5
1CN26DMB	-2.37	<-1.5
24DNP [f]	-1.42	-0.58, -1.22, -1.50
26DNP [f]	-1.46	-0.50, -0.85, -1.15, -1.70
1CN24DNB	-1.03	-0.47, -0.93
1CN26DNB	-1.06	-0.54, -0.92

a) lit:[5] -0.46V (ref: $^{n}Bu_4N.ClO_4$ (0.1M) /DMF).
b) lit:[5] -0.83V (ref: $^{n}Bu_4N.ClO_4$ (0.1M) /DMF).
c) 2,4-dinitroanisole, lit:[14] -1.28, -1.55, -1.88V (ref: $Ag/AgNO_3$ (0.1M) /DMSO).
d) lit:[14] -1.09, -1.43, -1.80V (ref: $Ag/AgNO_3$ (0.1M) /DMSO).
e) 1,5-Difluoro-2,4-dinitrobenzene.
f) 2,4- and 2,6-dinitrophenol.
g) Dropping mercury electrode.
h) Platinum electrode.

Polarographic measurements have been made to record the reduction potentials of some neutral substrates that have been used throughout this work. The reduction potentials observed are given in the table 5.2. The polaragraphs have been recorded

Figure 5.23

Polarographs (0 - $^{-}$1.5V) of $^{n}Bu_4N.Br$ (0.0078M) /DMSO

a) in the absence and b) in the presence of 13DNB ($5x10^{-4}$M),

and c) in the presence of 13DNB ($1x10^{-3}$M).

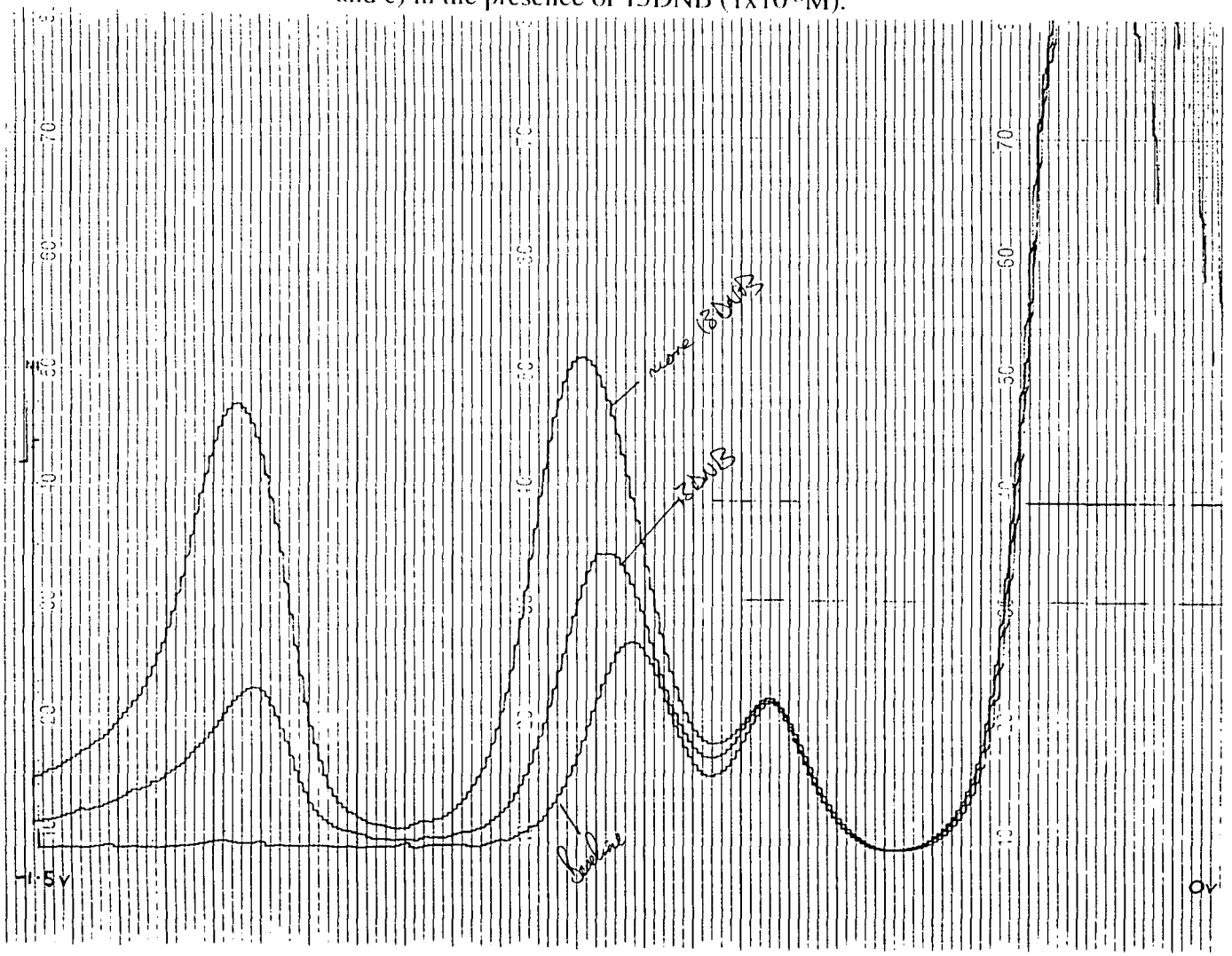
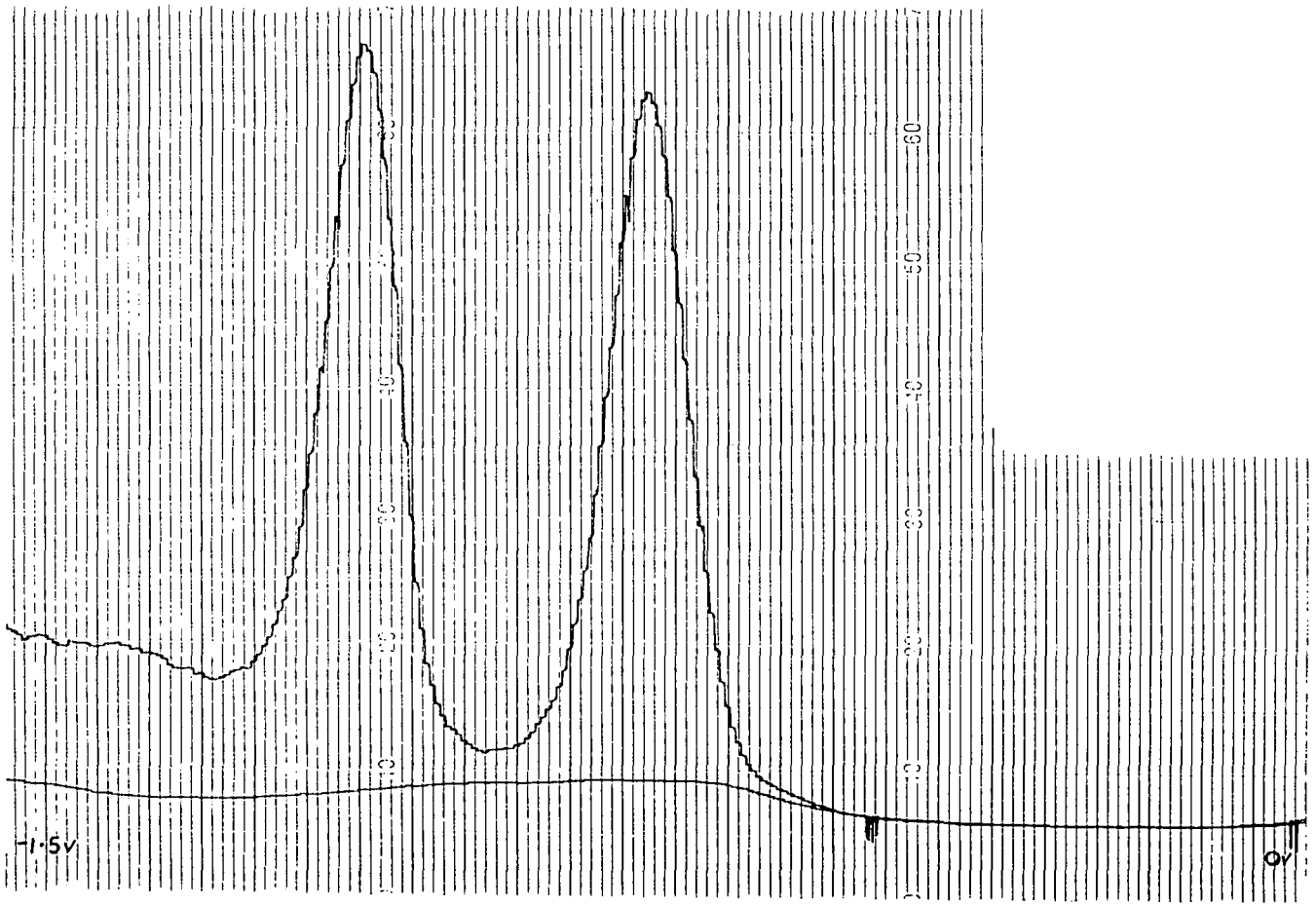


Figure 5.24

Polarographs (0 - $^{-}$1.5V) of $KClO_4$ (0.2M) /DMSO

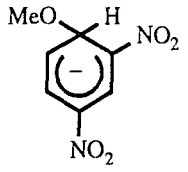
a) in the absence and b) in the presence of 13DNB ($5x10^{-4}$M).



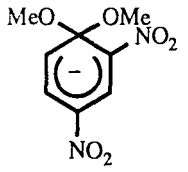
using two different media because tetrabutylammonium bromide shows two peaks at -0.38 and -0.54V (fig.5.23) which might have obscured peaks due to the substrates. Potassium perchlorate shows no peaks in the potential ranges studied. Figs. 5.23 and 5.24 show the polarographs of *meta*-dinitrobenzene in tetrabutylammonium bromide and potassium perchlorate respectively.

5.4.2 Oxidation Potentials of Some Sigma-Complexes.

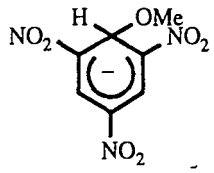
The oxidation potentials of the two methoxy sigma-complexes (5.15) and (5.16) have been recorded. Complex (5.15) was formed by mixing 13DNB ($5x10^{-4}$M) with a large excess of NaOMe (0.01M) in DMSO. An oxidation potential was observed at 0.77V using a platinum electrode. There were no other peaks between -0.2 and 1.3V. Complex (5.16) was formed by mixing 2,4-dinitroanisole ($5x10^{-4}$M) [15,16] or 1-chloro-2,4-dinitrobenzene ($5x10^{-4}$M) [17,18] with a large excess of NaOMe (0.01M) in DMSO. An oxidation potential was observed at 0.93V using a platinum electrode. There were no other peaks observed between -0.2 and 1.3V.



(5.15)



(5.16)



(5.17)

When TNB ($5x10^{-4}$M) was added to a large excess of NaOMe (0.01M) in DMSO no oxidation peaks could be observed below 2.0V although the solution was the characteristic orange colour [19] of the complex (5.17).

1-Chloro-2,4-dinitrobenzene ($5x10^{-4}$M) was added to a large excess of KCN (0.01M) in DMSO but no oxidation potential was observed below 1.3V with a platinum electrode. The solution rapidly turned the characteristic yellow colour of phenols.

5.4.3 The Reactions of 2,4-Dinitrobenzonitrile, 1-Fluoro-2,4-dinitrobenzene and *meta*-Dinitrobenzene with Cyanide in DMSO.

Polarographs have also been recorded for the reactions of 1CN24DNB, 1-fluoro-2,4-dinitrobenzene and 13DNB with an excess of KCN in DMSO between 0.8 and -1.2V. Some common peaks are observed for these reactions. A platinum electrode with potassium perchlorate as the background electrolyte is used throughout.

When 1CN24DNB ($5x10^{-4}M$) is mixed with KCN (0.005M) in dry DMSO under nitrogen the polarograph of the mixture after 2min shows (fig.5.25) peaks at 0.30, -0.19 and -0.78V. These peaks fade slowly with time, but are still evident after 90min. A small amount of air was allowed into the system after 90min. The polarograph then showed further small peaks at -0.97 and -1.10V. On further aeration only the peaks at -0.97 and -1.10V were observed.

Similar behaviour is observed when 1-fluoro-2,4-dinitrobenzene ($5x10^{-4}M$) is mixed with KCN (0.005M) in dry DMSO under nitrogen. The initial polarograph (fig.5.26) shows peaks at 0.30, -0.19 and -0.77V. These peaks slowly fade with time. After aeration these peaks have faded completely, and new peaks are observed at -0.62, -0.89 and -1.04V.

Similar behaviour is also observed when 13DNB ($5x10^{-4}M$) is mixed with KCN (0.005M) in dry DMSO under nitrogen. The initial polarograph (fig.5.27) shows peaks at 0.29, -0.17, -0.70 and -1.10V. These peaks slowly fade with time. After aeration these peaks have faded completely, and new peaks are observed at -0.52, -0.68, -0.94 and -1.08V.

Some similarities between these systems are evident. The initial polarographs in the absence of oxygen show peaks at 0.30, -0.19 and *c.a.* -0.77V; all of which appear to fade at the same rate. On aeration, these peaks are no longer observed, and two new peaks appear at *c.a.* -0.94 and -1.08V.

Unfortunately, in the systems studied in this section cyano sigma-complexes have been shown to be short lived and so the author has been unable to produce polarographic data for these species. However, oxidation potentials for two methoxy sigma-complexes (5.15 and 5.16) have been recorded. The results indicate that it may be possible for a sigma-complex to reduce its parent substrate in these systems. This is often an essential step in the mechanisms proposed throughout this thesis.

Common intermediates and products have also been observed in this work for the reactions of these three substrates with cyanide in DMSO using uv/vis spectroscopy, NMR and e.s.r. spectrometry. The possible natures of these species are discussed in the section that follows (section 5.5).

Figure 5.25

Polarographs (0.8 - $^{-}$1.2V) of 1CN24DNB ($5x10^{-4}M$)
+ KCN (0.005M) /DMSO 1) 2min, 2) 7min, 3) 16min, 4) 90min,
5) slightly aerated and 6) fully aerated.

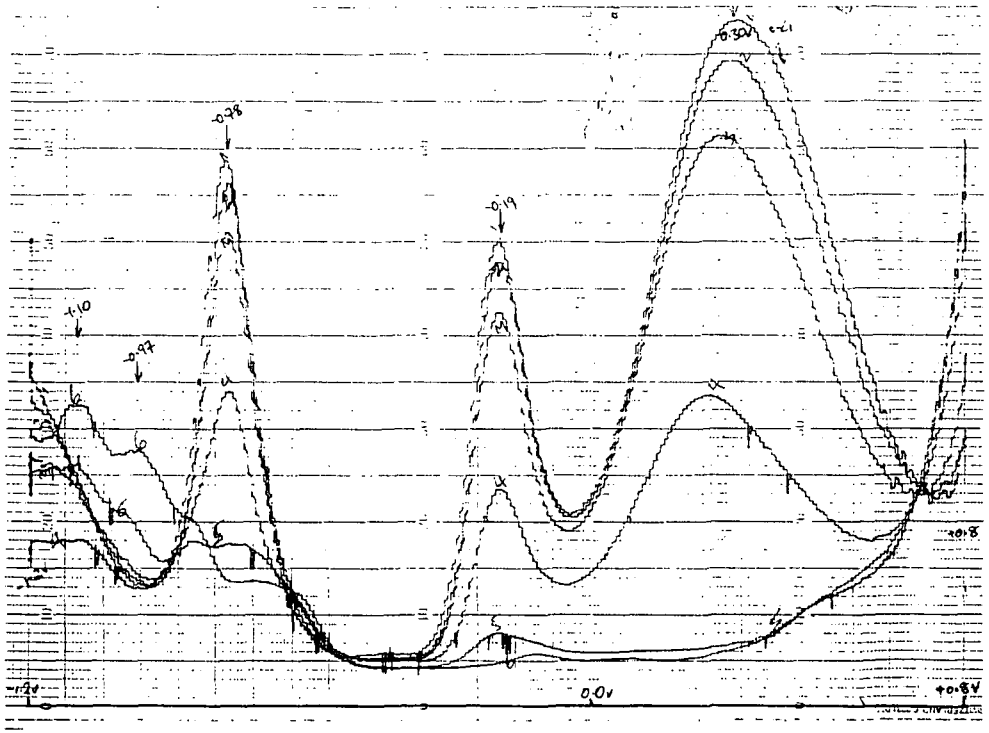


Figure 5.26

Polarographs (0.8 - -1.2V) of 1F24DNB ($5x10^{-4}$M)
+ KCN (0.005M) /DMSO 1) 2min, 2) 5min, 3) 20min,
4) 40min, and 5) fully aerated.

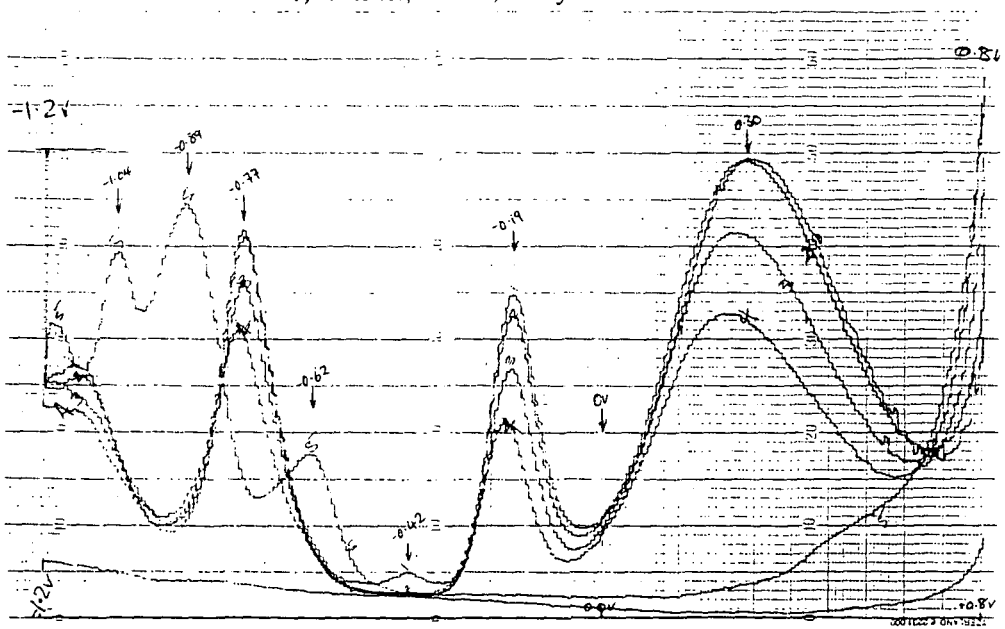
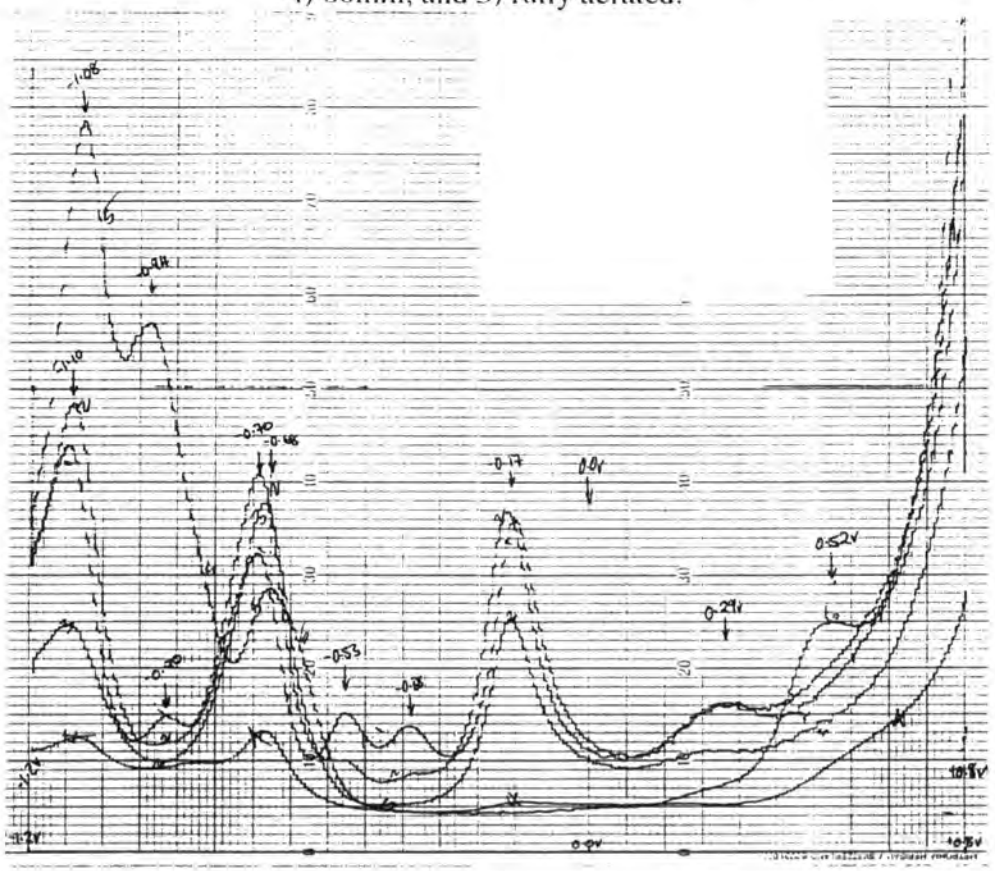


Figure 5.27

Polarographs (0.8 - $^{-}$1.2V) of 13DNB ($5x10^{-4}$M)
+ KCN (0.005M) /DMSO 1) 2min, 2) 5min, 3) 20min,
4) 60min, and 5) fully aerated.



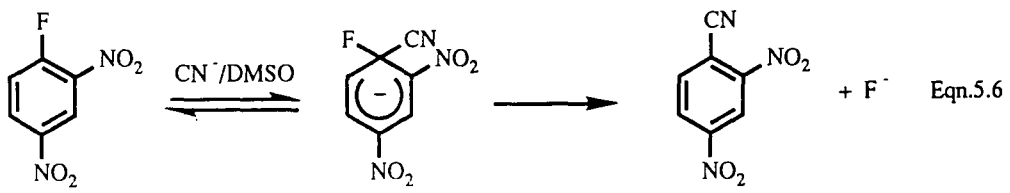
5.5 THE NATURE OF THE COMMON INTERMEDIATE.

5.5.1 The Evidence.

The author has reported evidence for the existence of a common intermediate in the reactions of 2,4-dinitrobenzonitrile (section 5.1), *meta*-dinitrobenzene (section 5.2) and 1-fluoro-2,4-dinitrobenzene (section 6.3) with excess cyanide in DMSO-rich media. The uv/vis spectrum of this species shows a narrow absorbance band at 550nm, with a shoulder at 520nm. 2,4-Dinitrobenzonitrile and 1-fluoro-2,4-dinitrobenzene with excess cyanide in DMSO both give a common e.s.r. spectrum (section 5.3); the e.s.r. spectrum of the reaction of *meta*-dinitrobenzene with excess cyanide in DMSO appears to include this common spectrum. The polarographs of each of the three reactions (section 5.4) show common bands, both during and at completion of the reactions.

5.5.2 Discussion.

It will be shown later (chapter 6) that the reaction of 1-fluoro-2,4-dinitrobenzene with cyanide ions differs markedly from the reaction of 1-chloro-, 1-bromo- and 1-iodo-2,4-dinitrobenzenes with cyanide. This difference probably derives from the rate of attack by the nucleophile at the 1-position relative to attack at unsubstituted ring-positions in these substrates. It is known [4] that nucleophilic attack at the 1-position of 1-fluoro-2,4-dinitrobenzene is faster than attack at unsubstituted ring positions, while attack at the 1-position in other 1-halo-2,4-dinitrobenzenes is at least an order of magnitude slower than attack at unsubstituted positions. This difference probably arises i) because of the higher electronegativity of fluorine relative to the other halogens which increases the positive charge at the 1-position and ii) the smaller size of fluorine which will minimise any steric repulsion between the entering and leaving ions.



Eqn.5.6

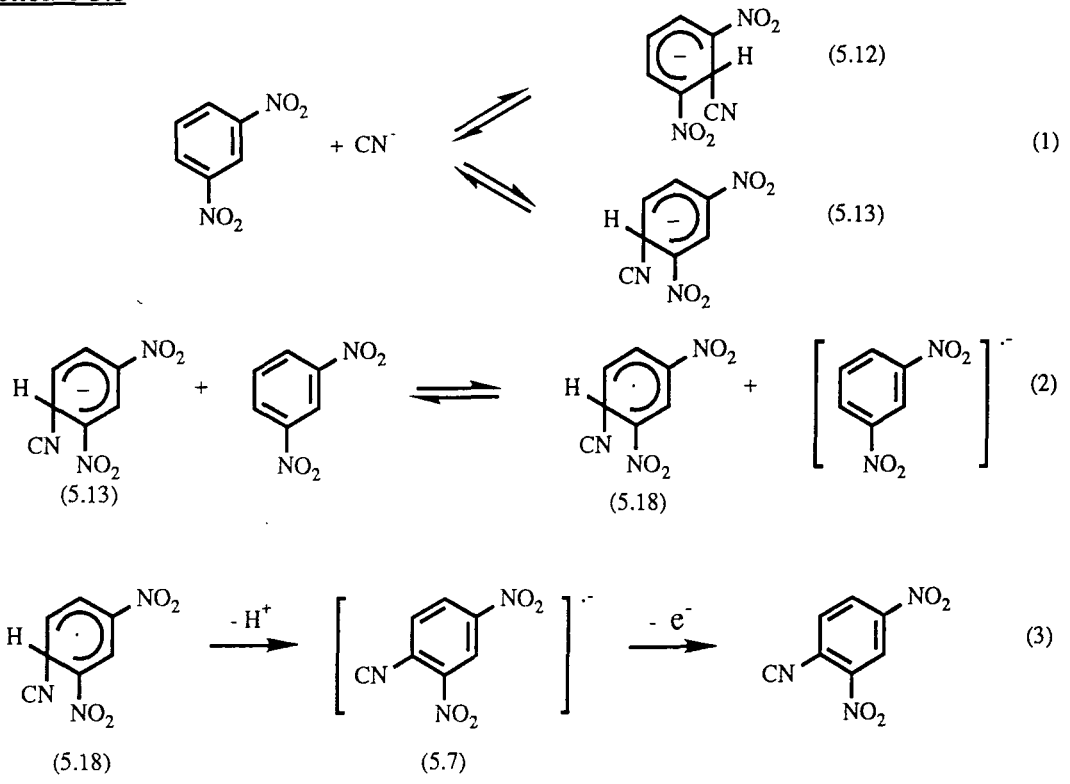
Hence the major reaction between 1-fluoro-2,4-dinitrobenzene and cyanide will be direct nucleophilic attack at the 1-position leading to rapid formation of 2,4-dinitrobenzonitrile (eqn.5.6). There is no evidence for build-up of an intermediate sigma-complex so that the first step, cyanide addition, is likely to be rate determining.

The initial reaction of the other 1-halo-2,4-dinitrobenzenes with cyanide will involve attack at an unsubstituted position and this leads on to other products as discussed in chapter 6.

The fact that there are common features in the reactions of 2,4-dinitrobenzonitrile and 1-fluoro-2,4-dinitrobenzene with excess cyanide is thus explained. It also appears that a common species is also produced by reaction of *meta*-dinitrobenzene with excess cyanide in DMSO. However, the evidence from uv/vis and e.s.r. spectroscopies is that this species is produced much more slowly from *meta*-dinitrobenzene.

A possible mechanism for the production of 2,4-dinitrobenzonitrile from *meta*-dinitrobenzene and cyanide is shown below (scheme 5.3).

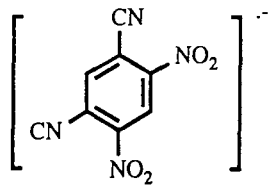
Scheme 5.3



The production of the adducts (5.12) and (5.13) (step 1) has been discussed above (section 5.2).

Hydride is a poor nucleofuge, consequently *meta*-dinitrobenzene is unlikely to yield 2,4-dinitrobenzonitrile by simple nucleophilic aromatic substitution *via* (5.13). Hence a mechanism involving electron transfer from (5.13) to the parent (step 2) is proposed. It has previously been shown (section 5.4.3) that this step may be possible. The rate-determining step may be proton abstraction from (5.18) (step 3), yielding the relatively stable radical anion of 2,4-dinitrobenzonitrile (5.7). This step involves the cleavage of a chemical bond, and is therefore likely to be slower than the fast electron transfers involved in this mechanism. It is known [5] that nitro-aromatics can act as

electron acceptors and so it is possible that any free parent may oxidise (5.7) to 2,4-dinitrobenzonitrile. The presence of radicals other than (5.8) in this mechanism (scheme 5.3) explains the recording of other e.s.r. signals in the reaction of *meta*-dinitrobenzene with cyanide (section 5.3).



(5.8)

It seems probable that the species giving the observed visible and e.s.r. spectra and polarographs is the radical (5.8) which is intermediate in the conversion of 2,4-dinitrobenzonitrile to 2,4-dicyano-5-nitrophenoxide (5.1) described in section 5.1. It has been shown that the e.s.r. spectrum observed is compatible with this structure. Also the radical anion might well be expected to show an oxidation potential corresponding to loss of an electron, so that the band at +0.3V may be attributed to this. The reduction potentials at -0.19 and -0.78V would correspond to electron additions to the radical anion. The new polarograph obtained after exposure to oxygen can be attributed to oxidation possibly resulting in phenolic products.

The above arguments do not of course constitute a proof that the radical anion (5.8) is actually responsible for the observed characteristics. A method to test this would be to synthesise 1,3-dicyano-4,6-dinitrobenzene and then generate the radical anion from it. Unfortunately time did not allow an attempt of this synthesis.

5.6 REFERENCES.

1 R.B.Chapas, R.D.Knudsen, R.F.Nystrom & H.R.Snyder, *J. Org. Chem.*, (1975), **40**, 3746.

2 J.H.Gorvin, *J. Chem. Res.*, (1990), (S) 198, (M) 1662; (1991), (S) 88, (M) 738.

3 R.Bacaloglu, C.A.Bunton & F.Ortega, *J. Am. Chem. Soc.*, (1989), **111**, 1041.

4 M.R.Crampton, A.B.Davies, C.Greenhalgh & A.J.Stevens, *J. Chem. Soc., Perkin Trans. II*, (1989), 675.

5 C.Mariani, G.Modena, G.P.Pizzo, G.Scorrano & L.Kistenbrugger, *J. Chem. Soc., Perkin Trans. II*, (1979), 1187.

6 M.R.Crampton & V.Gold, *J. Chem. Soc. B*, (1966), 498.

7 Y.Hasegawa, *Bull. Chem. Soc. Jpn.*, (1974), **47**, 2186.

8 E.J.Fendler, J.H.Fendler, N.L.Arthur & C.E.Griffin, *J. Org. Chem.*, (1972), **37**, 812.

9 P.H.Rieger, I.Bernal, W.H.Reinmuth & G.K.Fraenkel, *J. Am. Chem. Soc.*, (1963), **85**, 683.

10 C.J.W.Gutch, W.A.Waters & M.C.R.Symons, *J. Chem. Soc. B*, (1970), 1261.

11 L.S.Degtyarev, M.P.Ponomarchuk & L.S.Kasukhin, *Zh. Org. Khim.*, (1972), **8**, 2353.

12 F.Gerson, *"High Resolution E.S.R. Specroscopy."*, J.Wiley & Sons Ltd., (1970), 137.

13 C-Y.Ling & J.Gendell, *J. Chem. Phys.*, (1967), **46**, 400.

14 C.K.Mann & K.K.Barnes, *"Electrochemical Reactions in Non-Aqueous Systems"*, Marcel Dekker Inc., New York, (1970), 353.

15 R.Foster, C.A.Fyfe, P.H.Ernslie & M.I.Foreman, *Tetrahedron*, (1967), **23**, 227.

16 W.E.Bryne, E.J.Fendler, J.H.Fendler & C.E.Griffin, *J. Org. Chem.*, (1967), **32**, 2506.

17 Y.Hasegawa, *Bull. Chem. Soc. Jpn.*, (1974), **47**, 2186.

18 K.Bowden & N.S.Nadvi, *J. Chem. Soc., Perkin Trans. II*, (1987), 189.

19 F.Terrier, *Chem. Revs.*, (1982), **82**, 77.

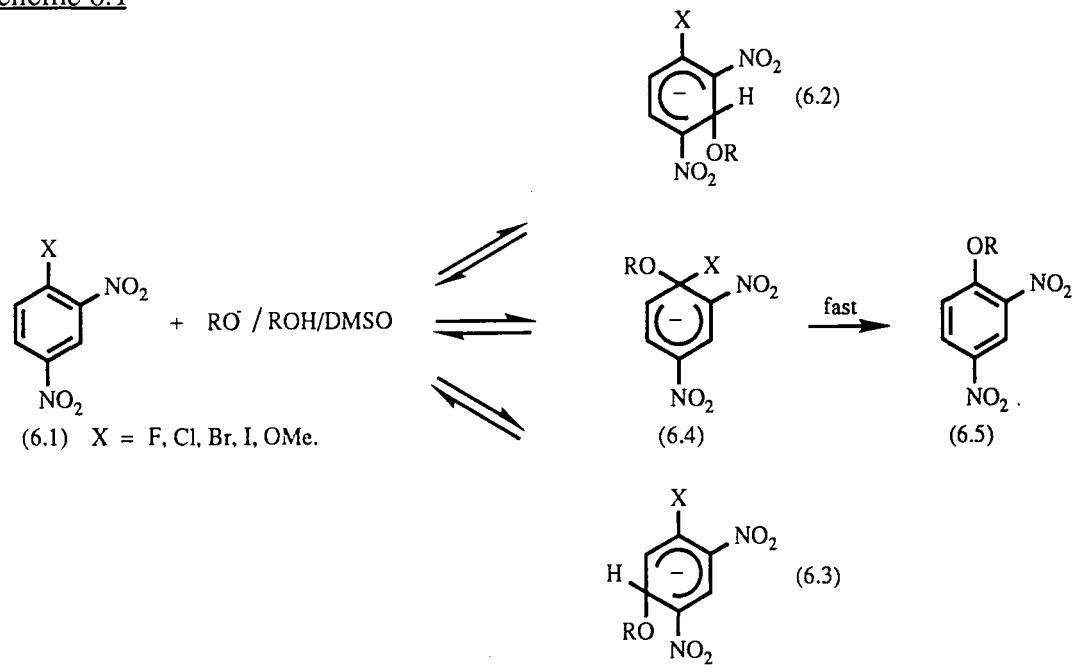
CHAPTER 6

THE REACTIONS OF 1-HALO-2,4-DINITROBENZENES AND 2,4-DINITROANISOLE WITH CYANIDE IONS IN METHANOL AND DMSO.

6.1 INTRODUCTION.

It is well known [1,2] that 2,4-dinitrophenol (6.5, R=H) (or phenoxide) is produced from the reactions of 1-halo-2,4-dinitrobenzenes (6.1, X=F,Cl,Br,I) with hydroxide ions in aqueous DMSO (scheme 6.1). There is uv/vis spectrophotometric evidence [1,3] for two sigma-complex intermediates (6.2 and 6.3, R=H).

Scheme 6.1



When 1-chloro-2,4-dinitrobenzene (6.1, X=Cl) is reacted with hydroxide in aqueous DMSO it is possible to observe the 3-hydroxy complex (6.2, R=H, X=Cl) by rapid-scan spectrophotometry.[3] The thermodynamically more stable 5-hydroxy complexes (6.3, R=H, X=Cl,Br,I) have been observed [1] by slower uv/vis spectrophotometry in 20%/80% v/v water/DMSO. No 1-hydroxy complexes (6.4, R=H) have been observed, implying that loss of halide ion is fast. The phenolic product (6.5, R=H) exists as the phenoxide in these basic systems.

Similarly, 2,4-dinitroanisole (6.5, R=Me) is produced from the reactions of 1-halo-2,4-dinitrobenzenes with methoxide ions in methanolic DMSO,[4,5] and there is uv/vis spectrophotometric evidence for two sigma-complex intermediates (6.2 and 6.3, R=Me). When 1-chloro-2,4-dinitrobenzene is reacted with deficient sodium methoxide

in 2%/98% v/v MeOH/DMSO [4] the first species observed is the 3-methoxy complex (6.2, R=Me, X=Cl); with other 1-halo-2,4-dinitrobenzenes (6.1, X=Cl,Br,I) the kinetically controlled formation of (6.3, R=Me, X=Cl,Br,I) can also be observed. In high concentrations of DMSO (>55%) with excess methoxide the product 2,4-dinitroanisole reacts further to produce the 1,1-dimethoxy sigma-complex (6.4, R=Me, X=OMe).

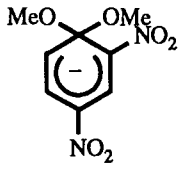
1-Chloro-2,4-dinitrobenzene undergoes normal nucleophilic aromatic substitution with excess sulphite ions in aqueous DMSO.[6] There is kinetically controlled production of the C-5 sigma-complex (6.3, RO=SO_3^-, X=Cl) together with slower attack at the 1-position to give the C-1 sigma-complex (6.4, RO=SO_3^-, X=Cl) which loses chloride yielding the expected product (6.5, RO=SO_3^-). Attack of the nucleophile at the C-5 is twelve times as fast as attack at C-1. No phenolic/phenoxide products are reported.

Electron transfer reactions have been observed in reactions of 1-chloro- and 1-iodo-2,4-dinitrobenzenes [7] with potasssium *iso*-propoxide in *iso*-propanol/benzene mixtures. In the absence of potassium-complexing crown ethers normal nucleophilic aromatic substitution yields quantitatively 1-*iso*-propoxy-2,4-dinitrobenzene (6.5, R=^{i}Pr). In the presence of potassium-complexing crown ethers (*e.g.* 18-crown-6) the production of (6.5, R=^{i}Pr) is faster, but production of significant amounts of 2,4-dinitrophenol *via* an electron transfer process prevents quantitative conversion to the substitution product. The nature of this process has been discussed elsewhere (sections 1.3.1 and 6.4.4).

The nucleophilic attack of 1-halo-2,4-dinitrobenzenes by cyanide has yet to be systematically investigated. The following sections describe the authors work in this area. Since the author has previously presented evidence (chapter 3) of the significance of methanolysis in methanolic cyanide solutions a brief study of the reactions of the possible product, 2,4-dinitroanisole, with cyanide and methoxide ions in DMSO and methanol-DMSO mixtures is reported.

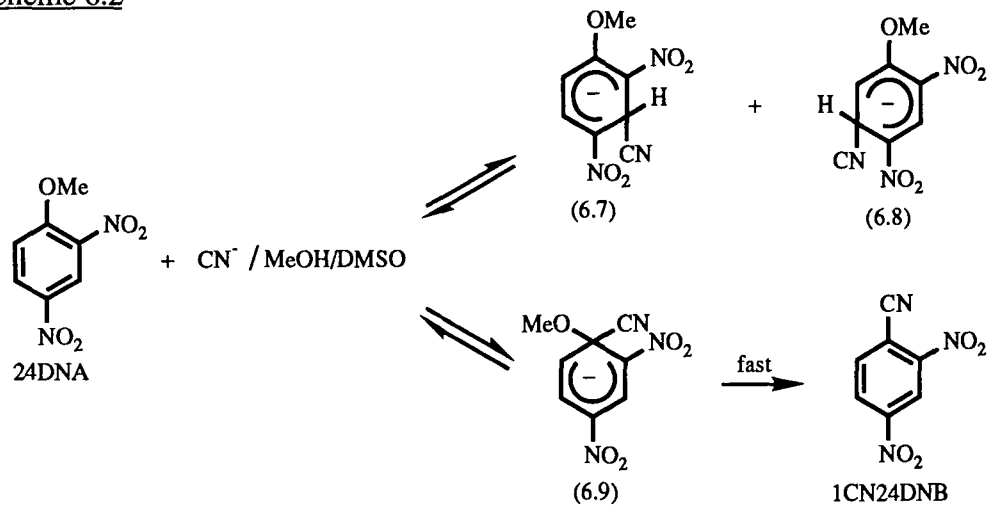
6.2 THE REACTIONS OF 2,4-DINITROANISOLE WITH METHOXIDE AND CYANIDE IN DMSO-RICH MEDIA.

2,4-Dinitroanisole (24DNA) in methanol/DMSO mixtures and DMSO shows an absorption at 295nm ($\varepsilon = 1x10^4 dm^3 mol^{-1} cm^{-1}$). In the presence of methoxide in media rich in DMSO the parent is converted to the adduct (6.6) [8] (λ_{max} 505nm, $\varepsilon = 2.2x10^4$ $dm^3 mol^{-1} cm^{-1}$) (figs.6.1 and 6.2). 24DNA ($1x10^{-4}$M) is stable (for at least 15min) in the presence of KCN (0.015M) in 25%/75% v/v MeOH/DMSO (fig.6.3); but a complicated reaction is observed in DMSO (fig.6.4). In the initial (after 20sec) spectrum absorbance bands at 595 and 300nm are seen. The spectrum 1min later shows these bands fading with two other bands at 490 and 550nm forming. The band at 490nm continues increasing over the next few minutes while the other three bands fade. An isosbestic point is observed at 331nm over the first few minutes. The spectrum after 90min shows three bands at 350, 400 and 425nm. An isosbestic point at 285nm is observed throughout the reaction.



(6.6)

Scheme 6.2



The data are interpreted in terms of the scheme 6.2. The band at 300nm is due to 24DNA, and this fades throughout the reaction due to the consumption of the substrate. The bands at 595 and 490nm are attributed to the sigma-complexes (6.7) and (6.8) respectively. Sharp absorption peaks at 550nm have also been observed in

DMSO-rich solutions of 1CN24DNB of 1F24DNB containing cyanide. Presumably the 1,1-complex (6.9) formed by cyanide attack at the 1-position would be unstable to methoxide loss, yielding the substitution product 1CN24DNB, and hence this band is attributed to a reaction product of the benzonitrile and cyanide. The nature of this species has been discussed above (secion 5.5).

Figure 6.1

UV/Vis spectra of 24DNA ($1x10^{-4}M$) + NaOMe (0.015M) /25%/75% v/v MeOH/DMSO.

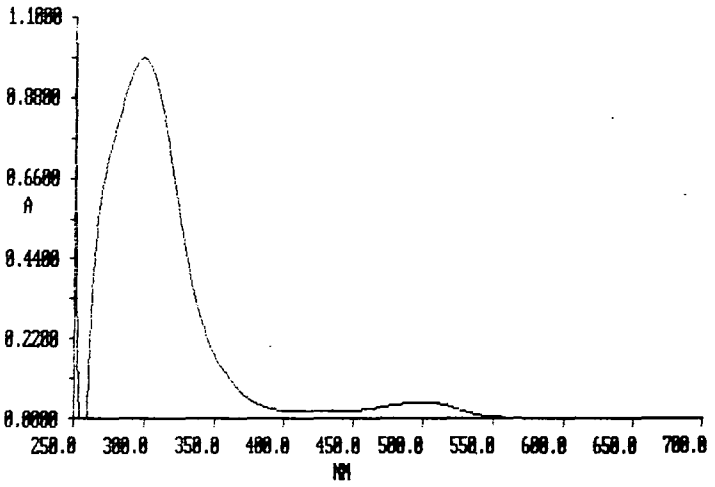


Figure 6.2

UV/Vis spectra of 24DNA ($1x10^{-4}M$) + NaOMe (0.015M) /DMSO.

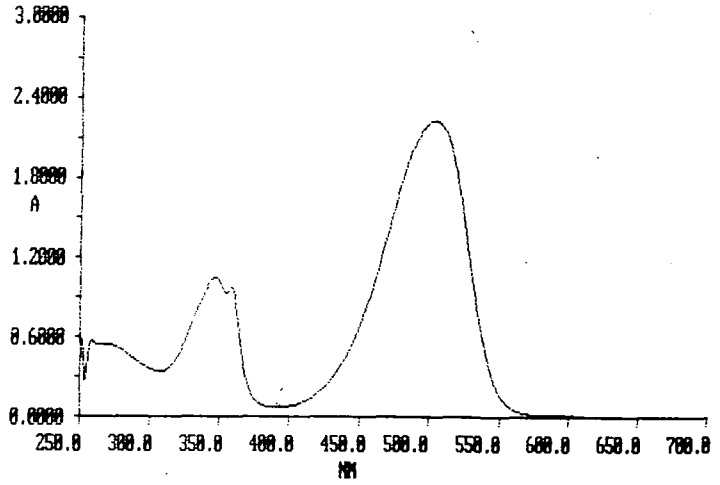


Figure 6.3

UV/Vis spectra of 24DNA ($1x10^{-4}M$) + KCN (0.015M) /25%/75% v/v MeOH/DMSO.

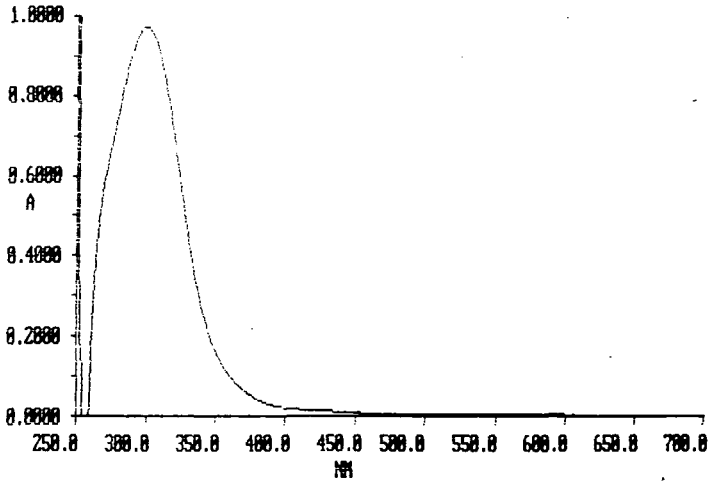
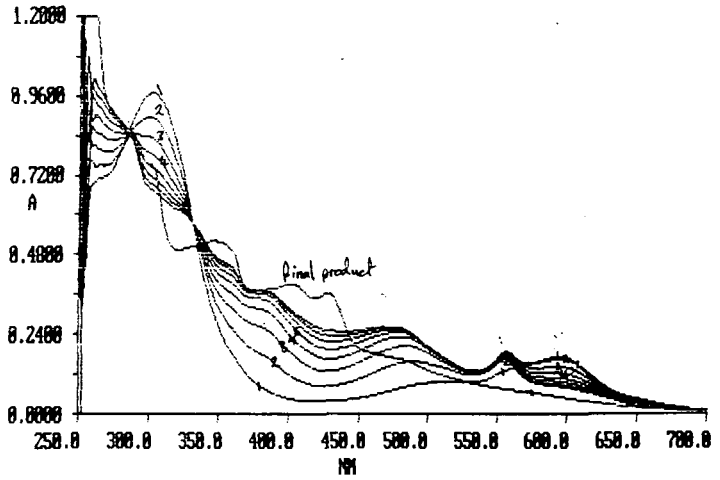


Figure 6.4

UV/Vis spectra of 24DNA ($1x10^{-4}M$) + KCN (0.015M) /DMSO (int = 1min).



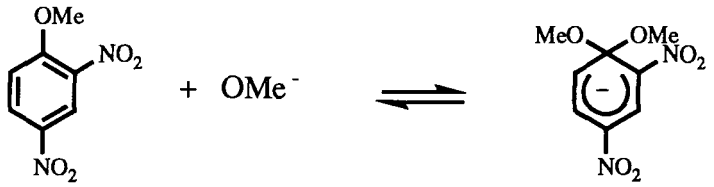
6.3 THE REACTIONS OF 1-FLUORO-2,4-DINITROBENZENE WITH METHOXIDE AND CYANIDE IN DMSO-RICH MEDIA.

6.3.1 UV/Vis Spectra.

There is evidence in cyanide solutions in methanolic media for competitive attack by cyanide and methoxide ions.

In DMSO, the addition to the parent of concentrated methanolic sodium methoxide (no cyanide present) results in the rapid and quantitative formation of the adduct (6.6) as shown in fig.6.5.

In 25%/75% v/v MeOH/DMSO the dominant reaction of 1F24DNB ($2x10^{-4}M$) with KCN (0.01M) and NaOMe (0.005M) produces 2,4-dinitroanisole. Fig.6.6 shows a strong absorption due to 24DNA with a weak band at 505nm due to the adduct (6.6). In this medium the equilibrium in eqn.6.1 will be to the left so that the adduct is relatively disfavoured. The equilibrium will shift to the right as the proportion of DMSO in the solvent is increased and as the methoxide concentration is increased.



(6.6)

Eqn.6.1

UV/Vis spectra were recorded for 1F24DNB ($1\text{-}4x10^{-4}M$) with KCN (0.002-0.02M) in 25%/75% v/v MeOH/DMSO. The most rapid reaction, observed by rapid-scanning spectrophotometry, showed the development of a band at 620nm, with a shoulder at 530nm (fig.6.7). This occurred within the first 5sec of the reaction. These bands faded and a narrow band at 550nm (shoulder 520nm) developed to reach a maximum intensity after 100sec and the final spectrum showed an absorption at 295nm (fig.6.7a, p170).

The data are interpreted in terms of scheme 6.3. The first bands observed after 5sec are attributed to the cyanide adducts (6.10) and (6.11). It is known [1,4-6,9] that 3-hydroxy adducts of 1-halo-2,4-dinitrobenzenes absorb in media rich in DMSO at 560-580nm, while the isomeric 5-hydroxy adducts absorb at 505-510nm. Carbon bonded adducts are expected [10] to absorb at longer wavelengths than oxygen bonded adducts so the bands at 620 and 530nm may be due to the adducts (6.10) and (6.11) respectively.

The strong sharp absorption at 550nm has been observed both in these solutions and also in solutions of 2,4-dinitrobenzonitrile containing cyanide. Hence this band is attributed to a reaction product of 2,4-dinitrobenzonitrile and cyanide. Presumably

Figure 6.5

UV/Vis spectra of 1F24DNB ($1x10^{-4}M$)

+ NaOMe (0.001M) /DMSO.

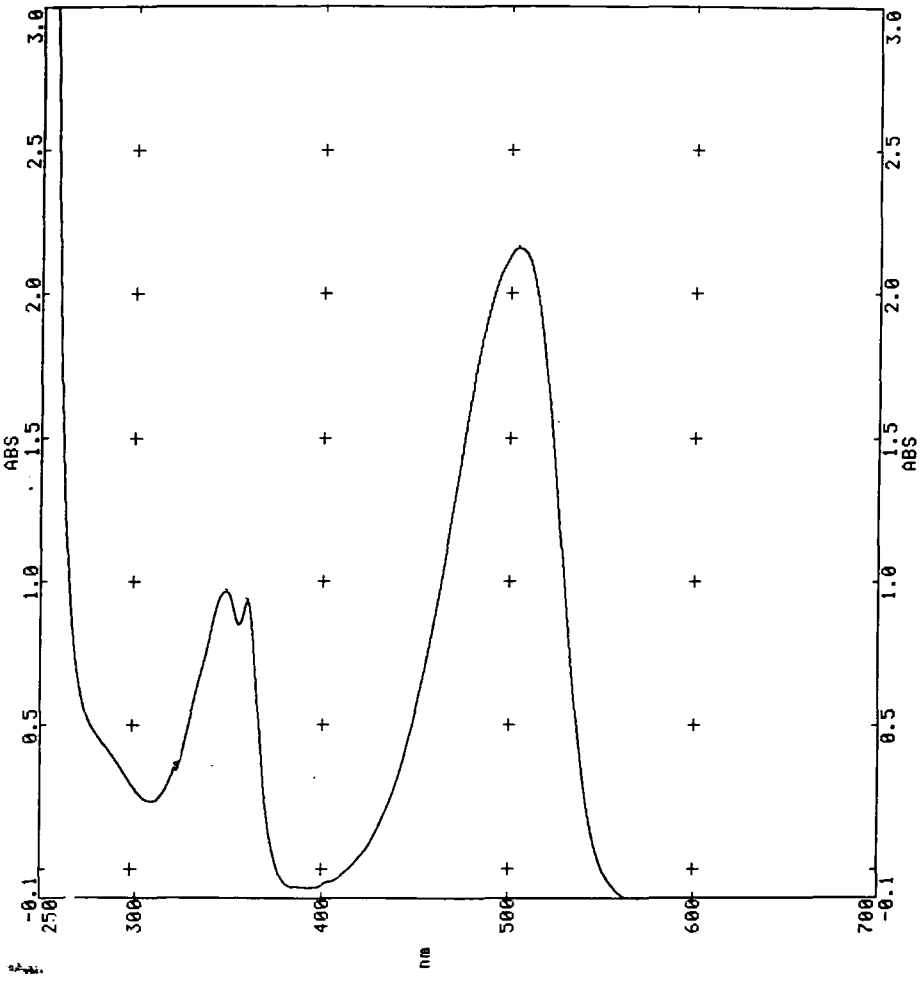


Figure 6.6

UV/Vis spectra of 1F24DNB ($2x10^{-4}M$) + KCN (0.01M)

+ NaOMe (0.001M) /25%/75% v/v MeOH/DMSO.

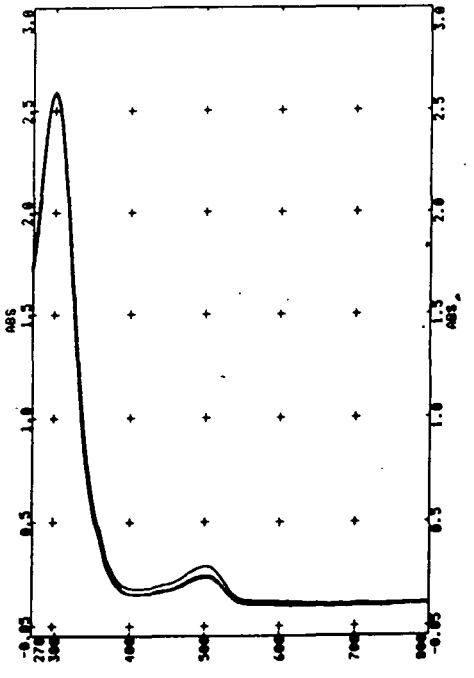


Figure 6.7

UV/Vis spectra of 1F24DNB ($4x10^{-4}$M) + KCN (0.002M)
/25%/75% v/v MeOH/DMSO (int = 1sec).

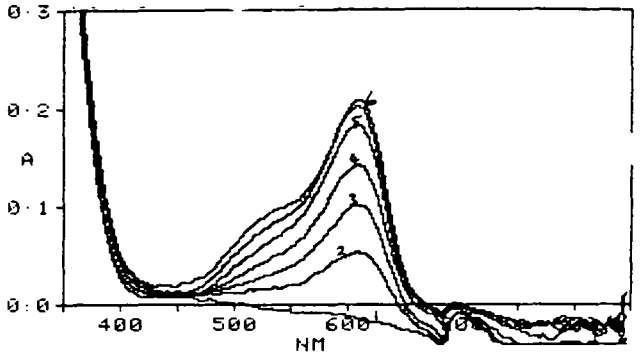
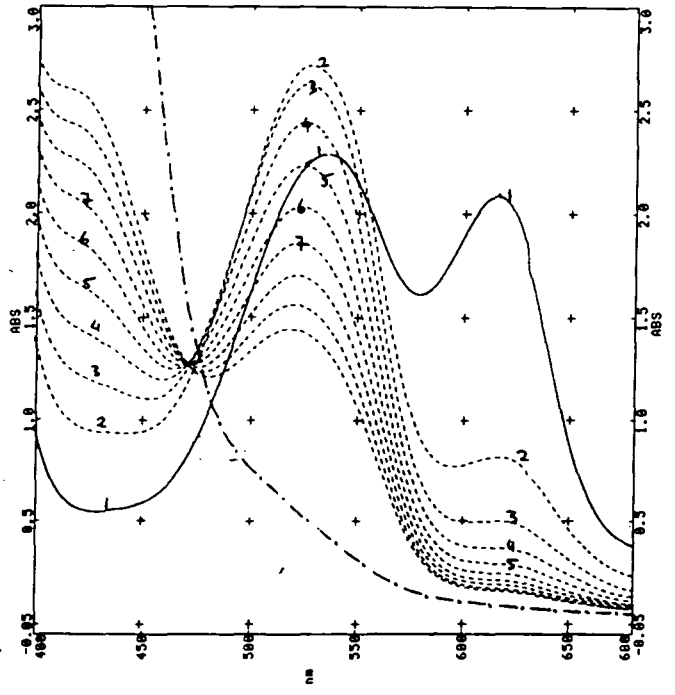


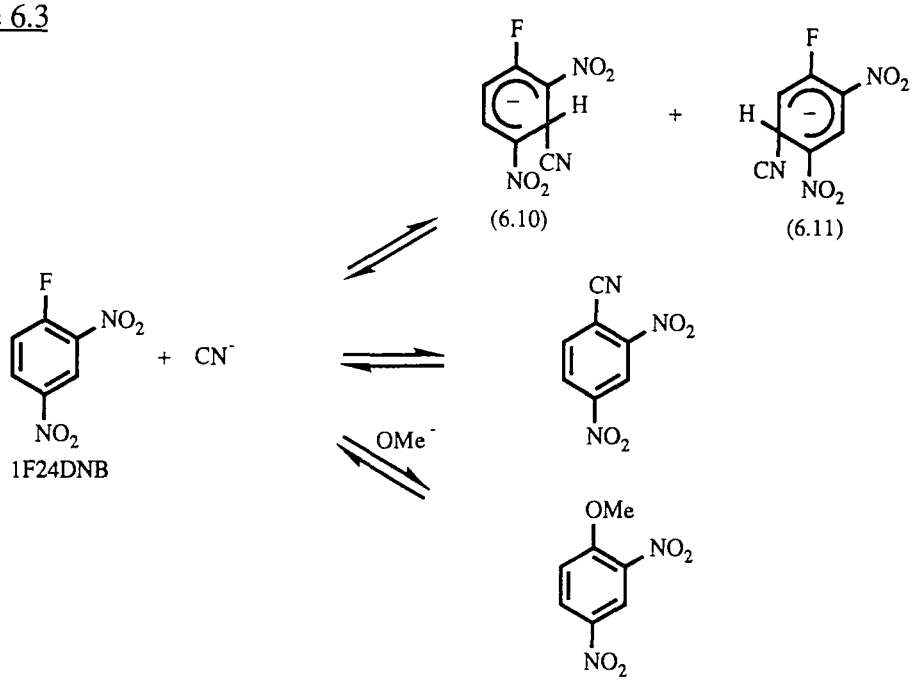
Figure 6.8

UV/Vis spectra of 1F24DNB (0.025M) + KCN (0.003M)
/25%/75% v/v MeOH/DMSO (int = 30sec).
(–·–·–·– = final product)



once the cyanide has displaced fluoride the reaction of the substitution product with excess cyanide is rapid.[5] The nature of this species has been discussed above (section 5.5). The shape of the band is much narrower than would be expected for a sigma-complex. E.S.R. signals have been observed that have a similar time dependance to this band in these reaction systems (section 5.3). The final spectrum shows absorption at 295nm indicating that some reaction with methoxide has occurred to produce 2,4-dinitroanisole.

Scheme 6.3



Spectra were also recorded (fig.6.8) in 25%/75% v/v MeOH/DMSO with 1F24DNB (0.025M) in excess of KCN (0.003M). The spectra provide evidence for the rapid formation of the 3-cyano adduct (6.9), with λ_{max} 620nm, followed by the formation of the 5-cyano adduct (6.11) with λ_{max} 530nm. These species gradually fade but the products were not investigated.

6.3.2 Proton NMR Spectra.

The proton NMR spectra of the reactions of 1-fluoro-2,4-dinitrobenzene with potassium cyanide in d_6-DMSO have been recorded.

The NMR of 1F24DNB shows three coupled signals due to the aromatic-ring protons at 8.84, 8.63 and 7.87ppm (table 6.1). In the presence of a deficiency of KCN (0.02M) in d_6-DMSO the NMR spectrum of 1F24DNB (0.03M) after 10min shows (fig.6.9) the signals of the parent, and those of 2,4-dinitrobenzonitrile (8.93, 8.74 and 8.50ppm) and 2,4-dinitrophenoxide (8.54, 7.73 and 6.26ppm) (table 6.1). After 1hr the

NMR shows a slight increase in the amount of phenoxide relative to benzonitrile. The formation of 1CN24DNB is presumably by nucleophilic aromatic substitution of the fluoride ion by cyanide *via* the C-1 sigma-complex. No sigma-complexes could be detected by NMR in this system. A water resonance at 3.3ppm shows that the d_6-DMSO used is wet, and this may cause the substitution of fluoride ion by hydroxide in the basic medium, forming 2,4-dinitrophenoxide. In this reaction with deficient cyanide there is no broadening of the NMR signals which could be caused by the presence of radical species.

Table 6.1

Proton NMR chemical shifts (δ) and coupling constants (J) of some 1,2,4-trisubstituted benzenes.

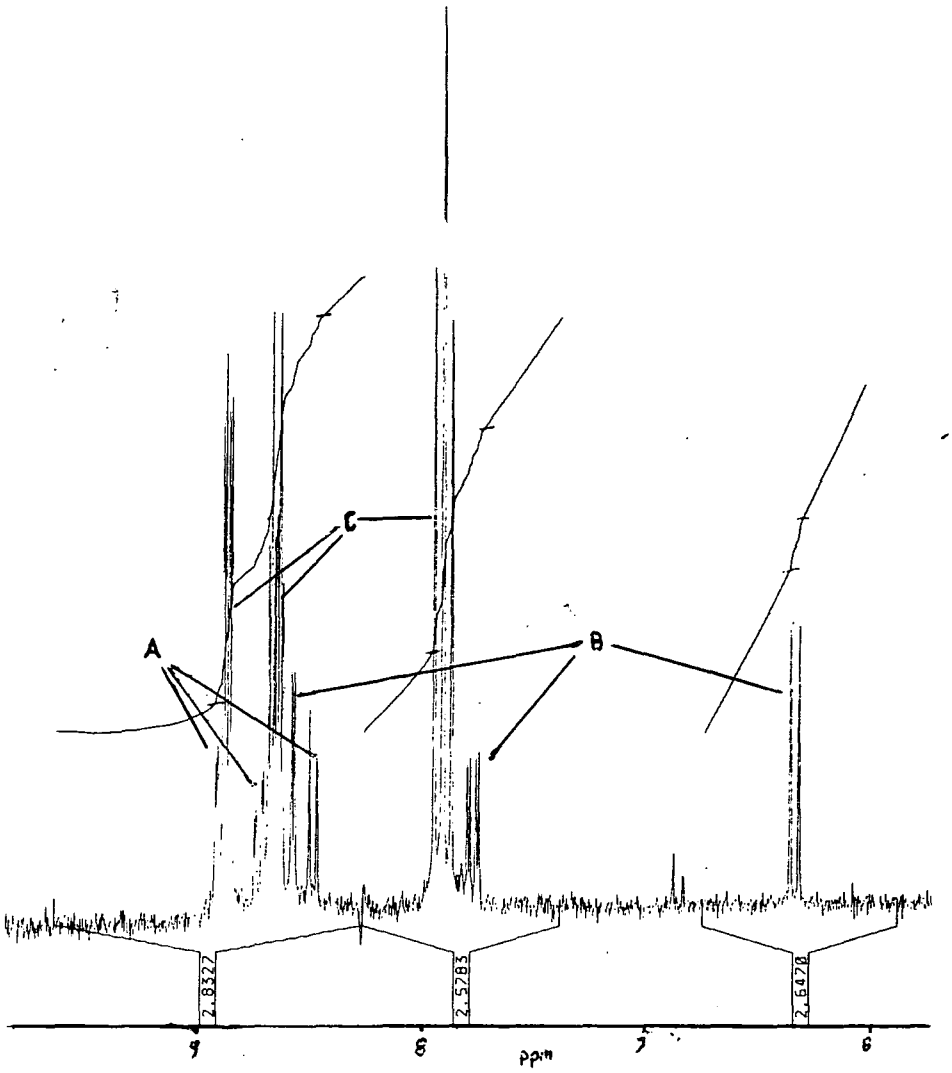
Substrate	Solvent	δ /ppm			J /Hz	
		H^3	H^5	H^6	J_{35}	J_{56}
1F24DNB[a]	d_6-DMSO	8.84	8.63	7.87	2.85	9.85
1Cl24DNB	CD_3OD/d_6-DMSO[b]	8.90	8.50	8.06	2.56	8.97
	d_6-DMSO	9.04	8.62	8.19	2.80	8.88
1I24DNB	CD_3OD/d_6-DMSO[b]	8.72	8.19	8.42	2.09	8.57
1CN24DNB	d_6-DMSO	8.93	8.74	8.50	2.21	8.62
	$CDCl_3$	9.04	8.47	7.35	2.93	9.26
2,4-Dinitro	CD_3OD/d_6-DMSO[b]	8.63	7.86	6.42	3.24	9.67
-phenoxide	d_6-DMSO	8.54	7.73	6.26	3.18	9.75
2,4-Dinitro	CD_3OD/d_6-DMSO[b]	8.73	8.38	7.38	2.78	9.12
-phenol	d_6-DMSO	8.59	8.33	7.23	2.86	9.11

a) $J_{6F} = 9.85$Hz, $J_{3(5)F} = 6.47$Hz.
b) 25%/75% v/v.

The NMR spectrum of the reaction mixture of 1F24DNB (0.025M) with a two times excess of NaCN (0.05M) in d_6-DMSO shows the simultaneous formation of the signals of 1CN24DNB and 2,4-dinitrophenoxide described above. No parent is observable after 90min (fig.6.10). Additional bands (singlets) are observed at 8.67, 8.17, 7.83, 6.88 and 6.83ppm. Some of these bands appear to be paired in terms of their intensities: 8.67 and 6.88ppm, 7.83 and 6.83ppm. Pairs of singlets are best interpreted in terms of 1,2,4,5-tetrasubstituted benzenes with the protons at the 3- and 6-positions giving single bands. Discussion of the nature of the species produced is given below (section 6.4.4). It is thought that the abnormally strong peak at 6.39ppm is not due to the reaction mixture since this peak remained at the same position and intensity throughout the reaction.

Figure 6.9

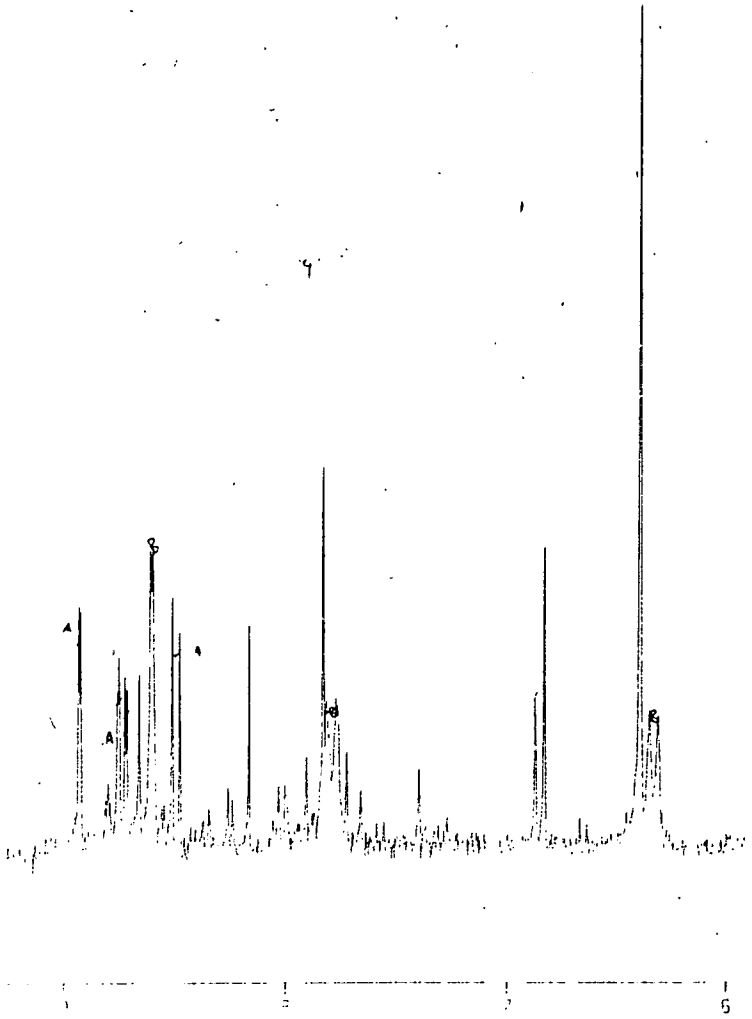
Proton NMR spectrum of 1F24DNB (0.03M) + KCN (0.02M) /d_6-DMSO (after 10min).



Bands labelled: A - 2,4-dinitrobenzonitrile, B - 2,4-dinitrophenoxide, C - 1-fluoro-2,4-dinitrobenzene.

Figure 6.10

Proton NMR spectrum of 1F24DNB (0.025M) + NaCN (0.05M) /d_6-DMSO (after 90min).



Bands labelled: A - 2,4-dinitrobenzonitrile, B - 2,4-dinitrophenoxide.

6.3.3 Preparative Experiments.

A simple preparative experiment has been performed using a slight excess of 1-fluoro-2,4-dinitrobenzene with potassium cyanide in dry DMSO.

1F24DNB (6.41g) was added to a solution of KCN (2.28g) in dry DMSO (350ml). The mixture was stirred for 5min and then swamped with ice-water and filtered. The filtrate was washed three times with chloroform. The organic layers were combined and the chloroform removed by evaporation leaving a brown liquid. This liquor was washed with water in an attempt to remove any parent or phenolic products (*e.g.* 2,4-dinitrophenol) present, leaving a small amount of thick brown liquid; the proton NMR spectra of which in d_6-DMSO is shown (fig.6.11). Together with the resonances of the parent described above the signals of relatively small amounts of 1CN24DNB and 2,4-dinitrophenol (table 6.1) can be observed.

In an attempt to improve the yield and quality of 1CN24DNB produced from 1F24DNB and cyanide equimolar quantities of reactants have been used, and the cyanide added more slowly.

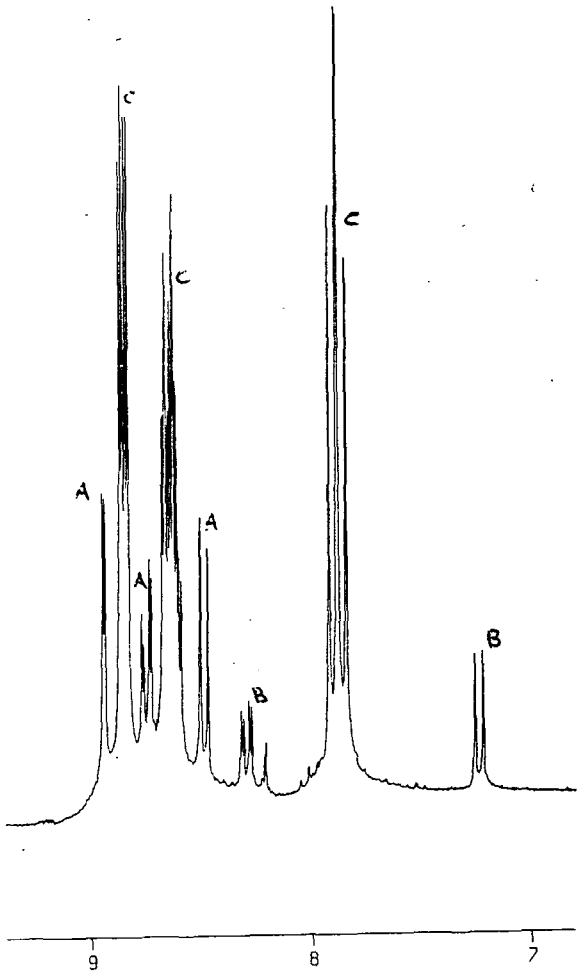
Small (0.4g) aliquots of solid KCN (16.3g, 0.25moles) were added over 3hr to a stirred solution of 1F24DNB (46.25g, 0.25moles) in dry DMSO (250ml). The reaction mixture was then stirred for a further hour and then swamped with ice-water (2l). The resulting mixture was filtered and washed three times with chloroform. The organic layers were collected and the solvent removed by evaporation. Water was added to the remaining viscous brown liquid and allowed to stand for 24hr. Filtration then yielded a solid that was washed throughly with warm water to yield a small amount of solid: m.pt, 94-98°C (lit:[11] 1CN24DNB 104-5°C); t.l.c. (CH_2Cl_2) gave two spots $r_f = 0.61$ and $r_f = 0.80$ (1CN24DNB = 0.63, 1F24DNB = 0.82); ^1H NMR in $CDCl_3$ (fig.6.12) shows the three coupled signals of 1CN24DNB at 9.09, 8.47 and 7.35ppm (table 6.1), a small triplet can be seen at 7.54ppm which is possibly due to unreacted parent.

6.3.4 Discussion.

It is reasonable to conclude that 2,4-dinitrobenzonitrile can be produced from the reaction of 1-fluoro-2,4-dinitrobenzene with cyanide. Presumably this reaction proceeds *via* normal nucleophilic aromatic substitution. Analysis of the unwashed viscous brown liquid showed that 2,4-dinitrophenol is a major by-product of this reaction; this is removed by washing with warm water. Production of 2,4-dinitrophenol may be due to residual water in the solvent despite distilling the DMSO, using dry glassware and performing the reaction in a vessel protected with a desiccator.

Figure 6.11

Proton NMR spectrum of the product of the reaction between excess 1F24DNB and KCN /d_6-DMSO.



Bands labelled: A - 2,4-dinitrobenzonitrile, B - 2,4-dinitrophenoxide, C - 1-fluoro-2,4-dinitrobenzene.

Figure 6.12

Proton NMR spectrum of the product of the reaction between equimolar quantities of 1F24DNB and KCN /$CDCl_3$.

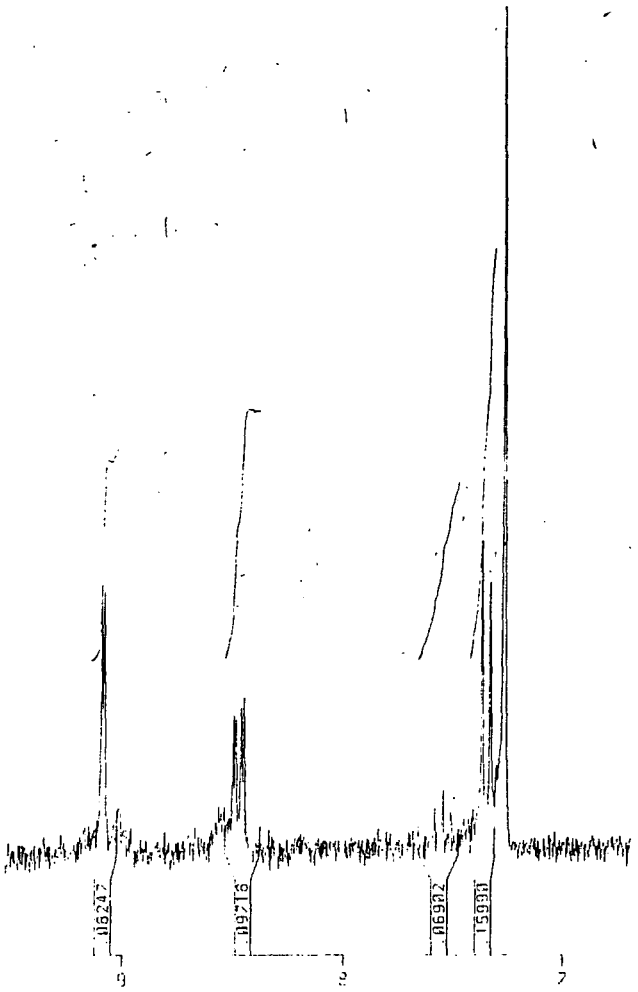
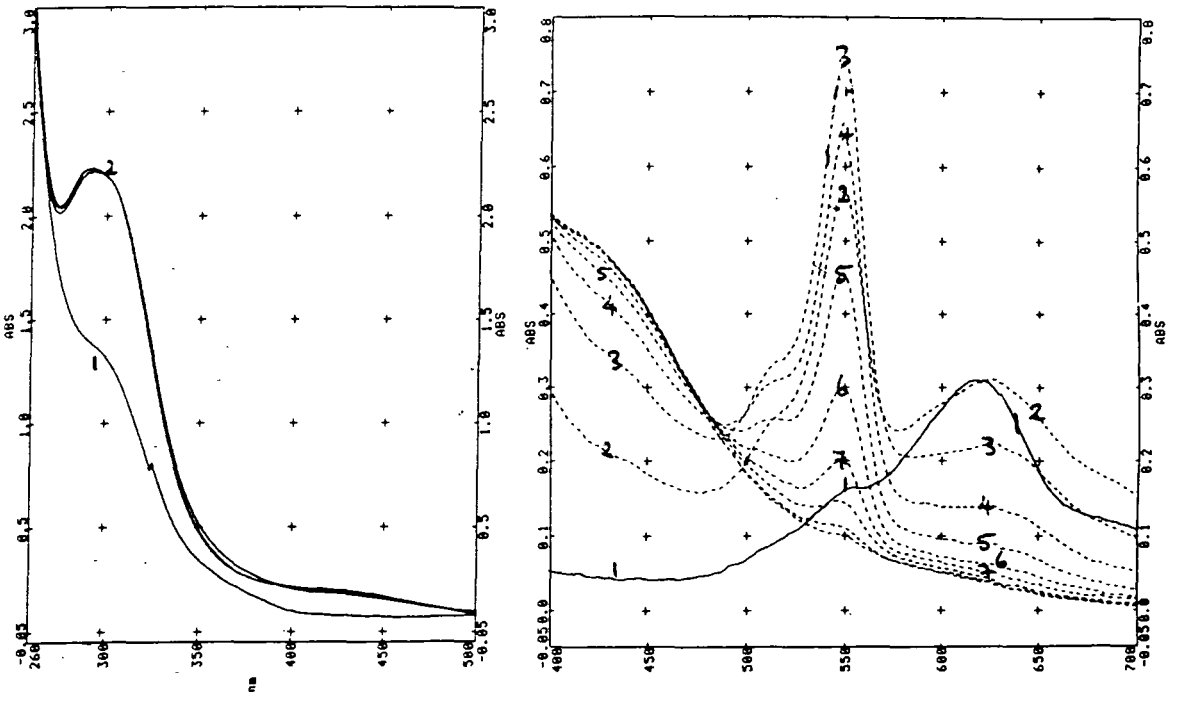


Figure 6.7a

1F24DNB (2x10-4M) + KCN (0.02M) / 25%/75% v/v MeOH/DMSO,

a) 150sec interval, b) 45sec interval.



a b

6.4 THE REACTIONS OF 1-CHLORO, 1-BROMO- AND 1-IODO-2,4-DINITRO-BENZENE WITH CYANIDE IN METHANOL-DMSO MIXTURES.

These reactions have been investigated using uv/vis spectrophotometry and also proton NMR spectroscopy. The concentration ranges of the substrates were necessarily very different in the two sets of experiments. Typically for the uv/vis work the parent concentration was *ca.* $1x10^{-4}$M and cyanide was in at least 100-fold excess. In the NMR experiments the parent concentrations were *ca.* 0.02M with cyanide in the range 0.02-0.08M.

The results are not clear cut and several attempts to isolate products of reaction did not yield conclusive results. Hence it is necessary to rely on spectroscopic measurements of the species present *in situ* in order to attempt to analyse the course of these reactions. It will be shown that there is sound evidence for formation of 2,4-dinitrophenol and of another phenol, probably 2,4-dinitro-5-cyanophenol, as major products of the reactions. The results will be described and then an analysis attempted.

6.4.1 UV/Vis Spectra.

The uv/vis spectra of the products of reaction between 1-chloro-, 1-bromo- and 1-iodo-2,4-dinitrobenzenes (1Cl24DNB, 1Br24DNB and 1I24DNB respectively) and large excesses of KCN in methanol-DMSO mixtures have been recorded. When these substrates are added to an excess of KCN in 50%/50% v/v MeOH/DMSO they produce a species with a uv/vis spectrum similar to that of 2,4-dinitrophenoxide (figs. 6.13 and 6.14). No transient colours are observed in this medium.

In higher concentrations of DMSO (25%/75% v/v MeOH/DMSO) a transient blue colour (λ_{max} 640-660nm) is initially observed when 1-chloro-, 1-bromo- and 1-iodo-2,4-dinitrobenzenes are mixed with an excess of KCN (figs.6.15-17). This colour fades within 2min. No absorption bands λ_{max} 550nm are observed (*c.f.* the reactions of 13DNB, 1F24DNB and 1CN24DNB). Throughout the reaction there is slow formation of a species with a spectrum similar to 2,4-dinitrophenol.

Addition of an excess of NaOMe (0.005M) to a solution of 1Cl24DNB ($1x10^{-4}$M) with an excess of KCN (0.013M) in 50%/50% v/v MeOH/DMSO causes steady build-up of a species λ_{max} 295nm (fig.6.18); presumably 2,4-dinitroanisole (fig.6.14). No transient species are observed. Buffering a solution of 1Cl24DNB and excess KCN in 50%/50% v/v MeOH/DMSO with HCl prevents any reaction. Degassing these systems appears to have no effect on the species produced, or their rate of formation.

Figure 6.13

UV/Vis spectra of the final products of i) 1F24DNB ($2x10^{-4}M$) + KCN (0.02M), ii) 1Cl24DNB ($1x10^{-4}M$) + KCN (0.01M), iii) 1Br24DNB ($1x10^{-4}M$) + KCN (0.013M) and iv) 1I24DNB ($2x10^{-4}M$) + KCN (0.025M) /50%/50% v/v MeOH/DMSO.

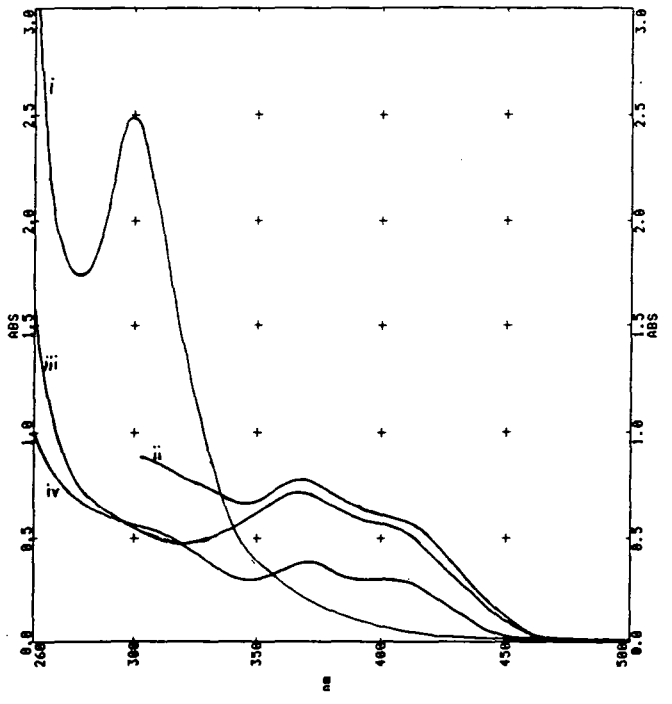


Figure 6.14

UV/Vis spectra of i) 24DNA ($2x10^{-4}M$) /50%/50% v/v MeOH/DMSO and ii) 2,4-dinitrophenol ($1x10^{-4}M$) /MeOH.

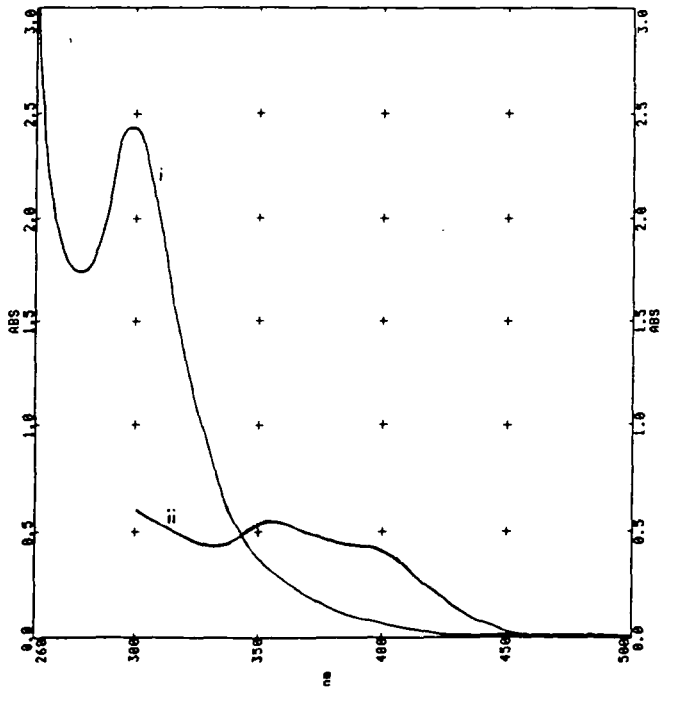


Figure 6.15

UV/Vis spectra of 1Cl24DNB ($2x10^{-4}$M) + KCN (0.02M)
/25%/75% v/v MeOH/DMSO (int = 2min).

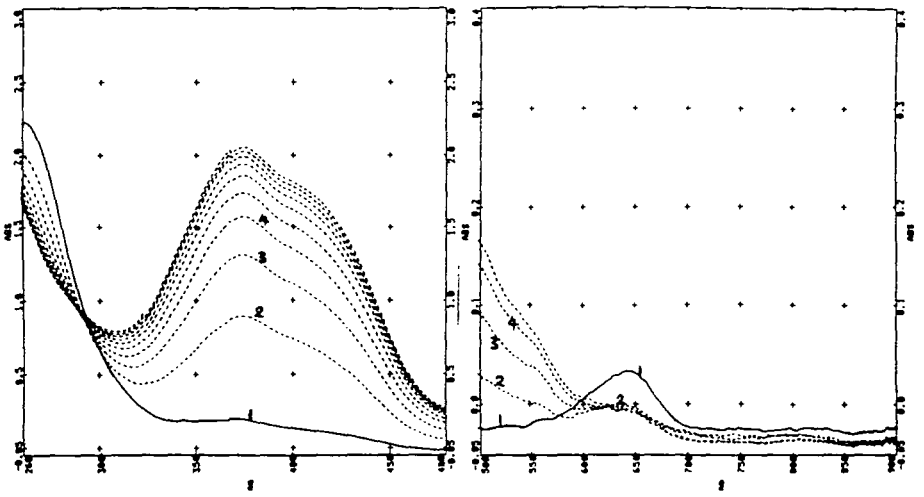


Figure 6.16

UV/Vis spectra of 1Br24DNB ($2x10^{-4}$M) + KCN (0.02M)
/25%/75% v/v MeOH/DMSO (int = 3min).

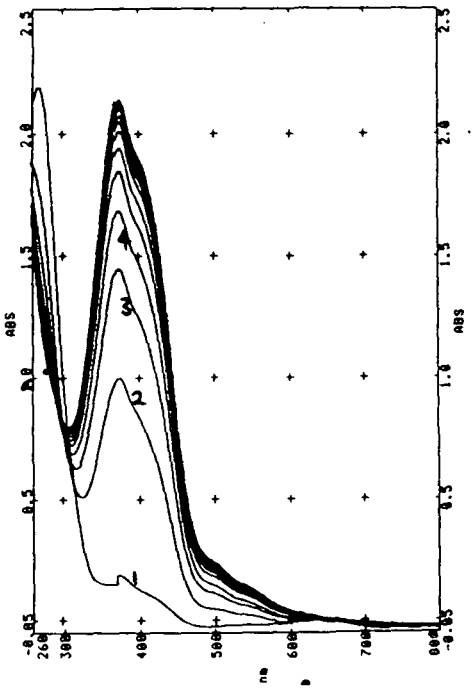


Figure 6.17

UV/Vis spectra of 1I24DNB ($2x10^{-4}$M) + KCN (0.02M) /25%/75% v/v MeOH/DMSO (int = 3min).

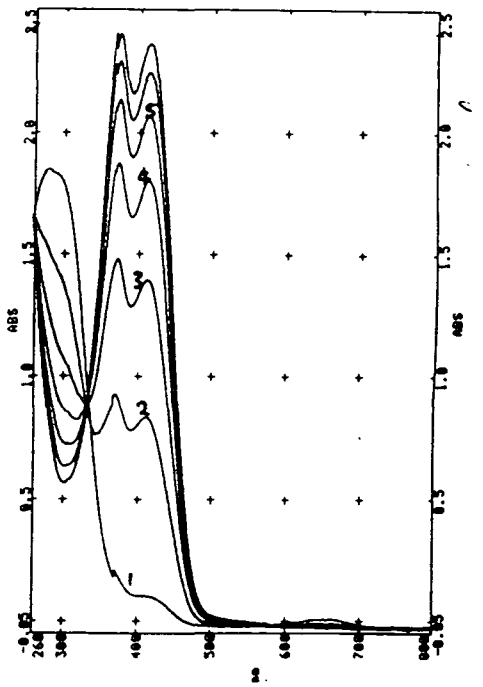
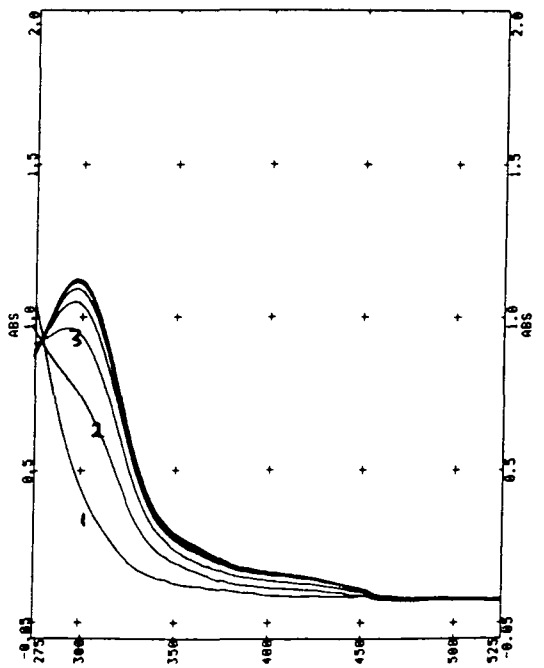


Figure 6.18

UV/Vis spectra of 1Cl24DNB ($1x10^{-4}$M) + KCN (0.013M) + NaOMe (0.005M) /25%/75% v/v MeOH/DMSO (int = 2min).



It is known [7] that alkoxide/alcohol systems can produce 2,4-dinitrophenol from 1Cl24DNB *via* an electron transfer process. In the reactions of 1-halo-2,4-dinitrobenzenes with excess KCN in methanol/DMSO mixtures, the uv/vis spectra of the products is compatible with the formation of 2,4-dinitrophenol as a major product. It is shown in fig.6.19 that 2,4-dinitrophenol is simply ionised to 2,4-dinitrophenoxide (λ_{max} 365nm, shoulder 410nm) by excess KCN in 25%/75% v/v MeOH/DMSO.

The rate coefficients for colour formation at 350nm in the reaction of 1Cl24DNB with excess cyanide in 25%/75% v/v MeOH/DMSO were measured. Individual runs showed good first-order kinetics, and values of rate coefficients obtained with the parent concentration of $1x10^{-4}$M and with varying concentrations of cyanide are shown in table 6.2. The plot of k_{obs} versus the cyanide concentration (fig.6.20) is an excellent straight line with gradient $0.38dm^3mol^{-1}s^{-1}$. The intercept is indistinguishable from the origin which might mean that the reaction being followed is irreversible or that the reverse reaction has a very low rate coefficient.

Table 6.2

Observed rate coefficients for the increase in absorption at 350nm in the reaction between 1Cl24DNB and varying concentration of KCN (25%/75% v/v MeOH/DMSO).

[KCN] /M	0.002	0.004	0.008	0.012	0.016	0.02
10^3 k_{obs} /s^{-1}	0.7	1.4	2.91	4.61	6.34	7.66

[1Cl24DNB] = $1x10^{-4}$M

Measurements were also made (table 6.3 and fig.6.21) of the rate coefficient at constant cyanide concentration (0.02M) but with varying substrate concentrations. The results show that as the substrate concentration increases the observed rate coefficient tends to decrease. The absorbance values at 350nm at completion of the reactions increase with increasing substrate concentration (fig.6.21).

1-Iodo-2,4-dinitrobenzene (1I24DNB) shows a band λ_{max} 280nm ($\varepsilon = 9x10^3$ $dm^3mol^{-1}cm^{-1}$) in 25%/75% v/v MeOH/DMSO. In the presence of a large excess of KCN (0.02M) 1I24DNB ($1x10^{-4}$M) in 25%/75% v/v MeOH/DMSO produces a species with two bands at 420 and 375nm (*c.f.* fig.6.17). The isosbestic point at 340nm indicates that the reaction is clean.

The observed rate constants under pseudo-first order conditions for the increase in absorbance at 375nm have been measured with varying concentrations of KCN. The results are shown in table 6.4. The plot of k_{obs} versus cyanide concentration (fig.6.22.)

Figure 6.19

UV/Vis spectra of 2,4-dinitrophenol ($1x10^{-4}$M) i) in the absence and, ii) in the presence of KCN (0.01M) /25%/75% v/v MeOH/DMSO.

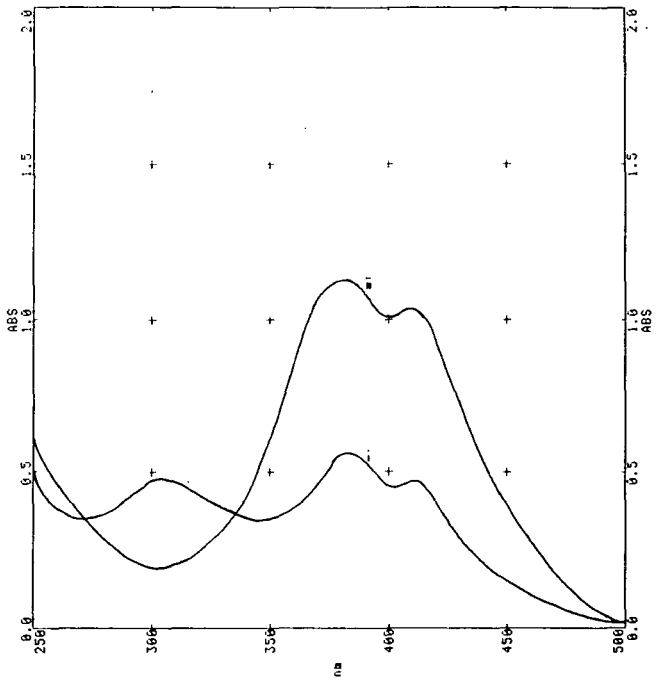


Figure 6.20

Graph of k_{obs} *vs.* [KCN] for the reaction of 1Cl24DNB ($1x10^{-4}$M) with excess KCN /25%/75% v/v MeOH/DMSO.

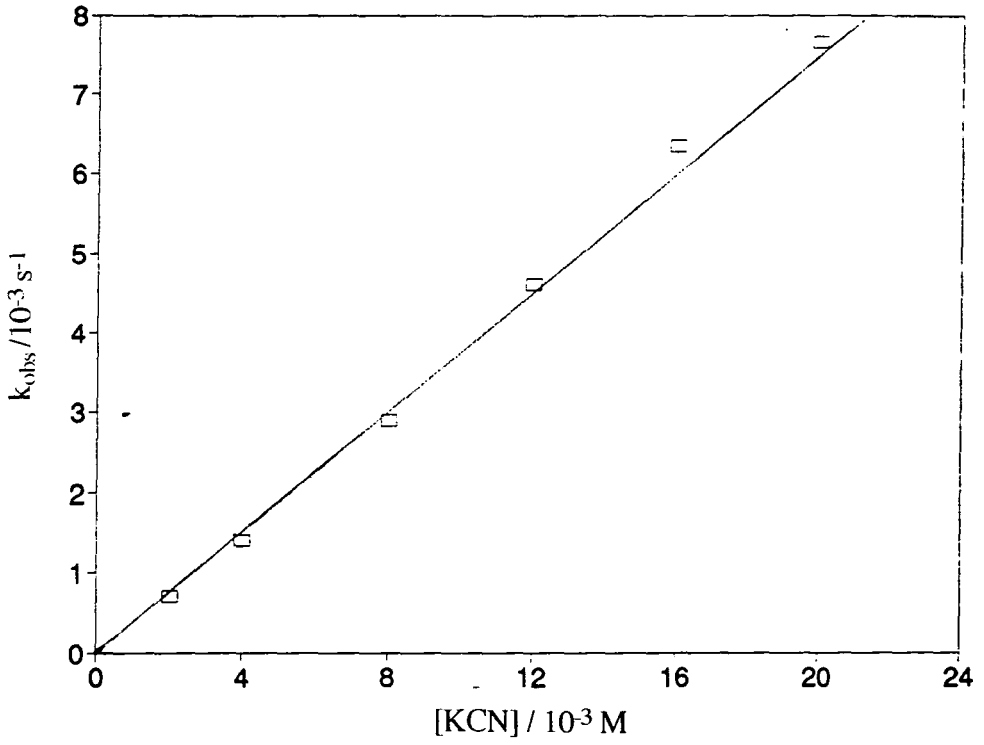


Figure 6.21

Graph of k_{obs} (■), and absorbance values (+) at 350nm at the completion of reaction (A_{max}), *vs.* [1Cl24DNB] for the reaction of excess KCN (0.02M) with 1Cl24DNB /25%/75% v/v MeOH/DMSO.

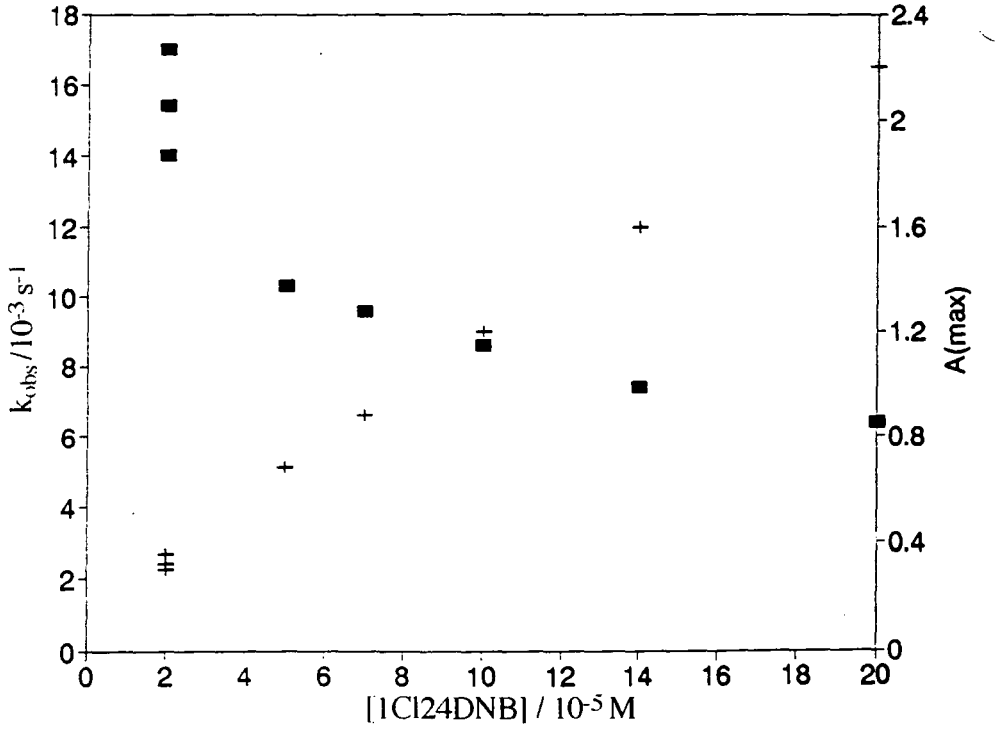
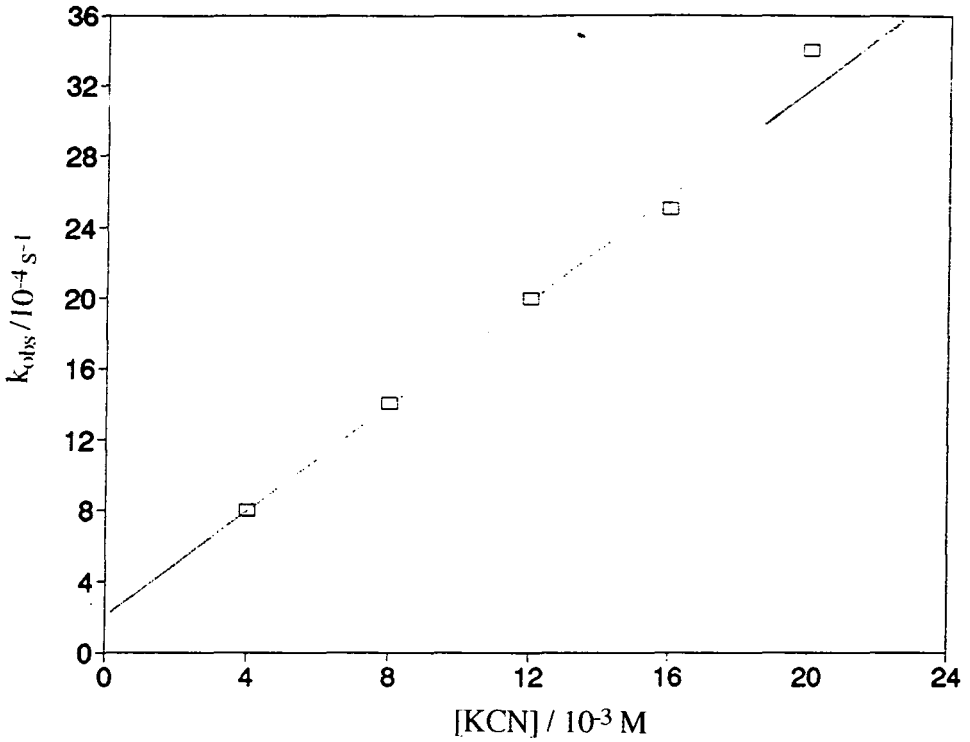


Figure 6.22

Graph of k_{obs} *vs.* [KCN] for the reaction of 1I24DNB ($1x10^{-4}$M) with excess KCN /25%/75% v/v MeOH/DMSO.



has a slope of $0.15 dm^3 mol^{-1} s^{-1}$ and there appears to be a small positive intercept, although a line through the origin would be within experimental error.

Table 6.3

Observed rate coefficients for the increase in absorption (k_{obs}) and absorbance at the end of the reaction (A_{max}) at 350nm in the reaction between KCN and varying concentration of 1Cl24DNB (25%/75% v/v MeOH/DMSO).

10^5 [1Cl24DNB] /M	10^3 k_{obs} /s^{-1}	A_{max} [a]
2.0	14.0	0.31
2.0	17.0	0.32
2.0	15.4	0.36
5.0	10.3	0.67
7.0	9.65	0.88
10.0	8.56	1.2
14.0	7.54	1.6
20.0	6.39	2.2

a) 1cm path length.

Table 6.4

Observed rate coefficients for the increase in absorption (k_{obs}) and absorbance at the end of the reaction (A_{max})at 375nm and in the reaction between 1I24DNB and varying concentration of KCN (25%/75% v/v MeOH/DMSO).

[KCN] /M	0.004	0.008	0.012	0.016	0.020
10^3 k_{obs} [a] /s^{-1}	0.81	1.4	2.0	2.5	3.4
A_{max} [b]	1.53	1.43	1.43	1.41	1.58

a) [1I24DNB] = 1×10^{-4}M
b) 1cm path length.

6.4.2 Proton NMR Spectra.

The proton NMR spectra of some reactions between 1Cl24DNB and 1I24DNB with potassium and sodium cyanides in d_6-DMSO and CD_3OD/d_6-DMSO mixtures have been recorded.

The spectrum of 1Cl24DNB in 25%/75% v/v CD_3OD/d_6-DMSO shows three coupled signals at 8.90, 8.50 and 8.06ppm (table 6.1). After 10min in the presence of a four-fold excess of NaCN (0.08M) in this medium, the signals due to three species can be observed (fig.6.23a). The signals of the parent are broad. Sharp coupled signals of 2,4-dinitrophenoxide can be seen at 8.63, 7.86 and 6.42ppm. Two sharp uncoupled signals are evident at 8.71 and 6.88ppm. After 50min no signals of the parent can be observed (fig 6.23b). The two singlets at 8.71 and 6.88ppm have grown in intensity relative to those of 2,4-dinitrophenoxide. Other uncoupled signals can be observed at 8.50, 7.97, 7.77 and 7.69ppm.

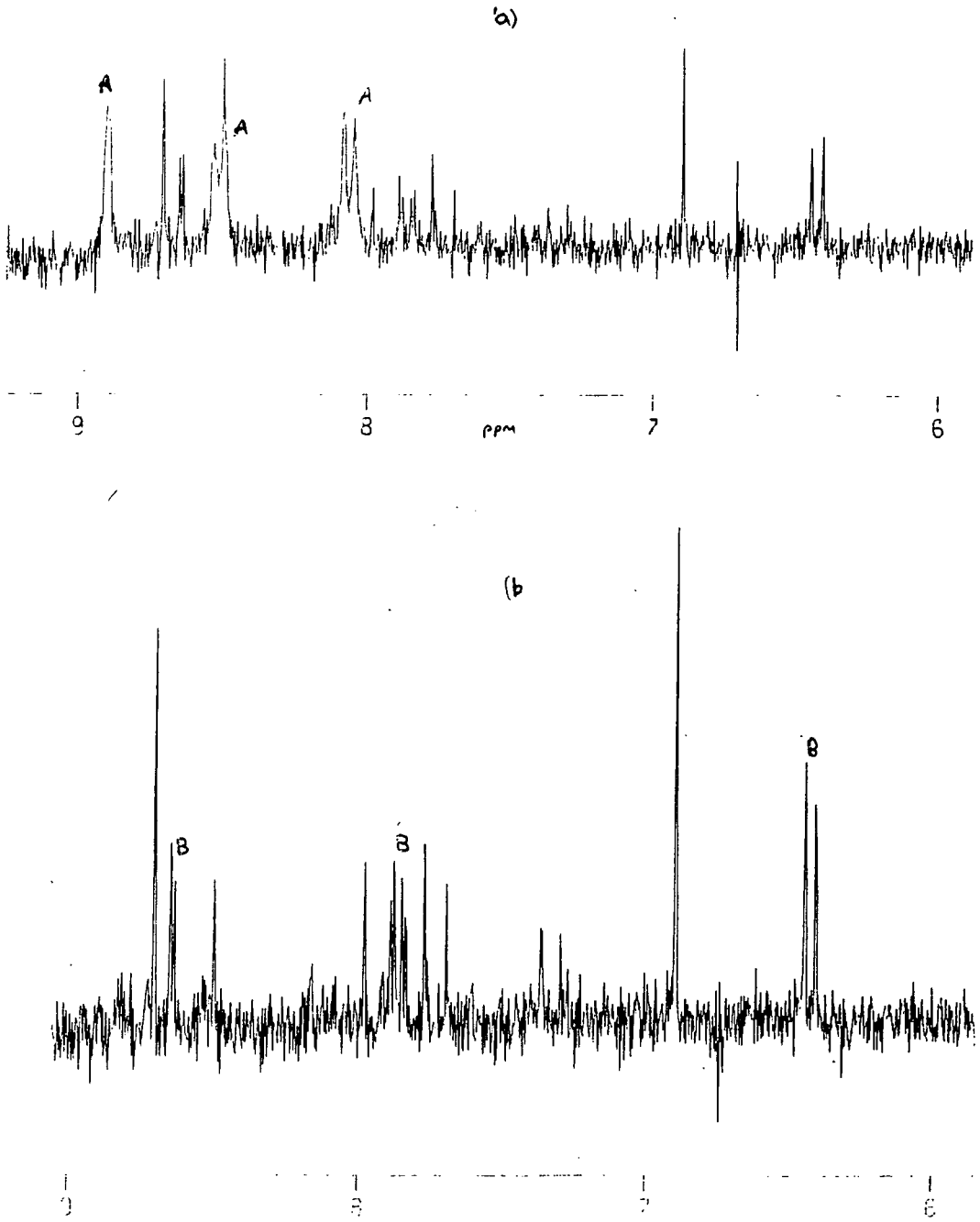
The system was also examined using a two-fold excess of cyanide. The spectrum of 1Cl24DNB (0.02M) with KCN (0.04M) in 25%/75% v/v CD_3OD/d_6-DMSO shows broad signals of the parent and sharp singlets at 8.71 and 6.88ppm after 5min. After 3hr the spectra of the same reaction mixture shows (fig.6.24) the sharp signals of 1Cl24DNB and 2,4-dinitrophenoxide (table 6.1); the most intense signals remain the two singlets at 8.71 and 6.88ppm, the nature of the species giving rise to these signals is discussed below (section 6.4.4).

When an equimolar amount of 1Cl24DNB (0.08M) was added to NaCN (0.08M) in 25%/75% v/v CD_3OD/d_6-DMSO the proton NMR spectrum recorded after 10min showed signals at 8.71 and 6.88ppm. Coupled signals due to 2,4-dinitrophenoxide were just apparent. The spectrum recorded after the reaction mixture had been left overnight showed signals due to the parent and 2,4-dinitrophenoxide, together with the two singlets at 8.71 and 6.88ppm (fig.6.25a). Acid (HCl 0.1M) was added to this mixture and the specrum recorded (fig.6.25b). The signals of 1Cl24DNB remain unchanged at 8.90, 8.50 and 8.06ppm. The coupled signals of 2,4-dinitrophenoxide are shifted downfield to 8.73, 8.38 and 7.38ppm, as expected for 2,4-dinitrophenol (table 6.1). The two singlets formerly at 8.71 and 6.88ppm are shifted downfield to 8.86 and 7.79ppm.

2,4-Dinitrophenoxide can be written as an equilibrium between four canonical forms (6.12). Consequently in the NMR spectrum the signal of the ring hydrogen in the 6-position is considerably upfield of the other ring hydrogen signals. When a basic solution of 2,4-dinitrophenoxide is acidified the phenoxide is protonated, forming 2,4-dinitrophenol. Hence the H-6 signal moves a relatively long way downfield. The other ring hydrogen signals move slightly downfield due to the inductive effect of protonation. That this phenomenon is observed in the reaction mixture above confirms the presence of 2,4-dinitrophenoxide, and also indicates that the species giving rise to the two singlets may also be an aromatic phenoxide in which one proton is *ortho* or *para* to the hydroxy group, and the other proton is *meta*. That these two signals are uncoupled (or coupled so poorly that splitting is not observed *i.e.* $J < 1Hz$) indicates that the species may contain a 1,2,4,5-tetrasubstituted benzene ring.

Figure 6.23

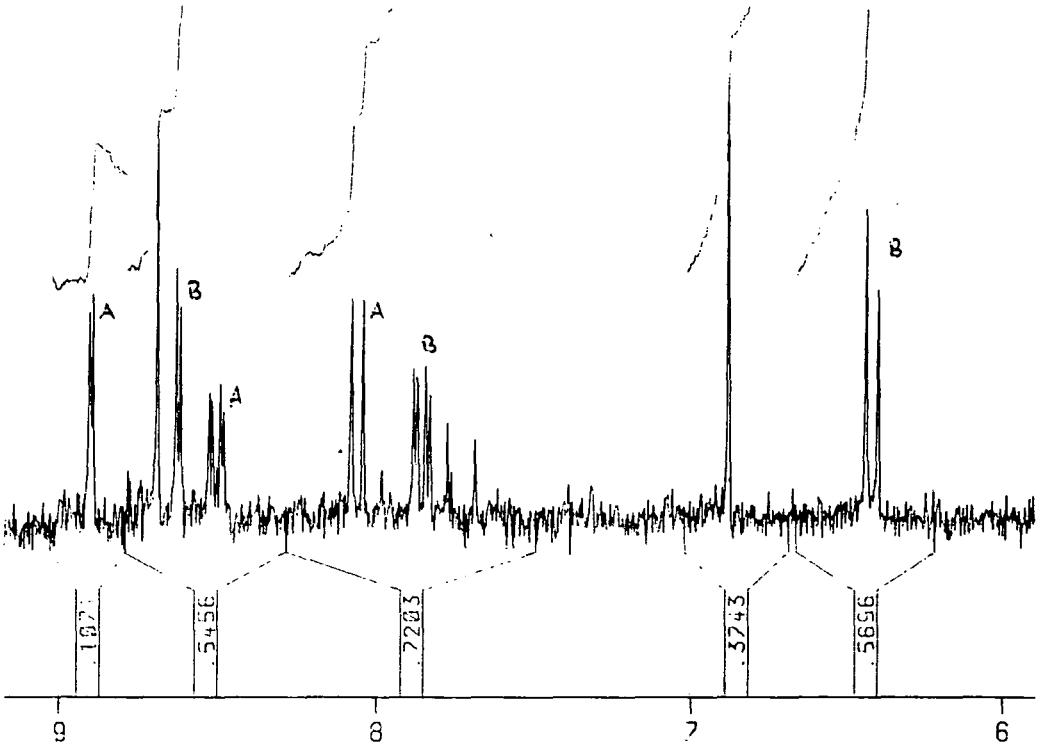
Proton NMR spectrum of 1Cl24DNB (0.02M) + NaCN (0.08M) /25%/75% v/v CD_3OD/d_6-DMSO, after a) 10min and b) 50min.



Bands labelled: A - 1-chloro-2,4-dinitrobenzene, B - 2,4-dinitrophenoxide.

Figure 6.24

Proton NMR spectrum of 1Cl24DNB (0.02M) + NaCN (0.04M) /25%/75% v/v CD_3OD/d_6-DMSO after 3hr.



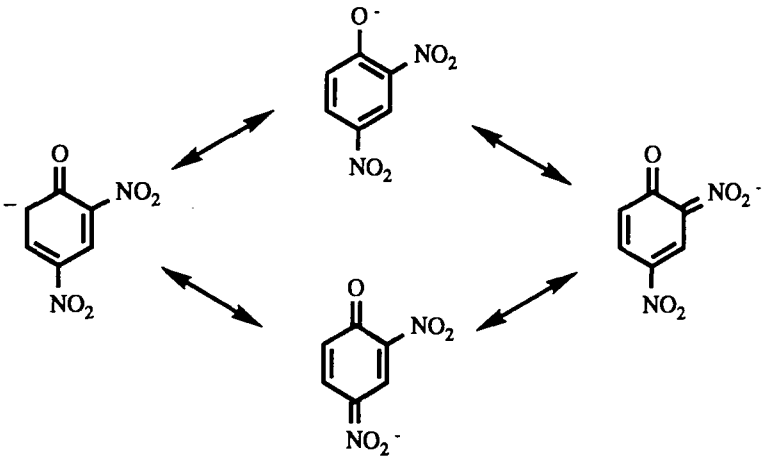
Bands labelled: A - 1-chloro-2,4-dinitrobenzene. B - 2,4-dinitrophenoxide.

Figure 6.25

Proton NMR spectra of 1Cl24DNB (0.08M) + NaCN (0.08M)
/25%/75% v/v CD_3OD/d_6-DMSO after 24hr
a) in the absence and, b) in the presence of acid.

Bands labelled: A - 1-chloro-2,4-dinitrobenzene, B - 2,4-dinitrophenoxide,
C - 2,4-dinitrophenol.

(6.12) Possible Canonical Forms of 2,4-Dinitrophenoxide.



In an attempt to determine the nature of this unknown species the reaction of 1Cl24DNB (0.02M) with a two-fold excess of NaCN (0.04M) in 25%/75% v/v CD_3OD/d_6-DMSO was follwed by NMR and then the reaction mixture was studied by mass spectroscopy.

The proton NMR spectrum of the reaction mixture after 45min showed two singlets at 8.71 and 6.88ppm (fig.6.26a). Also present were the signals of 2,4-dinitrophenoxide and singlets at 7.73, 7.66, 7.33 and 7.26ppm.

The electron ionisation (E.I.) mass spectrum of 1Cl24DNB shows the molecular ion peaks at 204 and 202mu of intensity 1:3 (fig.6.27). The chemical ionisation (C.I.) mass spectrum of 1Cl24DNB shows the peaks of 186 and 172mu, due respectively to the loss of oxygen and nitric oxide (NO) from the ^{35}Cl molecular ion (202) (fig.6.29). Peaks at 188 and 174mu of one-third intensity compared with 186 and 172mu are due to loss of the above fragments from the ^{37}Cl molecular ion (204). The E.I. spectrum of 2,4-dinitrophenol shows the M+1 peak at 185mu (fig.6.28). It is common for phenols to self-protonate in these systems. The C.I. spectrum shows a peak at 172mu. The carrier gas used was ammonia. It is common in this system for nitroaromatics to be ionised by addition of the ammonium ion (18mu) and then to lose nitric oxide (30mu), giving overall a M-12 peak (M=184mu).

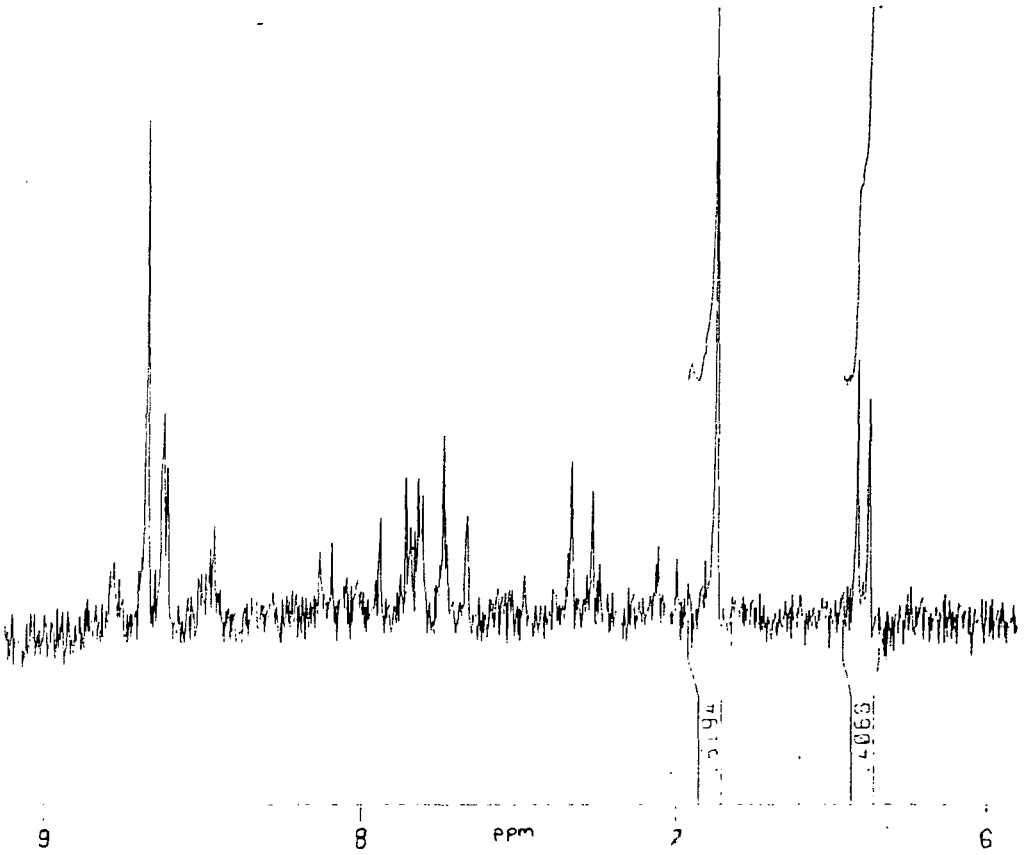
The E.I. mass spectrum of the acidified reaction mixture of 1Cl24DNB (0.02M) and NaCN (0.04M) in 25%/75% v/v CD_3OD/d_6-DMSO (as above) shows (fig.6.26b) peaks at 209 and 184mu. The peak at 149mu is an effect of the mass spectrophotometer. The peak at 84mu is due to d_6-DMSO. The peak at 184mu is the molecular ion of 2,4-dinitrophenol. It is therefore likely that the peak at 209mu is the molecular ion of the 2,4,5-trisubstitutedphenol which may cause the two singlets in the proton NMR spectra.

A species that satisfies the NMR an MS evidence is 2,4-dinitro-5-cyanophenol (6.13), and it is possible that the phenoxide of this species is a product of the reaction of 1Cl24DNB with cyanide in 25%/75% v/v MeOH/DMSO.

Figure 6.26

a) Proton NMR spectrum of 1Cl24DNB (0.02M) + NaCN (0.04M) /25%/75% v/v CD_3OD/d_6-DMSO after 45min.

b) Mass spectrum of the acidified reaction mixture.



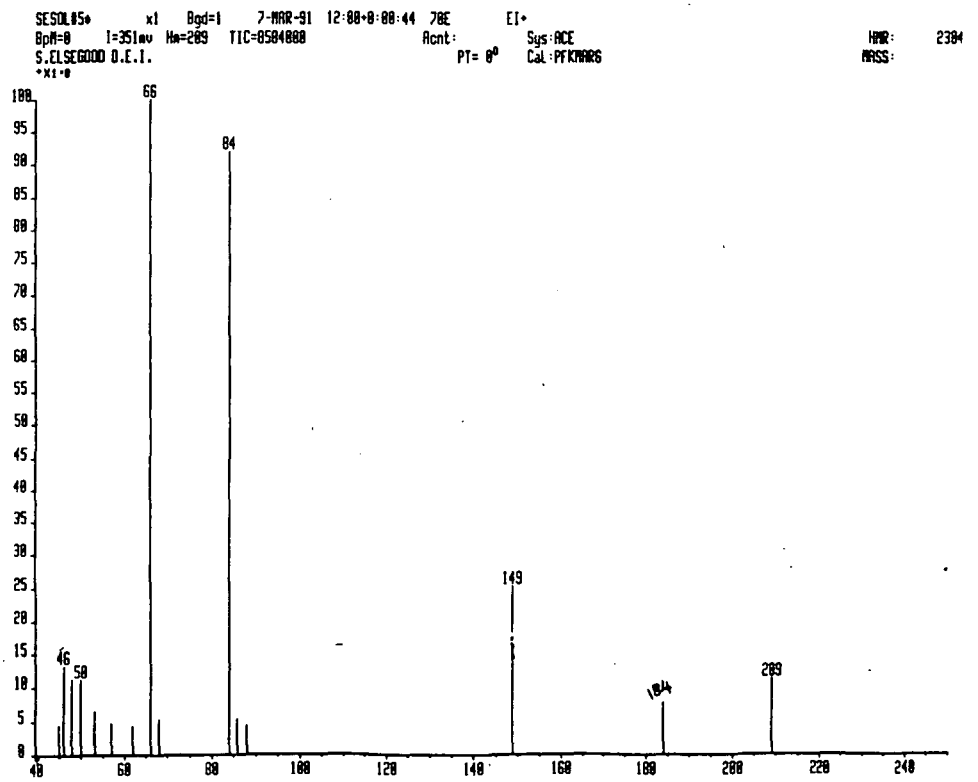


Figure 6.27

Mass spectra of 1Cl24DNB.

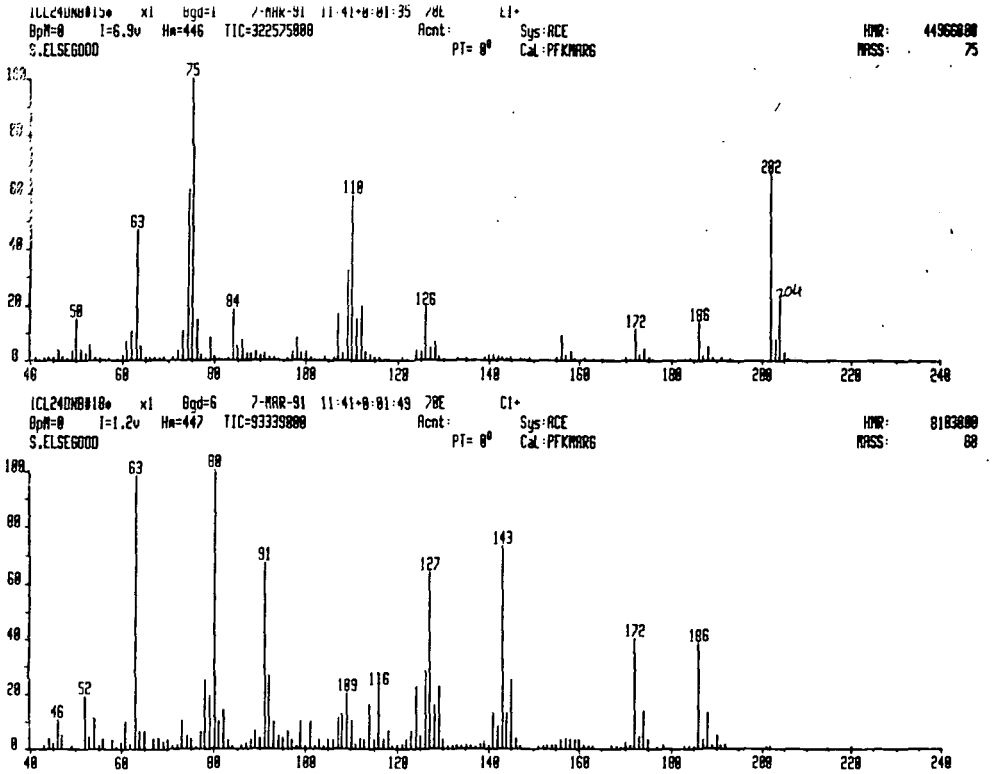
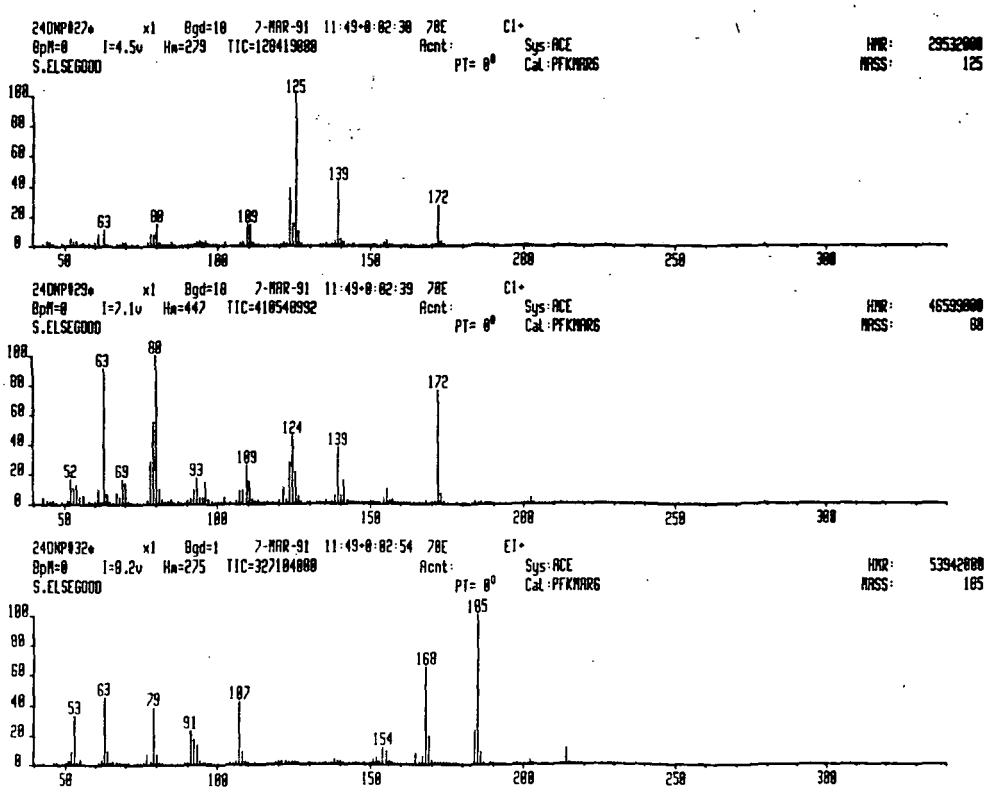
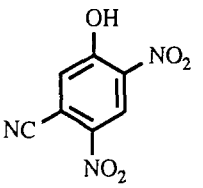


Figure 6.28

Mass spectra of 2,4-dinitrophenol.





(6.13)

The proton NMR spectrum of 1I24DNB in 25%/75% v/v CD_3OD/d_6-DMSO shows the three coupled signals of the three ring protons at 8.72, 8.42 and 8.19 (table 6.1). The spectrum after reaction between excess NaCN (0.08M) and 1I24DNB (0.02M) in 25%/75% v/v CD_3OD/d_6-DMSO after 30min shows the signals of three species: the parent, 2,4-dinitrophenoxide and the two singlets at 8.71 and 6.88ppm of 2,4-dinitro-5-cyanophenoxide. The spectrum of the reaction mixture left overnight shows no signals of the parent, only those of the two phenoxides (fig.6.29).

The proton NMR spectrum of 1Cl24DNB in d_6-DMSO shows three coupled signals at 9.04, 8.62 and 8.19ppm (table 6.1) due to the three ring protons. After 5min in the presence of excess KCN (0.02M), the spectrum of 1Cl24DNB (0.01M) shows (fig 6.30) the coupled signals of 2,4-dinitrophenoxide at 8.54, 7.73 and 6.26ppm, and the singlets of 2,4-dinitro-5-cyanophenoxide at 8.67 and 6.88ppm. Other signals are observed at 7.82, 7.52 and 6.82ppm. An identical spectrum is observed after 30min.

6.4.3 Preparative Experiment.

A simple preparative experiment was carried out with 1Cl24DNB and a two-fold excess of NaCN in 25%/75% v/v MeOH/DMSO in an attempt to prepare 2,4-dinitro-5-cyanophenol.

To a solution of NaCN (3.92g, 0.08moles) in 25%/75% v/v MeOH/DMSO (1l) solid 1Cl24DNB (8.10g, 0.04moles) was added and then stirred for 1hr. The reaction mixture was neutralised with dilute HCl and then washed with aliquots of dichloromethane. The organic layers were collected, washed with dil. acid to remove any DMSO and then dried overnight with sodium sulphate. The solution was then filtered and the dichloromethane removed by evaporation. The resulting solid was recrystallised from water to yield a small amount of solid: m.pt. 137-8°C; obs: 20.8% N, 43.5% C, 1.6% H (calc. for dinitro-cyanophenol: 20.1% N, 40.2% C, 1.4% H); ^{1}H NMR $\delta_{d6\text{-DMSO}}$ /ppm: 8.76(s) and 7.25(s) in base, 8.85(s) and 7.64(s) in acid; mass spectrum (direct current ionisation) shows molecular ion of 227 (M+18) and 197 (M+18-30(NO)). The uv/vis spectrum of the sample in the basic medium 25%/75% v/v MeOH/DMSO (fig.6.31) shows a definite band λ_{max} 420nm (shoulder 480nm).

Figure 6.29

Proton NMR spectum of 1I24DNB (0.02M) + NaCN (0.08M) /25%/75% v/v CD_3OD/d_6-DMSO after 30min.

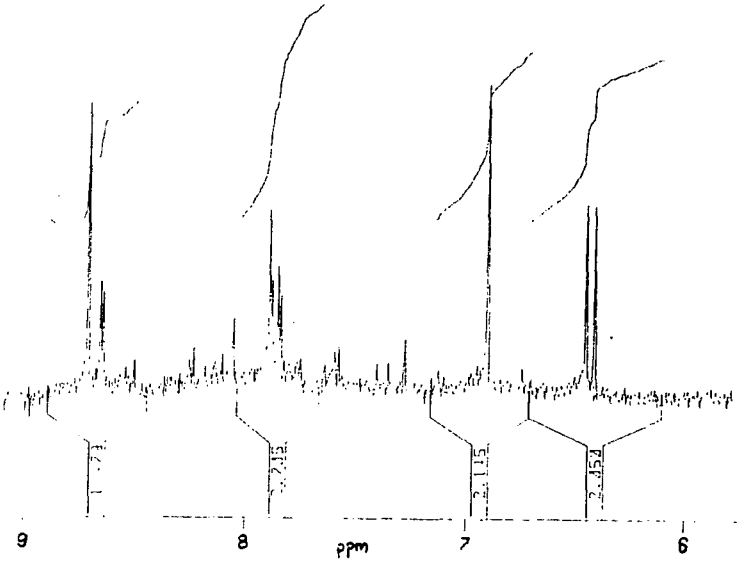


Figure 6.30

Proton NMR spectum of 1Cl24DNB (0.01M) + KCN (0.02M) /d_6-DMSO after 5min.

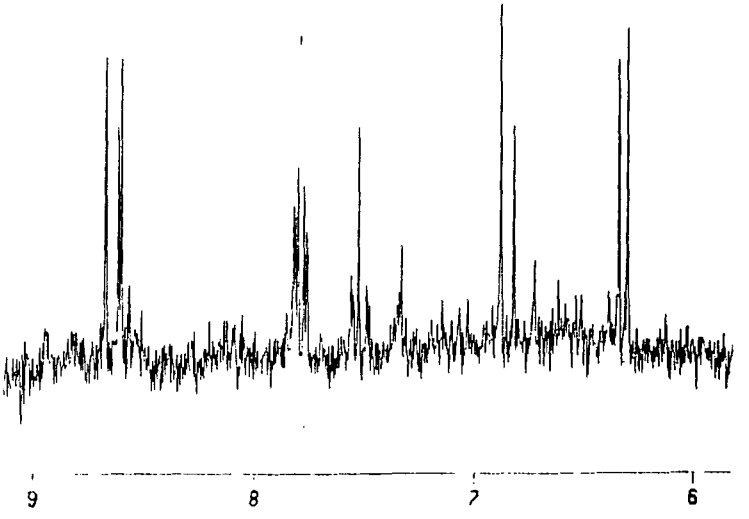
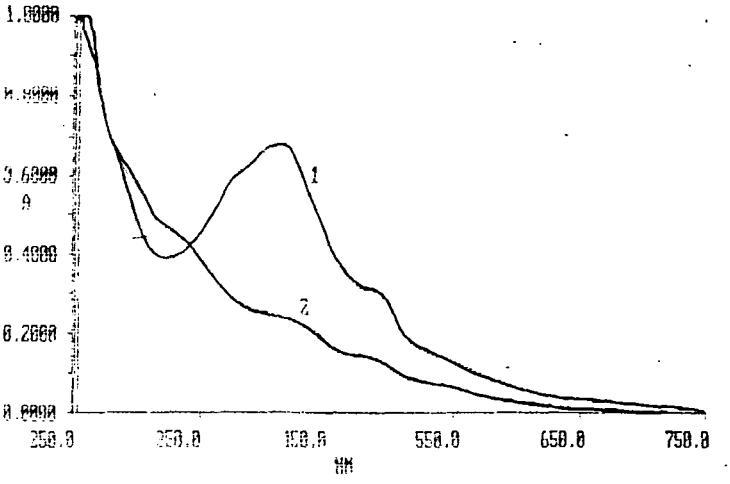


Figure 6.31

UV/Vis spectra of the product of 1Cl24DNB with excess NaCN /25%/75% v/v MeOH/DMSO 1) in the absence of, and 2) in the presence of acid.



However, when the sample is acidified in this medium no definite absorbance maxima are observed, but shoulders are evident at 420 and 480nm.

It seems doubtful that this preparation has produced the desired compound. The proton NMR spectrum shows two bands due to ring hydrogens, and these shift with pH as expected for a phenol. The decreased intensity of the uv/vis absorbance on acidification is also consistent with the product being a phenol. However the chemical shifts do not correspond to those, 8.67 and 6.88ppm, observed *in situ* when the reaction was followed by NMR spectroscopy. Also the elemental analysis is not very close to that expected for 2,4-dinitro-5-cyanophenol.

6.4.4 Discussion.

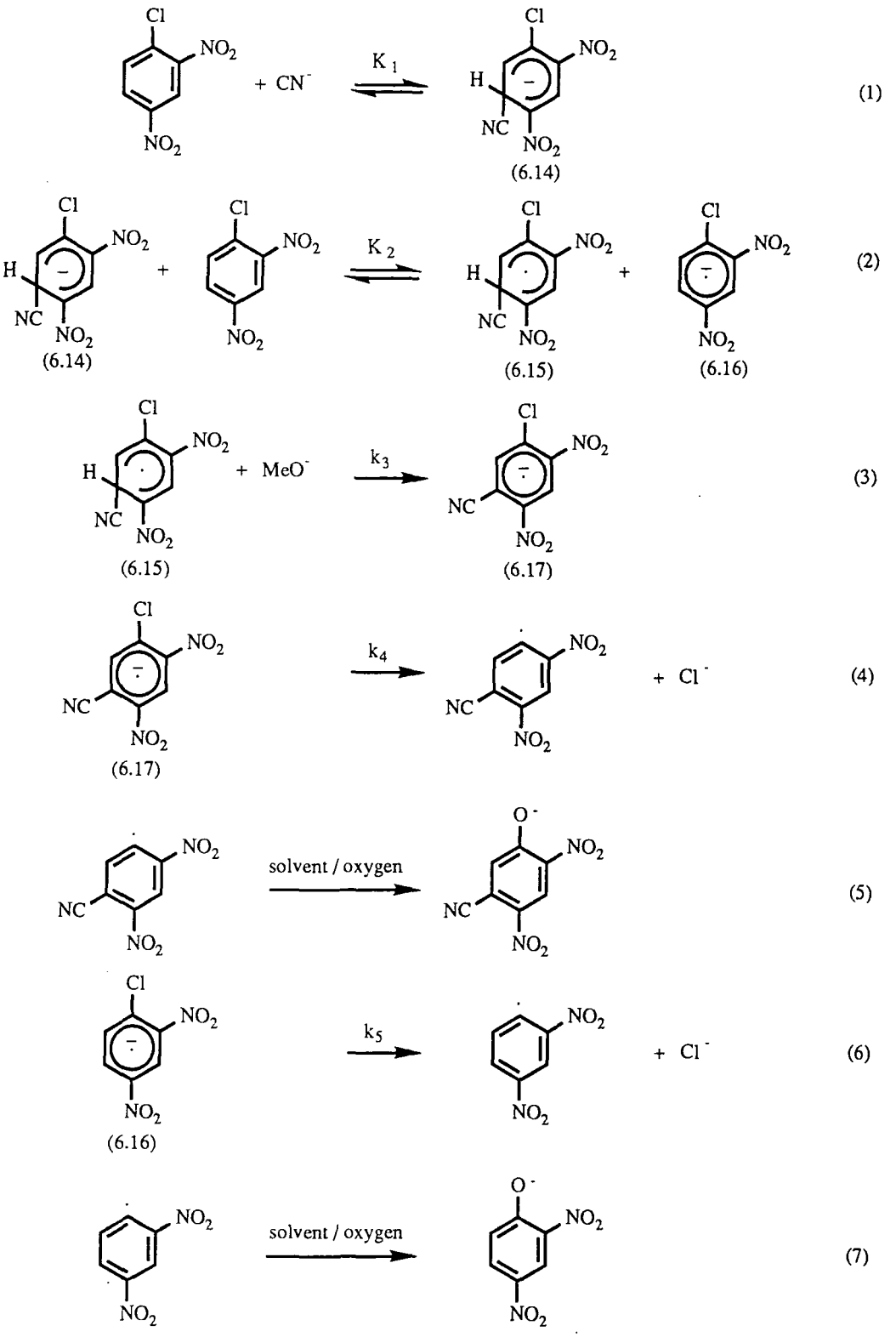
The proton NMR spectra obtained with relatively high concentrations of substrate and relatively small excess of cyanide are in accord with the formation of 2,4-dinitrophenol together with a second major product. The NMR and mass spectroscopic evidence is that this second species is 2,4-dinitro-5-cyanophenol. However, an attempt to isolate this product appears to have been unsuccessful.

The uv/vis measurements indicate formation of 2,4-dinitrophenol. However since the uv/vis spectrum of 2,4-dinitro-5-cyanophenol is not known it is possible that here also a mixture of the two products is formed. The kinetic experiments at constant substrate concentration ($1x10^{-4}M$) seem to indicate a straightforward reaction which is first order in substrate and first order in cyanide, with the 1-chloro-substrate being 2.5 times more reactive than 1-iodo-2,4-dinitrobenzene. However there is a complication here in that with increasing concentration of 1-chloro-2,4-dinitrobenzene the rate coefficient gradually decreases in value, indicating rather more complicated kinetics.

It is worthwhile to speculate on the possible pathways leading to 2,4-dinitrophenol and 2,4-dinitro-5-cyanophenol as products, and a tentative mechanism is given in the scheme (scheme 6.4).

The first step (1) involves attack by cyanide at the aromatic ring to give the sigma-adduct (6.14). The uv/vis spectra indicate the rapid formation in media rich in DMSO of species absorbing in the region of 600nm and this provides evidence for the sigma-complex. It is known [1] that sigma-adducts formed by nucleophilic attack at the 5-position of 1-halo-2,4-dinitrobenzenes have higher thermodynamic stabilities than the isomeric sigma-adducts formed by attack at the 3-position; so that structure (6.14) is likely. If cyanide attack were rate-determining this would lead to the observed kinetic behaviour, first order in parent and first order in cyanide. However the colour formation observed is instantaneous and much faster than product formation, hence it seems unlikely that this is the rate-determining step.

Scheme 6.4



(1)

(2)

(3)

(4)

(5)

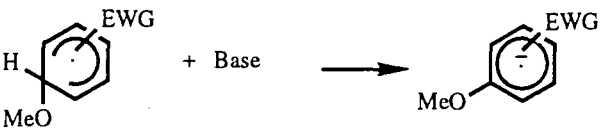
(6)

(7)

The second step (2) is an electron transfer to give a radical (6.15) and an anion radical (6.16). It is well known [7] that electron transfers may occur to and from nitro-substituted aromatics. Here the species transfering the electron (6.14) contains four electron withdrawing groups so there will not be a strong driving force to transfer an

electron to the parent. Nevertheless even though the value of K_2 is likely to be small, some electron transfer will occur to give (6.15) and (6.16).

A key step is the loss of a proton from (6.15) to give the radical anion (6.17), as shown in equation 3 (scheme 6.4). The proton lost from (6.15) will be acidic due to the neighbouring electron withdrawing groups, particularly the cyano group attached to the reaction centre. It is noteworthy that here and elsewhere in this work (chapters 4 and 5) there is evidence for replacement of ring hydrogens by cyanide. The facility of this reaction is unusual. For example with methoxide as nucleophile there are no examples of direct displacement of ring hydrogens. The difference can be understood in terms of the different electronic effects of the cyano and methoxy groups. The cyano group in (6.15) will acidify the adjacent hydrogen and will stabilise the anionic product (6.17). The analogous reaction with methoxide (eqn.6.2) is unlikely to occur because the methoxy group would not similarly acidify the adjacent hydrogen in (6.18) and would not stabilise the negative charge in (6.19). This appears to be a key difference in the reactions of methoxide and cyanide nucleophiles.



Eqn.6.2

(6.18) (6.19)

Steps (4) and (6) involve cleavage of halide ions from anion radicals. Such steps are well known in the $S_{RN}1$ radical chain mechanism.[7] However the intermediates (6.16) and (6.17) contain strongly electron withdrawing ring substituents so that the loss of halide would not be expected to be rapid. Nevertheless it is unlikely that halide loss is the rate determining step in the reaction since the kinetic experiments show that 1-chloro-2,4-dinitrobenzene reacts more rapidly than 1-iodo-2,4-dinitrobenzene and iodide should be more readily lost than chloride from an anion radical intermediate.

The final steps (5) and (7) involve formation of a bond to oxygen from the radicals. This oxygen might be derived from the solvent or from molecular oxygen.

It has been shown that the rate determining step in this scheme (scheme 6.4) is unlikely to be step (1) or steps (4) and (6). It is of interest to consider what kinetic form would be expected if step (3), the deprotonation of radical (6.15) were rate determining (calculation 6.1).

It is known [1] that values of the equilibrium constant for nucleophilic attack at the 5-position of 1-chloro-2,4-dinitrobenzene are larger than those for corresponding attack on 1-iodo-2,4-dinitrobenzene. Hence the larger value of K_1 for the chloro-derivative than for the iodo-derivative may contribute to its faster reaction.

Calculation 6.1

For step (3) as rate determining (scheme 6.4):

$$\text{velocity} = k_3[MeO^-][(6.15)]$$

assuming steps (1) and (2) are rapid equilibria:

$$K_1 = \frac{[(6.14)]}{[\text{parent}][CN^-]}$$

$$K_2 = \frac{[(6.15)][(6.16)]}{[(6.14)][\text{parent}]} = \frac{[(6.15)]^2}{[(6.14)][\text{parent}]}$$

therefore

$$[(6.15)] = \{K_2[(6.14)][\text{parent}]\}^{1/2}$$

$$= \{K_2K_1[\text{parent}]^2[CN^-]\}^{1/2}$$

$$= \{K_1K_2[CN^-]\}^{1/2}[\text{parent}]$$

But

$$CN^- + MeOH \underset{}{\overset{K_{Meth}}{\rightleftharpoons}} MeO^- + HCN \qquad \text{Eqn.3.4}$$

$$K_{Meth} = \frac{[MeO^-][HCN]}{[CN^-]} = \frac{[MeO^-]^2}{[CN^-]}$$

therefore

$$[MeO^-] = \{K_{Meth}[CN^-]\}^{1/2}$$

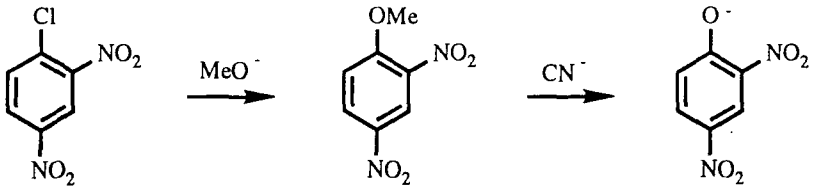
therefore

$$\text{velocity} = k_3\{K_{Meth}[CN^-]\}^{1/2}\{K_1K_2[CN^-]\}^{1/2}[\text{parent}]$$

$$= k_3\{K_1K_2K_{Meth}\}^{1/2}[CN^-][\text{parent}]$$

...giving the observed first order dependence on the concentrations of parent and of cyanide.

It is of interest to consider other possible routes to formation of the reaction products. One route to 2,4-dinitrophenol might be the attack of methoxide at the 1-postition of the substrate in an S_NAr reaction giving 2,4-dinitroanisole followed by demethylation to give the phenoxide (eqn.6.3). However it was shown (section 6.2) that 2,4-dinitroanisole is stable in the presence of cyanide under the conditions employed (25%/75% v/v MeOH/DMSO); hence this pathway is excluded.

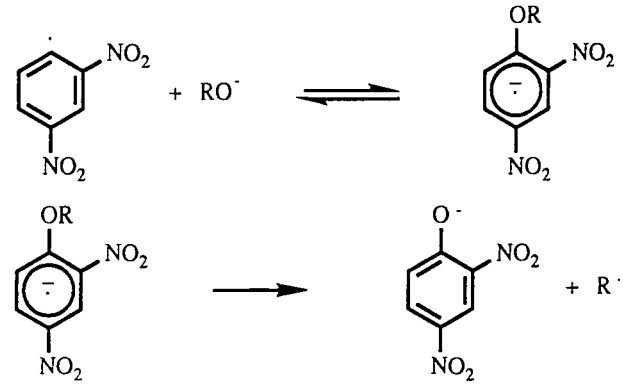


Eqn.6.3

It is also of interest to note that Scorrano *et.al.* [7] have shown that reaction of 1-halo-2,4-dinitrobenzenes with *iso*-propoxide ions in *iso*-propanol/benzene solvent

produced 2,4-dinitrophenol. Their proposed mechanism involved formation of the radical anion (6.16) followed by loss of halide to give the 2,4-dinitrobenzene radical (step 6). The final steps involved reaction of the radical with alkoxide to give a radical anion which subsequently fragmented to give the 2,4-dinitrophenoxide (scheme 6.5). These steps seem unlikely in the authors work since reaction can occur to give the same products in DMSO in the absence of methanol. In DMSO the base responsible for removal of the proton (step 3) is presumably the cyanide ion itself rather than methoxide.

Scheme 6.5



It should be stressed that the proposed scheme (scheme 6.4) is only tentative but it is an attempt to account for the observed features.

6.5 REFERENCES.

1 M.R.Crampton, A.B.Davies, C.Greenhalgh & A.J.Stevens, *J. Chem. Soc., Perkin Trans. II*, (1989), 675.

2 R.Bacaloglu, A.Blasko, C.A.Bunton, F.Ortega & C.Zucco, *J. Am. Chem. Soc.*, (1991), **113**, 238.

3 Y.Hasegawa, *Chem. Lett.*, (1972), 985.

4 Y.Hasegawa, *Bull. Chem. Soc. Jpn.*, (1974), **47**, 2186.

5 K.Bowden & N.S.Nadvi, *J. Chem. Soc., Perkin Trans. II*, (1987), 189.

6 M.R.Crampton & C.Greenhalgh, *J. Chem. Soc., Perkin Trans. II*, (1985), 599.

7 C.Mariani, G.Modena, G.P.Pizzo, G.Scorrano & L.Kistenbrugger, *J. Chem. Soc., Perkin Trans. II*, (1979), 1187.

8 R.Foster & C.A.Fyfe, *Tetrahedron*, (1967), **23**, 227.

9 K.Bowden & R.S.Cook, *Tet. Lett.*, (1970), 249.

10 E.Buncel, M.R.Crampton, M.J.Strauss & F.Terrier, *"Electron Deficient Aromatic- and Heteroaromatic-Base Interactions"*, Elsevier, Oxford, 1984.

11 R.Storrie, *J. Chem. Soc.*, (1937), 1746.

APPENDIX I.

RESEARCH COLLOQUIA, SEMINARS, LECTRURES AND CONFERENCES.

AI.1 COLLOQUIA, LECTURES AND SEMINARS GIVEN BY INVITED SPEAKERS AT THE UNIVERSITY OF DURHAM.

AI.1.1 1st August 1988 to 31st July 1989.

AVEYARD, Dr.R., (University of Hull), 15/3/89
Surfactants at your Surface.

AYLETT, Prof.B.J., (Queen Mary College, London), 16/2/89
Silicon-Based Chips:- The Chemist's Contribution.

* BALDWIN, Prof.J.E., (Oxford University), 9/2/89
Recent Advances in the Bioorganic Chemistry of Penicillin Biosynthesis.

* BALDWIN & WALKER, Drs.R.R. & R.W., (University of Hull), 24/11/88
Combustion: Some Burning Problems.

* BUTLER, Dr.A.R., (St. Andrews University), 15/2/89
Cancer in Linxiam: The Chemical Dimension.

* CADOGAN, Prof.J.I.G., (British Petroleum), 10/11/88
From Pure Science to Profit.

CASEY, Dr.M., (University of Salford), 20/4/89
Sulphoxides in Stereoselective Synthesis.

CRICH, Dr.D., (University College, London), 27/4/89
Some Novel Uses of Free Radicals in Organic Synthesis.

DINGWALL, Dr.J. (Ciba-Geigy), 18/10/88
Phosphorus-Containing Amino Acids: Biologically Active Natural and Unnatural Products.

ERRINGTON, Dr.R.J., (University of Newcastle-Upon-Tyne), 1/3/89
Polymetalate Assembly in Organic Solvents.

FREY, Dr.J., (Southampton University), 11/5/89
Spectroscopy of the Reaction Path: Photodissociation Raman Spectra of NOCl.

* GRADUATE CHEMISTS, (Polytechnics and Universities in the North-East of England), 12/4/89
R.S.C.Symposium for the presentation of papers by postgraduate students.

HALL, Prof.L.D., (Addenbrooke's Hospital, Cambridge), 2/2/89
NMR-A Window to the Human Body.

HARDGROVE, Dr.G., (St. Olaf College, U.S.A.), Dec., 1988
Polymers in the Physical Chemistry Laboratory.

HARWOOD, Dr.L., (Oxford University), 25/1/89
Synthetic Approaches to Phorbols *via* Intramolecular Furan Diels-Alder Reactions: Chemistry Under Pressure.

JAGER, Dr.C., (Friedrich-Schiller University, G.D.R.), 9/12/88
NMR Investigations of Fast Ion Conductors of the NASICON Type.

JENNINGS, Prof.R.R., (Warwick University), 26/1/89
Chemistry of the Masses.

JOHNSON, Dr.B.F.G., (Cambridge University), 23/2/89
The Binary Carbonyls.

* LUDMAN, Dr.C.J., (University of Durham), 18/10/88
The Energetics of Explosives.

MACDOUGALL, Dr.G., (Edinburgh University), 22/2/89
Vibrational Spectroscopy of Model Catalytic Systems.

MARKO, Dr.I., (Sheffield University), 9/3/89
Catalytic Assymmetric Osmylation of Olefins.

McLAUCHLAN, Dr.K.A., (Oxford University), 16/11/88
The Effect of Magnetic Fields on Chemical Reactions.

MOODY, Dr.C.J., (Imperial College, London), 17/5/89
Reactive Intermediates in Heterocyclic Synthesis.

PAETZOLD, Prof.P., (Aachen), 23/5/89
Iminoboranes XB=NR: Inorganic Acetylenes?

PAGE, Dr.P.C.B., (University of Liverpool), 3/5/89
Stereocontrol of Organic Reactions Using 1,3-Dithiane-1-oxides.

POLA, Prof.J., (Czechoslovak Academy of Sciences), 15/6/89
Carbon Dioxide Laser Induced Chemical Reactions - New Pathways in Gas-Phase Chemistry.

REES, Prof.C.W., (Imperial College, London), 27/10/88
Some Very Heterocyclic Compounds.

SCHMUTZLER, Prof.R., (Technische Universitat Braunschweig), 6/10/88
Fluorophosphines Revisited - New Contributions to an Old Theme.

SCHROCK, Prof.R.R., (M.I.T.), 13/2/89
Recent Advances in Living Metathesis.

SINGH, Dr.G., (Teeside Polytechnic), 9/11/88
Towards Third Generation Anti-Leukaemics.

* SNAITH, Dr.R., (Cambridge University), 1/12/88
Egyptian Mummies: What, Where, Why and How?

STIBR, Dr.R., (Czechoslovak Academy of Sciences), 16/5/89
Recent Developments in the Chemistry of Intermediate-Sited Carboranes.

* VON RAGUE SCHLEYER, Prof.P., (Universitat Erlangen Numberg), 21/10/88
The Fruitful Interplay between Calculation and Experimental Chemistry.

WELLS, Prof.P.B., (University of Hull), 10/5/89
Catalyst Characterisation and Activity.

AI.1.2 1st August 1989 to 31st July 1990.

BADYAL, Dr.J.P.S., (University of Durham), 1/11/89
Breakthroughs in Heterogenous Catalysis.

BECHER, Dr.J., (Odense University), 13/11/89
Synthesis of New Macrocyclic Systems using Heterocyclic Building Blocks.

BERCAW, Prof.J.E., (California Institute of Technology), 10/11/89
Synthetic and Mechanistic Approaches to Ziegler-Natta Polymerisation of Olefins.

BLEASDALE, Dr.C., (University of Newcastle-Upon-Tyne), 21/2/90
The Mode of Action of some Anti-Tumour Agents.

* BUTLER, Dr.A.R., (St. Andrews University), 7/12/89
The Discovery of Penicillin: Facts and Fancies.

* CHEETHAM, Dr.A.K., (Oxford University), 8/3/90
Chemistry of Zeolite Cages.

CLARK, Prof.D.T., (I.C.I. Wilton), 22/2/90
Spatially Resolved Chemistry (Using Nature's Paradigm in the Advanced Materials Arena).

COLE-HAMILTON, Prof.D.J., (St. Andrews University), 29/11/89
New Polymers from Heterogenous Catalysis.

* CROMBIE, Prof.L., (Nottingham University), 15/2/90
The Chemistry of Cannabis and Khat.

DYER, Dr.U., (Glaxo), 31/1/90
Synthesis and Conformation of C-Glycosides.

FLORIANI, Prof.C., (University of Lausanne, Switzerland), 25/10/89
Molecular Aggregates - A Bridge between Homogenous and Heterogenous Systems.

GERMAN, Prof.L.S., (U.S.S.R. Academy of Sciences, Moscow), 6/7/90
New Syntheses in Fluoroaliphatic Chemistry: Recent Advances in the Chemistry of Fluorinated Oxiranes.

* GRAHAM, Dr.D., (B.P.Research Centre), 4/12/89
How Proteins Absorb to Interfaces.

GREENWOOD, Prof.N.N., (University of Leeds), 9/11/89
Novel Cluster Geometries in Metalloborane Chemistry.

* HOLLOWAY, Prof.J.H., (University of Leicester), 1/2/90
Noble Gas Chemistry.

* HUGHES, Dr.M.N., (King's College, London), 30/11/89
A Bug's-Eye View of the Periodic Table.

* HUISGEN, Prof.R., (Universitat Munchen), 15/12/89
Recent Mechanistic Studies of [2+2] Additions.

KLINOWSKI, Dr.J., (Cambridge University), 13/12/89
Solid State NMR Studies of Zeolite Catalysts.

LANCASTER, Rev.R., (Kimbolten Fireworks), 8/2/90
Fireworks - Principles and Practice.

LUNAZZI, Prof.L., (University of Bologna), 12/2/90
Application of Dynamic NMR to the Sudy of Conformational Enantiomerism.

PALMER, Dr.F., (Nottingham University), 17/10/89
Thunder and Lightning.

PARKER, Dr.D., (University of Durham), 16/11/89
Macrocycles, Drugs and Rock 'n' Roll.

PERUTZ, Dr.R.N., (York University), 24/1/90
Plotting the Course of C-H Activations with Organometallics.

PLATONOV, Prof.V.E., (U.S.S.R. Academy of Sciences, Novosibirsk), 9/7/90
Polyfluoroindanes: Synthesis and Transformation.

POWELL, Dr.R.L., (I.C.I.), 6/12/89
The Development of CFC replacements.

* POWIS, Dr.I. (Nottingham University), 21/3/90
Spinning Off in a Huff: Photodissociation of Methyl Iodide.

ROZHKOV, Prof.I.N., (U.S.S.R. Academy of Sciences, Moscow), 9/7/90
Reactivity of Perfluoroalkyl Bromides.

STODDART, Dr.J.F., (Sheffield University), 1/3/90
Molecular Lego.

SUTTON, Prof.D., (Simon Fraser University, Vancouver B.C.), 14/2/90
Synthesis and Applications of Dinitrogen and Diazo Compounds of Rhenium and Iridium.

THOMAS, Dr.R.K., (Oxford University), 28/2/90
Neutron Reflectometry from Surfaces.

THOMPSON, Dr.D.P., (University of Newcastle-Upon-Tyne), 7/2/90
The Role of Nitrogen in Extending Silicate Crystal Chemistry.

AI.1.3 1st August 1990 to 31st July 1991.

* ALDER, Dr.B.J., (Lawrence Livermore Laboratories, California), 15/1/91
Hydrogen in all its Glory.

*# BELL, Prof.T., (S.U.N.Y., Stoney Brook, U.S.A.), 14/11/90
Functional Molecular Architecture and Molecular Recognition.

\# BOCHMANN, Dr.M., (University of East Anglia), 24/10/90
Synthesis, Reactions and Catalytic Activity of Cationic Titanium Alkyls.

* BRIMBLE, Dr.M.A., (Massey University, New Zealand), 29/7/91
Synthetis Studies towards the Antibiotic Griseusin-A.

BROOKHART, Prof.M.S., (University of North Carolina), 20/6/91
Olefin Polymerisations, Oligomerisations and Dimerisations using Electrophilic Late Transition Metal Catalysts.

* BROWN, Dr.J., (Oxford University), 28/2/91
Can Chemistry Provide Catalysts Superior to Enzymes?

*# BUSHBY, Dr.R., (University of Leeds), 6/2/91
Biradicals and Organic Magnets.

COWLEY, Prof.D., (University of Texas), 13/12/90
New Organometallic Routes to Electronic Materials.

* CROUT, Prof.D., (Warwick University), 29/11/90
Enzymes in Organic Synthesis.

*# DOBSON, Dr.C.M., (Oxford University), 6/3/91
NMR Studies of Dynamics in Molecular Crystals.

*# GERRARD, Dr.D., (British Petroleum), 7/11/90
Raman Spectroscopy for Industrial Analysis.

HUDLICKEY, Prof.T., (Virginia Polytechnic Institute), 25/4/91
Biocatalysis and Symmetry Based Approaches to the Efficient Synthesis of Complex Natural Products.

*# JACKSON, Dr.R., (University of Newcastle-Upon-Tyne), 31/10/91
New Synthetic Methods: α-Amino Acids and Small Rings.

*# KOCOVSKY, Dr.P., (Uppsala University), 6/11/90
Stereo-Controlled Reactions Mediated by Transition and Non-Transition Metals.

* LACEY, Dr.D., (University of Hull), 31/1/91
Liquid Crystals.

LOGAN, Dr.N., (Nottingham University), 1/11/90
Rocket Propellants.

* MACDONALD, Dr.W.A., (I.C.I.Wilton), 11/10/90
Materials for the Space Age.

* MARKHAM, Dr.A.J., (I.C.I.Phamaceuticals), 7/3/91
DNA Fingerprinting.

* PETTY, Dr.M.C., (University of Durham), 14/2/91
Molecular Electronics.

\# PRINGLE, Dr.P.G., (Bristol University), 5/12/90
Metal Complexes with Functionalised Phosphines.

PRITCHARD, Prof.J., (Queen Mary & Westfield College, London), 21/11/90
Copper Surfaces and Catalysts.

* SADLER, Dr.P.J., (Birkbeck College, London), 24/1/91
Design of Inorganic Drugs: Precious Metals, Hypertension and H.I.V.

* SARRE, Dr.P., (Nottingham University). 17/1/91
Comet Chemistry.

SCHROCK, Prof.R.R., (M.I.T.), 24/4/91
Metal-Ligand Multiple Bonds and Metathesis Initiators.

* SCOTT, Dr.S.K., (University of Leeds), 8/11/90
Clocks, Oscillations and Chaos.

\# SHAW, Prof.B.L., (University of Leeds), 20/2/91
Syntheses with Coordinated, Unsaturated Phosphine Ligands.

\# SINN, Prof.E., (University of Hull), 30/1/91
Coupling of Little Electrons in Big Molecules. Implications for the Active Sites of (Metalloproteins and other) Macromolecules.

*# SOULEN, Prof.R., (South Western University, Texas), 26/10/90
Preparation and Reactions of Bicycloalkenes.

*# WHITAKER, Dr.B.J., (University of Leeds), 28/11/90
Two-Dimensional Velocity Imaging of State-Selected Reaction Products.

* Attended

\# Invited specifically for the postgraduate training programme.

AI.2 CONFERENCES ATTENDED.

European Symposium on Organic Reactivity II, University of Padova, Italy. (27/8/89 - 1/9/89).
Royal Society of Chemistry Organic Reactivity Group Meeting, I.C.I., Blackley, Manchester; paper presented. (1/10/90).

AI.3 FIRST YEAR INDUCTION COURSE, OCTOBER 1988.

The course consisted of a series of one hour lectures on the services available in the department: departmental organisation, safety matters, electrical appliances and infra-red spectroscopy, choromatography and microanalysis, atomic absorptiometry and inorganic analysis, library facilities, mass spectroscopy, nuclear magnetic resonance spectroscopy, and glassblowing technique.