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MEISENHEIMER COMPLEXES: SOME STRUCTURAL, EQUILIBRIUM AND KINETIC STUDIES

by

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Chemistry Department

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I would also like to thank the many staff members and technical staff of the department for their co-operation.

CONTENTS

ABSTRACT

Structural and equilibrium studies of Meisenheimer complexes formed from activated anisoles and from 1-X-3,5-dinitrobenzenes have been carried out. Specific effects of cations on the stabilities of such σ-complexes were observed and an explanation has been put forward.

The results of ^1H n.m.r. and visible spectroscopy for the interaction of 1-chloro-2,6-dinitro-4-X-benzenes (X = Cl, CO_2Me, CF_3) with sodium methoxide in dimethyl sulphoxide solutions show that initially base addition takes place at an unsubstituted aromatic carbon, forming a σ-complex. However the faster addition of base at the unsubstituted ring position is followed by nucleophilic replacement of chloride ion forming the corresponding anisole.

Visible spectroscopy was used for the equilibrium and kinetic study of σ-complex formation from activated anisoles and methoxide ion in methanol. The values of stoichiometric equilibrium constants so obtained show an increase with base concentration when sodium, potassium or tetra-n-butylammonium methoxide is used as the base, while no such increase is observed with lithium methoxide. It is suggested that the observed increase in stoichiometric equilibrium constants is due to the stabilisation of the complexes by association with the cations present. As a result of this observation it seems more appropriate to use lithium methoxide for the measurements of thermodynamic equilibrium constants. The specific effects of cations are also observed with bivalent barium and calcium ions, in whose presence large increases in the stoichiometric equilibrium constants for methoxide addition to 2-methoxycarbonyl-4,6-dinitroanisole, 4-methoxycarbonyl-2,6-dinitroanisole and 2-chloro-4,6-dinitroanisole are found. This effect, attributed to cation association with the Meisenheimer complexes, is

demonstrated in the case of the methoxide σ-complex from 2,4,6-trinitroanisole, by change in visible spectrum in the presence of various cations. However the σ-complex formed from 1,3,5-trinitrobenzene and methoxide ions shows little tendency to form ion associates with cations. It is therefore suggested that when ion pairs are formed the cation is held by a cage effect by the two oxygen atoms of the methoxyl group at the position of addition and by the electronegative substituent at the ortho-position.

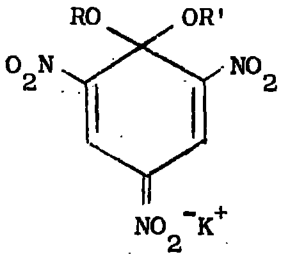
Structural and equilibrium studies for the formation of Meisenheimer complexes from some 1-X-3,5-dinitrobenzenes and methoxide ions were also made. ^{1}H n.m.r. results in conjunction with visible spectroscopy indicate initial addition of base at an aromatic carbon para to the substituents X, however rearrangement occurs so that at equilibrium the isomeric adduct formed from addition of base at a ring carbon para to a nitro-group usually dominates. The measurements of indicator ratios in methanol-dimethyl sulphoxide mixture containing ($\sim 10^{-1}\underline{\underline{M}}$) sodium methoxide allowed the simultaneous determination of the J_M acidity function and the thermodynamic equilibrium constants, K, for complex formation. Similar measurements of indicator ratios with the less reactive anisoles in methanol-dimethyl sulphoxide mixtures lead to the determination of an alternative J_M acidity function and the thermodynamic equilibrium constants for the complex formation from anisoles and methoxide ions. The two J_M scales as well as the stability constants of the adducts formed from 1-X-3,5-dinitrobenzenes and similarly activated anisoles are compared.

CHAPTER 1

INTRODUCTION

General Introduction

The interactions of electron-deficient aromatics with a variety of bases to give brightly coloured solutions have attracted chemists since before 1900.[1] Since then the nature of these interactions and the structure of the species formed have been the subject of comprehensive investigations. Jackson and Gazzolo in 1900 described the species produced from the reaction of picryl ethers with base by the quinonoid structure (1.1) (R=R'=alkyl) and later Meisenheimer[2] endorsed this structure by isolating the same product from the reaction of 2,4,6-trinitroanisole with potassium ethoxide and 2,4,6-trinitrophenetole with potassium methoxide. More recently spectroscopic and crystallographic studies have provided further evidence for this structure, although the modern representation would be (1.2) when the negative charge is delocalised about the nitro-groups and aromatic ring.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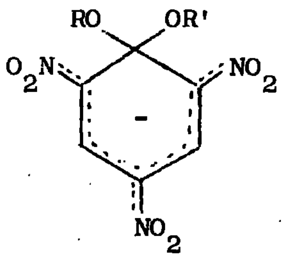
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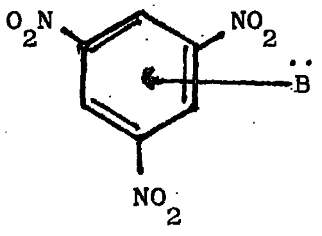
A considerable volume of literature now exists on these 'Meisenheimer complexes' as they have become known and several reviews have been written.[3-7] It is therefore neither necessary nor desirable to give a comprehensive treatment in this introduction. Instead some of the more important features will be brought to attention.

In fact a number of other possibilities apart from Meisenheimer complex formation are possible from the interaction of bases with electron-deficient aromatics. A π-complex (1.3) could result from the partial transfer of electric charge from the base to the aromatic nucleus. This type of complex is also known as a 'charge-transfer complex'.[8] It is also possible



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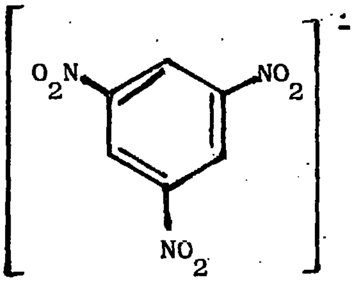

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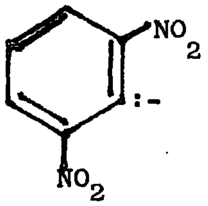

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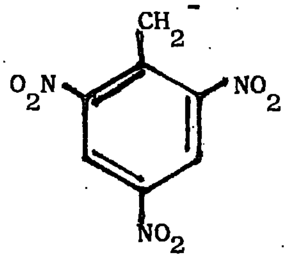


(1.6)

for an electron from the base to be completely transferred to the electron depleted aromatic compound giving a radical anion (1.4). On the other hand if the unshared electron pair of the base is used in formation of a covalent bond to an aromatic carbon atom Meisenheimer complex formation will result. Nucleophilic aromatic substitution may also occur if the parent compound contains a readily displaceable group, such as halogen. Another possibility is for proton-abstraction to occur yielding an aryl carbanion (1.5). Proton abstraction from a side chain in compounds such as 2,4,6-trinitroaniline or 2,4,6-trinitrotoluene may also occur giving an anion such as (1.6).

I. Structural Studies of the Complexes Formed

(a) Use of spectroscopic methods

Many spectroscopic and crystallographic techniques have been used to elucidate the structural and kinetic problems faced in the study of Meisenheimer complexes.

Foster and Hammick[9] studied the infrared absorption of the crystalline Meisenheimer complex formed from potassium ethoxide and trinitroanisole. The shift of the N-O symmetrical stretching frequency from 1343 cm^{-1} in the parent anisole to 1291 cm^{-1} in the adduct and of the N-O asymmetrical stretching frequency from 1552 to 1492 cm^{-1} are consistent with the increased negative charge on the nitro-groups, supporting structure (1.2), (R=Me, R'=Et). Dyall[10] has made a detailed study of infrared spectrum of the adducts formed by picryl ethers with different alkoxides. His results show strong bands characteristic of a 'ketal' as would be expected from a fully covalent structure (1.2) rather than a charge-transfer structure.

Visible spectroscopy has been a popular tool in the investigation of structural and kinetic behaviour of Meisenheimer complexes. Foster[11] measured the visible spectrum of the product obtained from potassium methoxide and 2,4,6-trinitrophenetole and from potassium ethoxide and 2,4,6-trinitroanisole. The similarity of the two spectra led Foster to postulate that the two products contain the same complex with structure (1.2). However further studies[12,13] showed that the visible spectra of a variety of dialkoxy-Meisenheimer complexes symmetrically (R=R') or unsymmetrically ($R \neq R'$) substituted are all very similar and show two maxima in the region 400-800 nm.

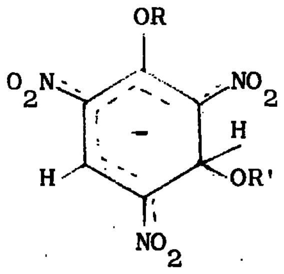
More recently crystallographic studies[14-16] have shown that the bond angle between C_6-C_1-C_2 is 109^o which is very close to the tetrahedral angle required from sp^3 hybridized carbon. The bond between C_4 and nitrogen atom of the nitro group in para position is significantly shorter than the bond between C_2 and nitrogen atom of the ortho nitro groups, indicating that a large proportion of negative charge is localised on the nitro group in para position to C_1. This conclusion is in agreement with the infra-red results.

More specific and unambiguous results as o the structure of Meisenheimer complexes was obtained by Crampton and Gold[17], through ^{1}H n.m.r. studies of the adducts formed by 2,4,6-trinitroanisole and 1,3,5-trinitrobenzene with potassium methoxide in solutions. As a result of their observations it is now possible to identify the complexes formed by these substrates with methoxide as Meisenheimer complexes with unambiguity.

In n.m.r. spectroscopy positions of the resonance lines are expressed in p.p.m. and are relative to tetramethylsilane as internal reference. The exact location of absorption depends somewhat on the solvent used but does not usually vary by more than ~ ±·15 p.p.m. In the following section are detailed some examples of the uses of spectroscopic methods in structural studies with a variety of different types of nucleophile. Because of the large volume of literature on this subject these give examples of complexes formed with different structure types rather than a comprehensive review of the literature.

(b) Complexes with alkoxides

The ^{1}H n.m.r. spectrum of 2,4,6-trinitroanisole in dimethyl sulphoxide shows two bands at δ 9·07 and 4·07 p.p.m. and with relative intensities 2:3 attributed respectively to the ring protons and methoxyl protons.[17] The spectrum of the complex dissolved in dimethyl sulphoxide also shows two bands which are shifted to high field relative to the positions in the parent molecule. The new locations are at δ 8·64 and 3·03 p.p.m. with relative intensities 2:6. The single band due to the six methoxyl proton in the complex show their equivalence and indicates the structure (1.2) (R=R'=Me) for the complex. If however[18] a concentrated solution of methanolic methoxide is added to a dimethyl sulphoxide solution of 2,4,6-trinitroanisole the initial spectrum shows two doublets at δ 8·4 and 6·2 p.p.m. due to ring protons of complex (1.7) (R=R'=Me). These bands decrease in intensity with time as the 1,3-adduct (1.7) rearranges to the thermodynamically more stable 1,1-adduct (1.2) (R=R'=Me).



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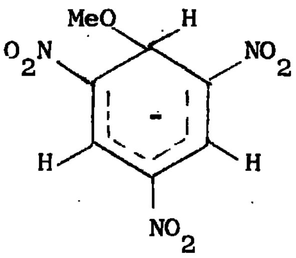
In the case of 1,3,5-trinitrobenzene[17,19] the resonance in dimethyl sulphoxide solution is located at δ 9·2 p.p.m., the addition of methanolic methoxide results in the appearance of two spin coupled bands at 8·4 and 6·1 p.p.m. The resonance at 8·4 p.p.m. appears as a doublet (J = 1·5 Hz) and is attributed to the two equivalent C_3 and C_5 protons in the complex (1.8), while the band at 6·1 p.p.m. appears as a triplet and corresponds to the proton at the site of addition.



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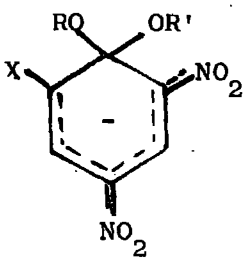
Formation of Meisenheimer complexes of greater than 1:1 stoichiometry from 2,4,6-trinitroanisole and 1,3,5-trinitrobenzene in the presence of high concentration of base has also been reported.[12,19,20]

The visible spectra produced by the addition of alkoxides to a number of 2,4-dinitro-6-X-anisoles and 2,6-dinitro-4-X-anisoles were reported by Pollitt and Saunders.[21] They interpreted their results in terms of the formation of structures (1.9) and (1.10). In general the band at low energy



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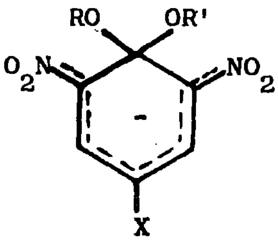
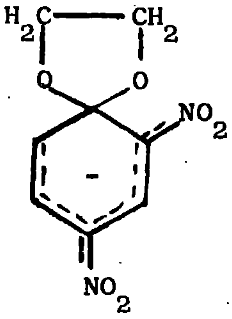


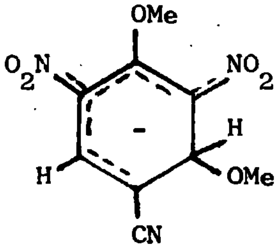
(1.10)

was found to undergo a hypsochromic shift as the electronegativity of the X-substituent increased. The formation of solid complexes of structure (1.9) and (1.10) (R=R'=alkyl, X=H) were reported by Gitis et al[22,23] from the addition of alkoxides to 2,4-dinitroanisole and 2,6-dinitroanisole. More recently the structures (1.9) and (1.10) have been confirmed by ^1H n.m.r. spectroscopy[24], some such cases studied during the present work are also discussed in Chapter IV. The spiro structure of glycol-2,4-dinitrophenyl ether in basic solution has been shown from ^1H n.m.r. measurements.[25] The methylene protons give an A_2B_2 pattern due probably to the hindered rotation of the spiro group indicating structure (1.11).



(1.11)

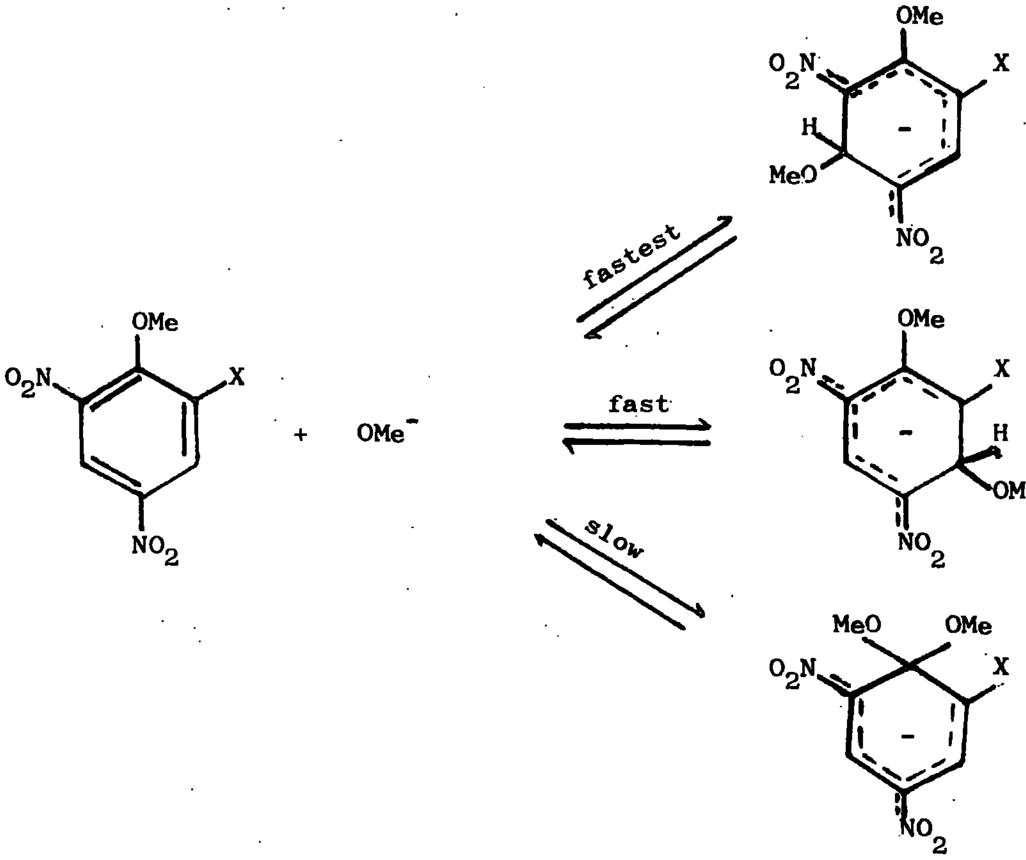
Fendler et al[24] have prepared and isolated potassium-1,1-dimethoxy-2-cyano-4,6-dinitrocyclohexadienate and potassium-1,1-dimethoxy-4-cyano-2,6-dinitrocyclohexadienate. Their results confirm the earlier findings of Dyall et al[26], the replacement of a nitro group by a cyano group decreases the stability of the complexes.[26] The initial formation of the 1,3-adduct (1.12) is also confirmed by ^{1}H n.m.r. spectrum.[24] This, however, transfers



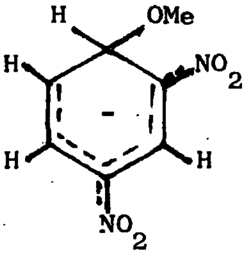
(1.12)

to thermodynamically more stable 1,1-adduct (1.10) (R=R'=Me, X=CN) with time.

In the case of 2-X-4,6-dinitroanisoles, Terrier and his co-workers[27,28] have evidence using ^{1}H n.m.r. spectroscopy and stopped-flow kinetic techniques for the formation of two transient adducts produced by alkoxide addition at the C_3 and C_5 positions followed by eventual formation of the stable C_1 adduct. They suggested the following scheme:



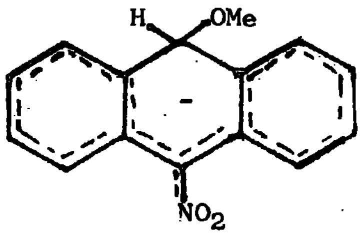
The addition of methanolic sodium methoxide to 1,3-dinitrobenzene in dimethyl sulphoxide produces a red solution (λ_{max} = 520 nm) which has been attributed[29,30] to the adduct (1.13). Pollitt and Saunders[31] have also



(1.13)

reported nuclear proton exchange of 1,3-dinitrobenzene using isotopic exchange although it has been shown that the carbanion formed by proton loss is not responsible for the colour in the solutions. Recently the structure (1.13) has been confirmed by ^{1}H n.m.r. results.[32]

Substituted multi-ring aromatics are also reported to form Meisenheimer type adducts. Foster et al[33] observed the deep red colour (λ_{max} = 505 nm) solution by the addition of methoxide to a dimethyl sulphoxide solution of 9-nitroanthracene, and described it as due to complex (1.14) on the evidence



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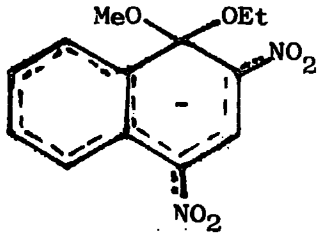
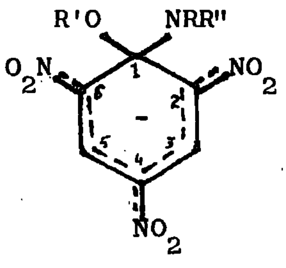


(1.15)

of ^{1}H n.m.r. spectrum which shows an upfield shift of the resonance of C_{10} proton from 8·9 p.p.m. in the parent compound to ~ 4·9 p.p.m. in the coloured species formed, this being consistent with base addition at this position. Similarly alkyl ethers of 2,4-dinitronaphthalenes are reported to to give complexes such as (1.15), with alkoxides, the structure has been confirmed by ^1H n.m.r. spectroscopy.[34]

The reaction of nitroaromatic amines in basic media could result either in the abstraction of an amino proton or the addition of base.[18,35-37] Early workers[38,39] suggested formula (1.16) (R=H,alkyl,phenyl; R'=H,alkyl; R''=H) for the addition product. Deprotonation of amine was also suggested[40]



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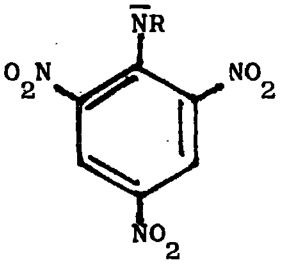

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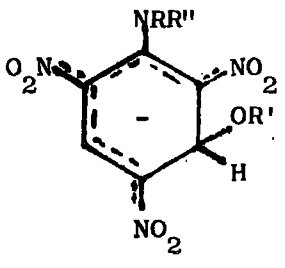
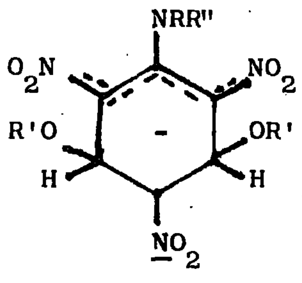


(1.18)

to give anion of the type (1.17). More recently Gold and Rochester[41] suggested that either base addition or proton loss occurred, but that the adduct formed was in fact of structure (1.18) where alkoxide adds to a ring position carrying hydrogen. 1:2 Interactions resulting in the formation of adducts (1.19) or (1.20) were also postulated.



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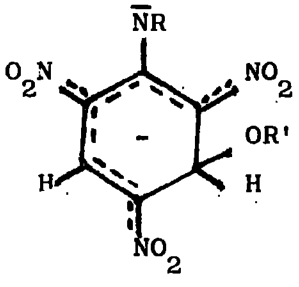
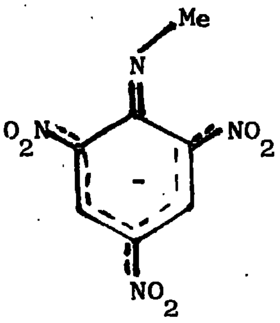


(1.20)

Crampton and Gold[30] studied the reactions of a number of nitroaromatic amines with base, using ^1H n.m.r. as the main source of information; their results show that for anilines containing two nitro groups proton loss in the basic medium is predominant reaction. However, for anilines containing three nitro groups ionisation by proton loss and addition of base, are both important.

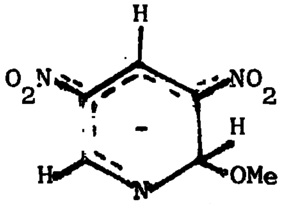
^{1}H n.m.r. spectrum measured by Servis[20] of solutions of N-methyl-2,4,6-trinitroaniline and sodium methoxide results from a mixture of the anion (1.18) (R=H; R'=R"=Me) and anion (1.17) (R=CH_3) resulting from proton abstraction. The former adduct gives spin coupled bands at 8·5 and 6·2 p.p.m. resulting from C_5 and C_3 protons respectively. Servis found that in the anion (1.17) (R=Me) the two ring protons are non-equivalent and gave spin coupled bands. He argued that this was due to restricted rotation about the nitrogen ring carbon bond giving a structure (1.17a). At higher methoxide concentration a dianion of the type (1.20) was formed (R=R'=Me).



(1.17a)

There have been a number of studies of the interactions of heterocyclic aromatics with bases. Mariella et al[42] observed the formation of highly coloured solutions from substituted pyridines in basic solutions. More recently different workers[26,43-47] have confirmed the formation of Meisenheimer type complexes from substituted pyridines and pyrimidines. Apparently the role of the aza group as an activating function is similar to that of the nitro group.[48] Fyfe[43] studied the visible and ^{1}H n.m.r. spectra of the dimethyl sulphoxide solution of 3,5-dinitropyridine with sodium methoxide. The bright red coloured solution produced has an absorption maxima at 487 nm, the ^{1}H n.m.r. spectrum shows the presence of new bands of equal intensity at 8·62, 8·3 and 6·08 p.p.m. while the bands in the parent molecule are at 9·73 and 9·14 p.p.m. This pattern is consistent with complex

(1.21). Although Fyfe[43] could not detect the formation of C_4 adduct (1.22),



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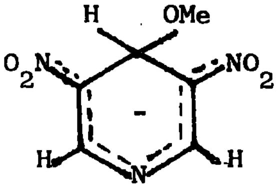

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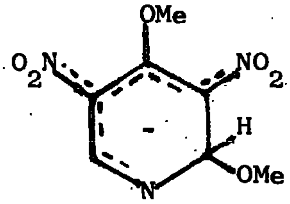

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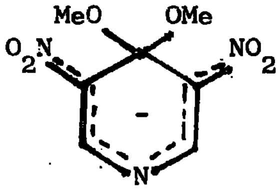
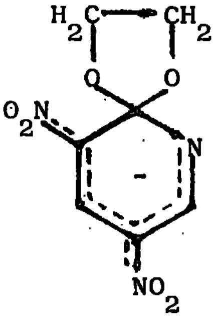


(1.24)

Biffin et al[49] have reported the initial addition of base at C_4 to give (1.22), which then decays to give more stable C_2 adduct (1.21). The same authors[49] have also confirmed the initial formation of C_2 adduct (1.23) from 4-methoxy-3,5-dinitropyridine with methoxide, which then transforms to the more stable C_4 adduct (1.24). Fyfe[43] also reported the formation of a spiro complex (1.25) from the addition of sodium methoxide to a dimethyl sulphoxide solution of 2-(2'-hydroxyethoxy)-3,5-dinitropyridine.



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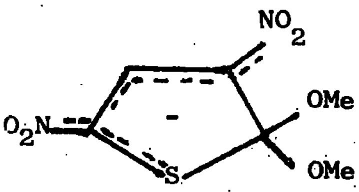

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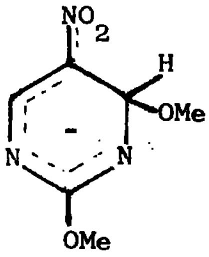
^1H n.m.r., visible and I.R. spectra are consistent for a Meisenheimer structure (1.26) for the product of high stability obtained from 2-methoxy-3,5-dinitrothiophene and sodium methoxide.[50] Biffin et al[51] also reported the formation of adducts (1.27) and (1.28) from 2-methoxy-5-nitropyrimidine and 5-nitropyrimidine, while 4-methoxy-5-nitropyrimidine gave the adduct (1.29).



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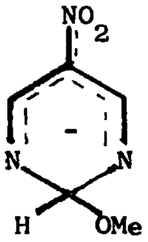

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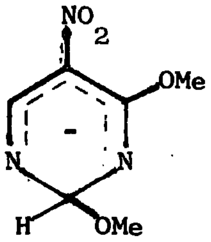
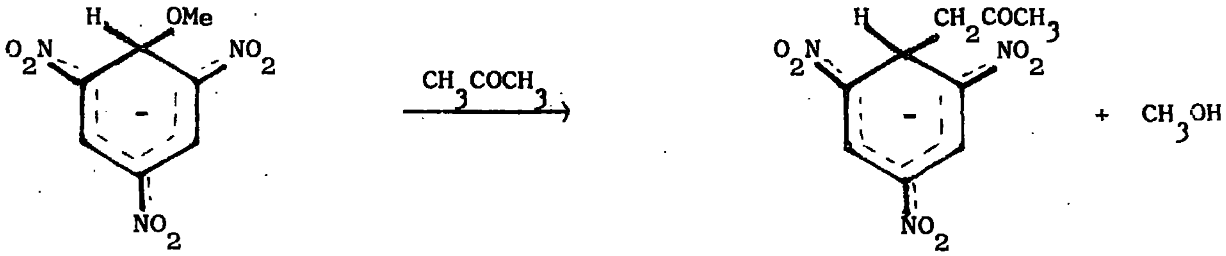


(1.29)

(c) Adducts with carbon bases

Foster and Fyfe[19], observed an alteration with time in the ^1H n.m.r. spectrum of the potassium methoxide adducts of 1,3,5-trinitrobenzene dissolved in acetone. The change indicates the transformation from (1.8) to (1.30).

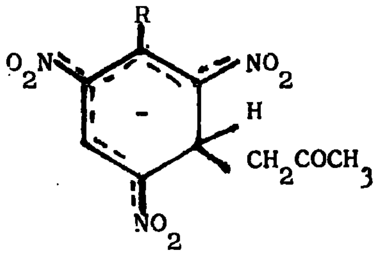


(1.8) (1.30)

The resonance of the proton at C_2 in (1.30) is at 5·70 p.p.m. and is split into a triplet (J ~ 9 Hz) through coupling with the adjacent methylene protons. Similar products can be obtained by the addition of base to solutions of 1,3,5-trinitrobenzene in a variety of ketones.[47,52,53] Acetonate ion is slowly generated by the loss of proton from ketone to amine:

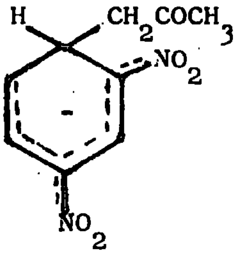
$$NEt_3 + CH_3COCH_3 \rightleftharpoons \overset{+}{N}HEt_3 + CH_3CO\overline{C}H_2$$

Thus 2,4,6-trinitrophenetole and 2,4,6-trinitrodiphenyl ether suffer acetonate attack at C_3 to give (1.31)[33], when triethylamine is added to a solution of the aromatic ether in acetone. The structure (1.31) is substantiated by ^1H n.m.r. spectrum.[33]

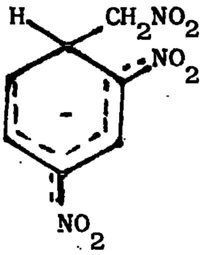


(1.31)

Carbanions can also give adducts with dinitrobenzenes. Thus Janovsky and Erb[54], reported the formation of intense purple colour when a solution of m-dinitrobenzene in acetone is treated with alkali. This reaction now more commonly known as 'Janovsky reaction' has been reviewed by Canback[55], who suggested structure (1.32) for the complex formed. Pollitt and Saunders[56] supported structure (1.32) by chemical and spectroscopic evidence.



(1.32)

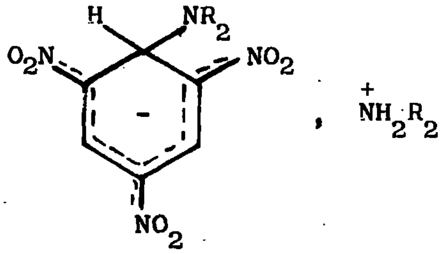


(1.33)

Recently the ^1H n.m.r. spectrum has been measured[36,47] and is consistent with structure (1.32).

Structure (1.33) is also reported to have been formed, when sodium methoxide is added to a solution of 1,3-dinitrobenzene in 60% dimethyl sulphoxide and 40% nitromethane. The ^1H n.m.r. and u.v. spectra bear close resemblance to that of (1.32).[47]

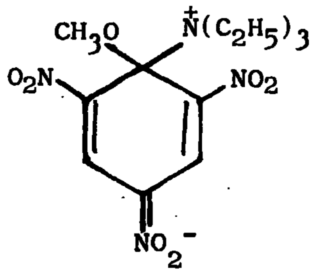
(d) Adducts with amines



(1.34)

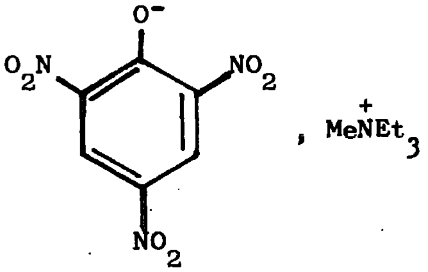
Structure (1.34) (R=H=alkyl) has been suggested[57] for the product of the reaction of 1,3,5-trinitrobenzene with primary and secondary amines, on the evidence of visible and ^1H n.m.r. spectra. The spectral characteristics of this adduct are similar to those of the 1,3,5-trinitrobenzene-methoxide adducts. The 2:1 stoichiometry for amine:1,3,5-trinitrobenzene is substantiated by conductance measurements[57] which show a linear increase in the conductance of solution of 1,3,5-trinitrobenzene in dimethyl sulphoxide with the increasing concentration of primary or secondary amine, up to a mole ratio of 2:1. Further increase in amine concentration results in little increase in conductance.

Picryl ethers form few Meisenheimer adducts with amines and usually dealkylation reactions occur with the formation of picric acid. An earlier report of the ^1H n.m.r. spectrum of Zwitterion (1.35) generated in dimethyl



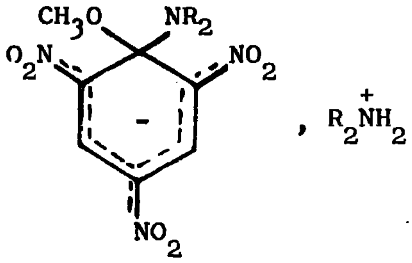
(1.35)

sulphoxide solution from 2,4,6-trinitroanisole and triethylamine[20] was later corrected; the spectrum was shown to result from methyltriethylammonium picrate (1.36).[58,59] With diethylamine the ^{1}H n.m.r. spectrum of 1,3,5-trinitroanisole in dimethyl sulphoxide solution has been attributed to C$_1$ adduct of structure (1.37) (R=C$_2$H$_5$)[20], but Strauss[7] argued that the ring proton resonance at 8·65 p.p.m.[20] could be that of the methyldiethylammonium picrate (1.36a). This would then explain the reported difficulty in equilibrating the product with its isomer (1.38) (R=Et), which can be prepared from sodium methoxide and N,N-diethylpicramide.

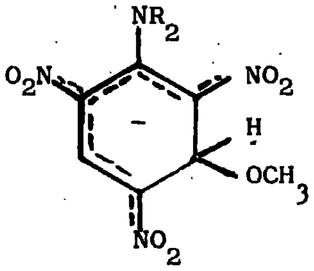


(1.36)

(1.36a, $\overset{+}{\mathrm{Me}\mathrm{N}}\mathrm{HEt}_2$)

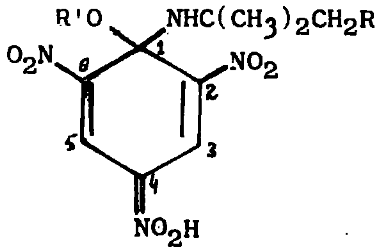


(1.37)



(1.38)

Clapp et al[60] reported the formation and characterisation of neutral complexes of the type (1.39) at low temperatures. Complex (1.39c), which is formed at -57° gives a deep red colour which changes to the bright yellow of a substituted picramide as the solution in tetrahydrofuran warms to room temperature. Complex (1.39a), in tetrahydrofuran solution gives a single ^{1}H



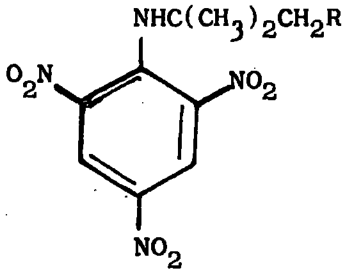
(1.39)

(1.39a, R=H; R'=C_6H_5)

(1.39b, R=H; R'=CH_3)

(1.39c, R=H; R'=$C_6H_2(CH_3)_3$)

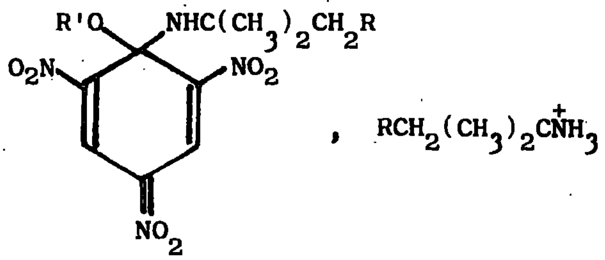
(1.39d, R=OH; R'=CH_3)



(1.40)

(In these complexes protonation of the 4-nitro group occurs)

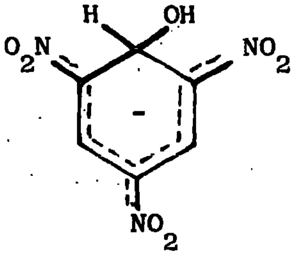
n.m.r. peak for the two equivalent ring protons at C_3 and C_5 (δ = 8·4 p.p.m.) the NO_2H proton resonate at 11·9 p.p.m., and the NH proton at C_1 gives a peak at 6·06 p.p.m. The low field peak at 11·9 p.p.m. disappears as the solution changes from red to yellow at room temperature, this being associated as the formation of picramide (1.40). When 2 moles of amine was used the low field peak at 11·9 p.p.m. due to NO_2H proton was not observed, instead a broad signal at 4·06 p.p.m. appeared, this is interpreted as being the salt of (1.39a), i.e. (1.41) (R=H, R'=C_6H_5).



(1.41)

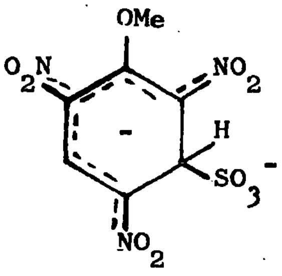
(e) Complexes with other nucleophiles

Foster and Fyfe[61] isolated red crystals from the reaction of 1,3,5-trinitrobenzene with hydroxide and assigned structure (1·42) to this complex. The visible and ^1H n.m.r. spectra are similar to those of the alkoxide analogue (1.8). Crampton[62] studied the visible and ^1H n.m.r. spectrum of 1,3,5-trinitrobenzene with sodium sulphite; the visible spectrum in aqueous solution shows a shift of absorption maximum from 462 nm to 490 nm with increased sulphite concentration; this change is attributed to the formation of a 1:2 stoichiometry adduct at higher nucleophile concentrations. The ^1H n.m.r. spectrum taken in water-dimethyl sulphoxide mixture also substantiated the visible results.

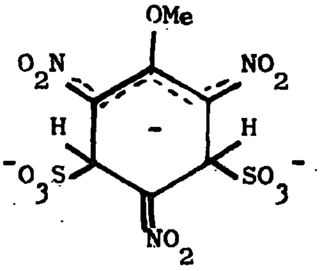


(1.42)

The ^1H n.m.r. spectra of 2,4,6-trinitroanisole with sodium sulphite[62] also indicates the formation of 1:1 and 1:2 adducts, (1.42) and (1.43) respectively.



(1.42)



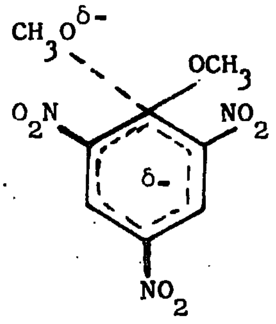
(1.43)

II. Relative Stabilities of Meisenheimer Complexes

(a) Variation with nature of parent molecule

The points which are demonstrated from the previous discussion are (i) the greater thermodynamic stability of adducts formed by alkoxide additions to a ring carbon already carrying an alkoxy group than those formed by addition at a ring carbon carrying hydrogen, and (ii) the kinetic preference for addition at an unsubstituted carbon atom. These two phenomena have been explained mainly in terms of steric arguments.[63-65] The greater stability of the adducts from alkoxy substituted substrates such as 2,4,6-trinitroanisole and 2,4-dinitroanisole over those from 1,3,5-trinitrobenzene and 1,3-dinitrobenzene is attributed to the steric relief experienced in the formation of 1,1-dimethoxypolynitrocyclohexadienate type complexes. It is argued that in compounds like 2,4,6-trinitroanisole the methoxyl group is subject to considerable strain by the flanking ortho nitro groups, but on complexation the two alkoxyl groups are no longer in the ring plane hence relieving steric strain. In the case of 1,3,5-trinitrobenzene and 1,3-dinitrobenzene there is no such driving force for the complexation. The crystallographic studies of Destro et al[14] and Ueda et al[16] substantiate the relief of steric strain on complex formation from 2,4,6-trinitrophenetol.

The kinetic preference for the formation of the thermodynamically less stable C_3 adduct in the case of 2,4,6-trinitroanisole and similar compounds has also been explained in terms of steric effects. It is argued[30] that although the C_1 complex is less strained than methyl picrate, nevertheless the transition state (1.44) leading to the formation of C_1 adduct is more strained than the transition state (1.45) leading to C_3 adduct. This rationalisation based on steric effects has been criticized[24], on the grounds that C_3 adducts were not observed with 1-methoxy-2,6-dinitrobenzene and



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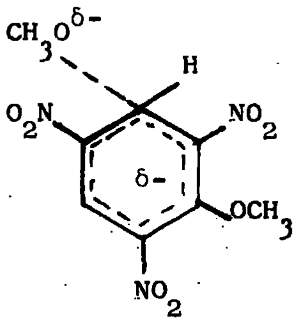
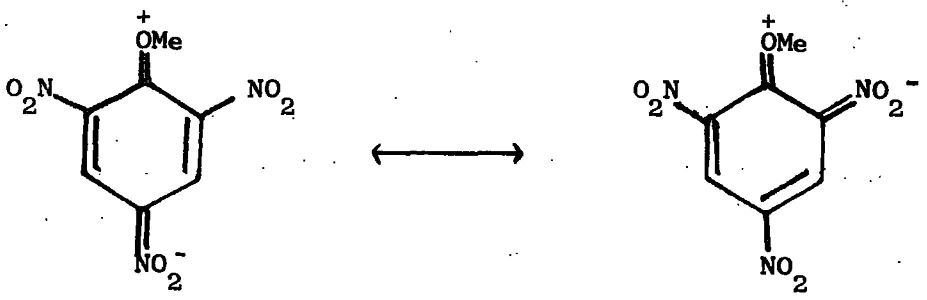
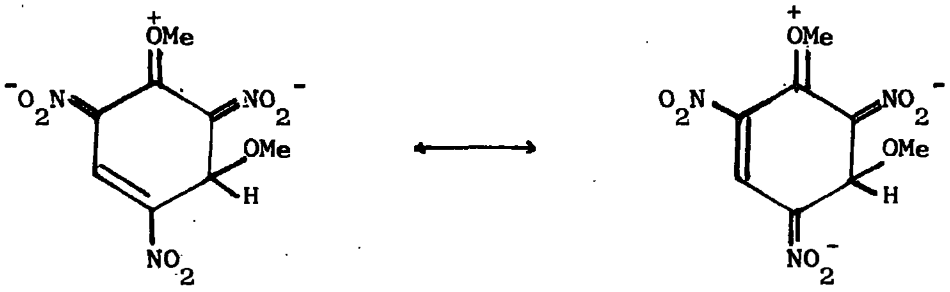


(1.45)

1-methoxy-2,4-dinitronaphthalene. The transition state leading to the C_3 adduct in the case of 1-methoxy-2,6-dinitrobenzene would be expected to be quite strongly favoured by steric factors, at the expense of the transition state leading to the C_1 complex. Bernasconi[66] argued that the greater stability of the C_1 adduct compared to C_3 adduct is due to the fact that multi-alkoxy substitution has a large stabilising effect on an sp^3 substituted carbon atom relative to a non-substituted or little substituted carbon atom as well as relative to an equally substituted sp^2 carbon. This explains the higher stability of the C_1 complex of 2,4,6-trinitroanisole compared to C_3 complex or the 1,3,5-trinitrobenzene complex. He further explained the faster formation of the C_3 complex relative to C_1 complex in terms of the ground state stabilisation of the parent anisole of the form:

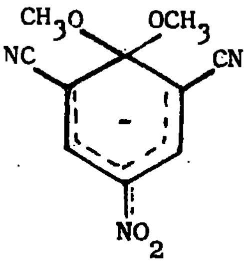


The above stabilisation factor still exists in a C_3 complex:

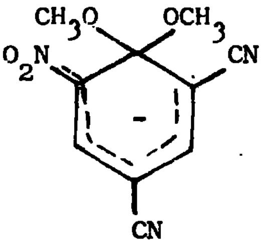


but fails to operate in an C_1 adduct. Thus reducing the rate of formation of C_1 complex, as this affects the ground state stabilisation of the parent compound.

Another important feature in the stabilisation of Meisenheimer complexes is the presence of a strongly electron withdrawing group para to the position of addition. Thus the equilibrium constant for the formation of (1.2) ($R=R'=CH_3$) is 500 times greater than that of (1.46) but 1700 times greater than (1.47). In general the stability of the Meisenheimer complexes increases with more efficient delocalisation of the negative charge.[7]



(1.46)



(1.47)

(b) Variations with attacking nucleophile

The subject was reviewed by Crampton.[3] Table 1.1 shows the equilibrium constants for the formation of 1:1 adducts from 1,3,5-trinitrobenzene with difference nucleophiles. However difference solvents have been used in obtaining these results so that it makes the comparison unrealistic as the stability of a given adduct depends considerably on the solvent used.

TABLE 1.1

Equilibrium Constants for Formation of Adducts from 1,3,5-Trinitrobenzene with Different Nucleophiles

Nucleophile	Solvent	K_1 (l.mole^{-1})	Reference
OMe^-	Methanol	$1{\cdot}54 \times 10^1$	63
SEt^-	Methanol	$3{\cdot}5 \times 10^3$	81
SPh^-	Methanol	$1{\cdot}95$	81
OPh^-	Methanol	$< 2 \times 10^{-3}$	81
OH^-	Water	$2{\cdot}7$	41
OEt^-	Ethanol	$1{\cdot}8 \times 10^3$	3
$SO_3^=$	Water	$2{\cdot}5 \times 10^2$	62
CN^-	Acetone	$1{\cdot}4 \times 10^5$	82
CN^-	Chloroform	$3{\cdot}5 \times 10^5$	82
OMe^-	D.M.S.O.	c.10^9	81
SPh^-	D.M.S.O.	8×10^4	81

Measurements made in methanol for different sulphur bases[7] give a decreasing order of affinity for 1,3,5-trinitrobenzene of $EtS^- > OMe^- > PhS^- > PhO^-$ which is not the same as the affinity of these nucleophiles towards protons $OMe^- > EtS^- > PhO^- > PhS^-$. These orders are dependent on the solvent used and are liable to change in different solvents. The equilibrium constants given in Table 1.1 measure the thermodynamic affinity of the nucleophiles towards an aromatic carbon atom, this affinity termed as 'carbon basicity', of the nucleophile differs from the 'Bronsted basicity', which measures the thermodynamic affinity for hydrogen, of the nucleophile.

It is also apparent from structural studies of Meisenheimer complexes, that the mode of interaction may also vary with the nature of the nucleophiles. Thus 2,4,5-trinitroanisole forms thermodynamically stable adducts with OMe^-, N_3^- or NEt_2^- by addition at C_1, while with $SO_3^=$ or $CH_3COCH_2^-$ stable adducts result from attack at unsubstituted ring carbon. This has been attributed to steric requirements. Similarly with nitroanilines where the nucleophile could either abstract an amino proton or form an addition complex, the ultimate product depends upon the base; thus while oxygen bases (OMe^-) abstract an amino proton, sulphur bases like SEt^- or SPh^- form addition complexes at an unsubstituted ring carbon.

(c) Solvent effects

The choice of solvent has a large effect on the stabilities of Meisenheimer complexes. This variation is partly due to the different solvating capacities of different solvents; for example the solvation of anions changes considerably between protic and dipolar aprotic solvents.[67-69] Protic solvents such as water formamide and methanol have 'strong' structures involving hydrogen bonds and are good hydrogen bond donors. Thus small anions which are strong hydrogen bond acceptors (e.g. OH^-, Cl^-, $CH_3CO_2^-$) are better solvated by protic solvents. In contrast dipolar aprotic solvents have 'weaker' structures and high dipole moments, and are very polarisable; thus large anions, which are polarisable but are poor hydrogen bond acceptors and fit poorly into the hydrogen bonded solvent structure (e.g. PhS^-, picrate$^-$) are better solvated by dipolar aprotic solvents such as dimethyl sulphoxide. In general polarisable large solutes whether anions, cations or polar molecules (e.g. nitroaromatics) are better solvated by dipolar aprotic solvents than by protic solvents like water or formamide in which usually only strong hydrogen bond acceptors (like small anions) are well solvated. The result is that the bimolecular reactions of anions are more accelerate and reactions of large polarisable anions are least accelerate, in the change from protic to dipolar aprotic solvent.

Fendler et al[70] have shown that the increase in the equilibrium constant for the formation of sodium-1,1-dimethoxy-2,4-dicyano-6-nitrocyclohexadienate and sodium-1,1-dimethoxy-2,6-dicyano-4-nitrocyclohexadienate with dimethyl sulphoxide concentration in the dimethyl sulphoxide-methanol solvent mixture is due to an increase in the rate constant for complex formation k_1, and a decrease in the rate constant for the decomposition of the complex k_{-1}. These results are rationalised as better solvation of methoxide ion in methanol through hydrogen bonding but gradual desolvation of this anion as the dimethyl sulphoxide concentration is increased, hence making methoxide ion more available for attack in higher dimethyl sulphoxide concentrations and thus increasing k_1. Similarly a decrease in the value of k_{-1} with increasing dimethyl sulphoxide concentration is associated with the better solvation of the highly polarisable Meisenheimer complex. It is now known[20,30] that in higher dimethyl sulphoxide concentrations the initial complex formed from 2,4,6-trinitroanisole and sodium methoxide is the C_3 adduct (1.7) (R=R'=Me). It seems that the formation of 1,1-adduct is catalysed by the increasing concentration of methanol in dimethyl sulphoxide-methanol solvent system.

It looks more probable that instead of changing the basic mode of interaction, dimethyl sulphoxide increases the efficiency of the interaction between base and the nitro compound. The arguments given so far are qualitative in nature and oversimplification of a much more complex phenomena. However the knowledge of relative enthalpies and entropies of reactants and transition states will provide with more quantitative insight of this problem, one should also consider the changes in the activity coefficients of the reactants and of the transition states as a function of solvent system.

Recently Larsen and Fendler et al[71-73] have measured the enthalpy changes for the reaction of 2,4,6-trinitroanisole with sodium methoxide. The heat of formation of the 1,1-Meisenheimer complex from sodium thiophenoxide and 1,3,5-trinitrobenzene have also been measured across the dimethyl sulphoxide-methanol solvent system. The enthalpies of transfer of the reactants and the products have also been measured in dimethyl sulphoxide-methanol solvent system. It is interesting to compare the heat of transfer from methanol to methanolic dimethyl sulphoxide. For sodium methoxide the enthalpy of transfer from pure methanol to 95% dimethyl sulphoxide-methanol (V/V) mixture is positive with $\Delta H \sim 10$ kcal/mole, while the ΔH value for sodium thiophenoxide for a similar solvent change is negative ($\Delta H \sim -0{\cdot}94$ kcal/mole). The heat of transfer of the complex (1.2) (R=R'=Me) is negative $\Delta H \sim -7$ kcal/mole on going from pure methanol to a 95% dimethyl sulphoxide-methanol (V/V) mixture. A similar change is observed for the complex of 1,3,5-trinitrobenzene with sodium thiophenoxide. Comparison of the enthalpies of solution indicates as expected[68], that for the small less polarisable methoxide anion the ΔH value is positive in aprotic dimethyl sulphoxide compared with pure methanol indicating the destabilisation of methoxide ion in the aprotic medium, probably by the loss of solvation enjoyed in methanol through hydrogen bonding. As expected the ΔH values for the complexes is negative in dimethyl sulphoxide compared with methanol indicating the better solvation of such highly polarisable species with greatly delocalised π system in aprotic solvent. Phenoxide ion which is much less polarisable with lesser delocalised system than Meisenheimer complex but more polarisable and much bigger than methoxide ion is stabilised in dimethyl sulphoxide but to a very much smaller extent than the complex. Similarly polarisable molecules 2,4,6-trinitroanisole and 1,3,5-trinitrobenzene also have a more negative enthalpy of solution in dimethyl sulphoxide than in methanol with $\Delta H \sim -1{\cdot}8$ kcal/mole and $-0{\cdot}91$ kcal/mole respectively in 95% dimethyl sulphoxide-methanol (V/V) solvent system compared to pure methanol.

The change in the heat of reaction between sodium methoxide and 2,4,6-trinitroanisole as the solvent is changed from pure methanol to dimethyl sulphoxide-methanol 95:5 (V/V) mixture is $\Delta H \sim -15$ kcal/mole; while the ΔH value for the reaction of 1,3,5-trinitrobenzene and sodium thiophenoxide changes from $\sim -3{\cdot}7$ kcal/mole in 10% dimethyl sulphoxide-methanol mixture to $\Delta H \sim -9{\cdot}9$ kcal/mole in 100% dimethyl sulphoxide. The greater change in ΔH for the former reaction is due to the fact that methoxide ion is destabilised as the concentration of dimethyl sulphoxide is increased, while the stability of thiophenoxide ion is greater in dimethyl sulphoxide, compared with pure methanol, however in both cases the complex formed is better solvated in dimethyl sulphoxide.

Fendler and Larsen[72] also measured the free energy changes for the reaction of sodium methoxide with 2,4,6-trinitroanisole, and the free energy and entropy of transfer of 2,4,6-trinitroanisole and complex from pure methanol to methanolic dimethyl sulphoxide solution. These results show that the largest change due to solvent variation is the increase in the free energy of sodium methoxide $\Delta G \sim 0{\cdot}91$ in 10% dimethyl sulphoxide-methanol (V/V) mixture to $\Delta G \sim 1{\cdot}93$ kcal/mole in 30% dimethyl sulphoxide-methanol mixture. This then substantiates the argument that the destabilisation of methoxide ion in dimethyl sulphoxide plays an important role in the ease of formation of Meisenheimer complexes in this media. The reaction between 1,3,5-trinitrobenzene and sodium thiophenoxide is isoentropic up to 95% dimethyl sulphoxide-methanol mixture ($\Delta S \sim 9$ e.u.), in contrast the change in entropy for the reaction of sodium methoxide with 2,4,6-trinitroanisole is from 3·05 e.u. in methanol to -2·45 e.u. in 30% dimethyl sulphoxide-methanol (V/V) mixture.

Buncel et al[74] investigated the effect of different alcoholic solvents on the equilibrium constant for the formation of the 1,3,5-trinitrobenzene adduct with cyanide ion. The large increase in the value of K in t-butanol (5×10^5 l/mole) compared with that in methanol (40 l/mole) is associated with a large enthalpy of reaction (-15 kcal/mole) and a large negative entropy change (-25 e.u.) in t-butanol while in methanol the enthalpy change is approximately zero and the entropy is small and positive. These results could be rationalised in terms of desolvation of cyanide ion in t-butanol compared to methanol which is a better hydrogen bond donor.

(d) Use of acidity functions

Hammett and Deyrup[75] described the acidity of concentrated solutions of strong acids as the ability of the acid solution to protonate a neutral solute species (also termed as indicator). Thus for the equilibrium of the type:

$$B + H^+ \rightleftharpoons BH^+$$

an acidity function was defined by equation 1.1

$$H_o = pK_{BH^+} - \mathrm{Log}_{10} \left(\frac{[BH^+]}{[B]}\right) \qquad 1.1$$

Where pK_{BH^+} is the acid dissociation constant for BH^+ which is the conjugated acid of B, and ($[BH^+]/[B]$) is the directly observable concentration ratio of the indicator in its two different forms.

In equation 1.1 the evaluation of H_o requires the knowledge of the ionisation ratios ($[BH^+]/[B]$) of the 'indicator' and the dissociation constant of their conjugate acids. The spectrophotometric methods provide a dependable means for the purpose. But to achieve reliable results from this method it is required that the indicator base should have an electronic absorption spectrum measureably different from that of its conjugate acid. Also the extinction coefficient of either B or BH^+ at the wavelength selected for study must be such that the concentration of indicator necessary for measureable absorption changes has negligible effect on the overall acidity of the medium.

The evaluation of pK_{BH^+} follows directly from knowledge of ($[BH^+]/[B]$) as a function of acid concentration. From the definition of pK_{BH^+} in equation 1.2 it follows for infinite dilution when all activity coefficients equal to unity that equation 1.3 is valid.

$$pk_{BH^+} = -\mathrm{Log}_{10} \left(\frac{[B]\ f_B}{[BH^+]\ f_{BH^+}} \cdot a_{H^+}\right) \qquad 1.2$$

$$pK_{BH^+} = \mathrm{Log}_{10} ([BH^+]/[B]) - \mathrm{Log}_{10} [H^+] \qquad 1.3$$

The knowledge of pK_{BH^+} provides the correct thermodynamic dissociation constant K_{BH^+} referred to pure solvent as standard state. For weaker bases direct determination of pK_{BH^+} is not feasible and therefore a stepwise comparison technique is used.[75] The subject has been reviewed by Paul and Long[76], which relates mostly to acid solutions. However more recently Rochester[77] reviewed the acidity function concept related to strongly basic media, the general rules and behaviour are essentially similar to those for strong acid solutions, and the H_- acidity function measures the ability of the strongly basic solution to abstract a proton from the weakly acidic neutral solute SH. It is defined by equation 1.4.[78,79]

$$SH + OH^- \rightleftharpoons S^- + H_2O$$

$$H_- = pK_{SH} + \mathrm{Log}_{10}\,([S^-]/[SH]) \qquad 1.4$$

The J_- acidity function applies for equilibria where instead of proton abstraction an addition of base takes place to a neutral indicator molecule R. The H_- acidity function and J_- function would not be expected to behave identically. In aqueous solutions the J_- function measures the ability of an aqueous base solution to add hydroxide ions to a neutral indicator molecule R,[80]

$$R + OH^- \rightleftharpoons ROH^-$$

quantitatively J_- is defined by equation 1.5,

$$J_- = p(KK_W) + \mathrm{Log}_{10}\,([ROH^-]/[R]) \qquad 1.5$$

where K denotes the formation of addition complex ROH^-. Similarly Rochester[77] defined a J_M acidity function for methanolic sodium methoxide referred to pure methanol as standard state, (e.g. equation 1.6).

$$J_M = p(KK_{MeOH}) + \mathrm{Log}_{10}\,([ROMe^-]/[R]) \qquad 1.6$$

Where pK_{MeOH} is the autoprotolysis constant of methanol and K is the thermodynamic equilibrium constant for methoxide addition to the neutral indicator molecule R.

CHAPTER 2

EXPERIMENTAL

I. Solvents

Methanol: A.R. methyl alcohol was used either as such or was boiled to remove carbon dioxide and subsequently protected from air with a soda-lime guard tube.

Dimethylsulphoxide: The commercial material was purified by standing over calcium hydride and subsequent distillation under reduced pressure. The middle fraction was collected and stored in a desiccator containing silica gel.

Acetone: A.R. acetone was used without purification.

II. Solution of Bases

Sodium Hydroxide: The solutions were prepared from A.R. sodium hydroxide. First the pellets were washed with distilled water and the washing discarded; the remaining solid, sodium hydroxide, was then dissolved in distilled water and standardised by titration with standard hydrochloric acid.

Sodium Methoxide: was prepared by dissolving sodium metal in A.R. methanol. The freshly cut pieces of the metal were first washed with methanol and then dissolved in methanol in a nitrogen atmosphere. The solutions of the alkali metal methoxide so obtained were clear, but more concentrated solutions were sometimes cloudy, such solutions were centrifuged to obtain clear solutions of alkali. The concentrations were determined by titration with standard hydrochloric acid.

Potassium Methoxide: The freshly cut pieces of potassium metal were dissolved in A.R. methanol taking the precautions as above with sodium methoxide.

Lithium Methoxide: The solution was prepared by dissolving lithium metal in A.R. methanol. The procedure being the same as with sodium methoxide preparation.

III. Nitro Compounds

1,3,5-Trinitrobenzene: Commerical 1,3,5-trinitrobenzene was recrystallised from methanol to constant m.p. 121°C (lit. 122·5°C).[83]

2,4-Dinitroanisole: was a recrystallised commercial sample m.p. 95°C (lit. 95°C).[83]

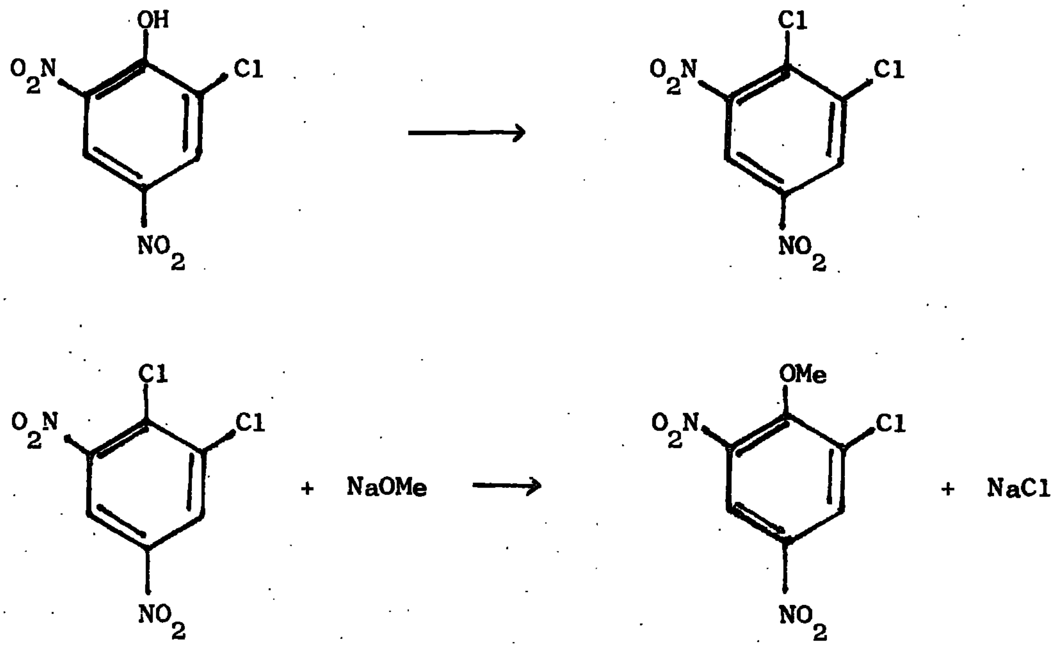
2,4,6-Trinitroanisole: M.p. 67°C (lit. 68°C)[83] and 2,6-dinitroanisole m.p. 118°C (lit. 118°C)[83] were samples prepared by Dr. M.A. El Ghariani.

1-Iodo-3,5-dinitrobenzene: Commercial specimen was used without purification.

1-Cyano-3,5-dinitrobenzene: Commercial specimen was used without purification.

1,3-Dimethoxy-4,6-dinitrobenzene: was prepared by the method of Holleman.[84] 10 g. of 4,6-dinitro-1,3-dichlorobenzene was dissolved in about 200 mls. of hot methanol, and 2 equivalents of conc. methanolic sodium methoxide ($\sim$ 5·0$\underline{\underline{M}}$) was added with stirring. The reaction mixture was refluxed for one hour. The solution was allowed to cool and the solid product was filtered and purified through recrystallisation from methanol. M p. 152°-154°C (lit. 154°-157°).[84] The ^{1}H n.m.r. spectrum of the purified sample in dimethylsulphoxide showed two bands of equal intensity at δ 8·66 and 7·06 p.p.m. due to the two ring protons and a more intense band at 4·12 p.p.m. due to the two equivalent methoxyl groups.

2-Chloro-4,6-dinitroanisole: was prepared by the method of Ulman and Sane[85] in two stages.



(a) Chlorination of 2-chloro-4,6-dinitrophenol: The substrate (22 g.) was warmed with 20 g. of toluene sulphonyl chloride and 30 g. of diethylaniline for five hours on a water bath at 100°C. The dark brown fused mass was treated with dilute hydrochloric acid when the required product is left as a grey crystalline mass. This was triturated with dilute hydrochloric acid several times and the solid was filtered off. The resulting solid mass was warmed with conc. sulphuric acid (d = 1·84) on a water bath for three hours and then poured onto crushed ice. The resulting solid was filtered off and washed with water. Yield 26 g. The crude product was decolourised with animal charcoal in ethanol and recrystallised from ethanol giving pale yellow crystals, m.p. 56°C.

(b) The dichloro compound obtained as above was dissolved in hot methanol and 1 equivalent of sodium methoxide was added with stirring. The reaction mixture was heated on a water bath for two hours, allowed to cool then acidified with dilute hydrochloric acid when the required anisole separates as a pale grey oil. This was separated and solidified by addition of solid CO_2, then recrystallised from methanol to give light yellow plates, m.p. 37°C (lit. 37°C).[84]

<u>4-Chloro-2,6-dinitroanisole</u>: was prepared in two stages by the method of Holleman and Hollander.[84] First the nitration of 1,4-dichloro-2-nitrobenzene (100 g.) was carried out by placing a nitrating mixture of 85 mls. of (70%) nitric acid and 183 mls. of oleum in a two litre round bottomed flask, and heated to 60°C. 100 g. of crude 1,4-dichloro-2-nitrobenzene was added gradually in the course of twenty minutes, with constant stirring and the temperature was kept below 75° by water cooling. The mixture was then heated at 75-85° for forty minutes, after which the temperature was raised to 120° in fifteen minutes and maintained for another eighty minutes. The temperature was allowed to fall to 80°, after which 200 mls. of water was slowly run in with stirring. The mixture was allowed to settle and the molten product separated. This was washed with boiling water until the washed water was no longer acidic. It was then allowed to solidify and the solid cake wiped dry from adhering moisture, then dried in the molten state at 100°C for a few hours.

The product so obtained is a mixture of two isomers, 2,6- and 2,3-dinitro-p-dichlorobenzene.[84] The separation of these two isomers was achieved by dissolving the reaction product in benzene so as to form a concentrated solution. Sufficient light petroleum (60-40) was added to precipitate about half of the dissolved substance, which was filtered off. The material in the mother liquor was recovered. Each of the two fractions was then separately dissolved in benzene and precipitated with light petroleum as before. The process was repeated twice and thus a less soluble and a more soluble fraction was obtained. The two fractions were separately recrystallised from carbon tetrachloride. The recrystallised product obtained from the less soluble fraction gives a melting point of 105-106°C and is 1,4-dichloro-2,6-dinitrobenzene. The other fraction has a m.p. of 101-102°C. The two isomers were isolated in similar quantities.

1,4-Dichloro-2,6-dinitrobenzene obtained as above was dissolved in hot methanol, and a little over one equivalent of conc. solution of methanolic sodium methoxide was added gradually with stirring. The reaction mixture was heated on a water bath for about an hour and allowed to cool, then acidified with dilute HCl when anisole separates. It was purified by recrystallisation from methanol, m.p. 65·5°C (lit. 66°).[84]

2-Methoxycarbonyl-4,6-dinitroanisole: was prepared from 2-chlorobenzoic acid in three stages.

(a) 62 g. of 2-chlorobenzoic acid and 300 mls. of conc. sulphuric acid (d = 1·84) were placed in a two litre round bottomed flask and warmed on an electrical mantle with mechanical stirring until the benzoic acid dissolved. 100 mls. of fuming nitric acid (sp. gr. 1·54) was added with stirring and the mixture was allowed to stand for about an hour, when a solid mass accumulated on the surface. The mixture was heated at 90-100°C for three hours, allowed to cool down and then 75 mls. of more fuming nitric acid (sp. gr. 1·54) was added with stirring and the reaction mixture was then heated at 100-110°C for a further three hours. The mixture was allowed to stand overnight and was then poured onto crushed ice. The resulting solid was filtered off and pump washed with water and dried, m.p. 199°C (lit. 199°C).[83]

(b) 20 g. of the resulting 3,5-dinitro-2-chlorobenzoic acid obtained as above was dissolved in about 150 mls. of Analar methanol and 10 mls. of conc. sulphuric acid (d = 1·84) was added. The mixture was then heated on a water bath for an hour and then allowed to cool, when the methyl ester of the acid separated as a crystalline solid. This was filtered and washed with aqueous sodium bicarbonate, then water, and recrystallised from methanol, m.p. 87°C (lit. 87°C).[83]

(c) The methyl ester of 2-chloro-3,5-dinitrobenzoic acid obtained as above was subjected to nucleophilic replacement of chlorine by methanolic sodium methoxide and the resulting anisole was crystallised from methanol, m.p. 68°C (lit. 69°C).[86]

<u>4-Methoxycarbonyl-2,6-dinitroanisole</u>: was prepared by the esterification of 4-chloro-3,5-dinitrobenzoic acid obtained commercially, followed by nucleophilic substitution of chlorine by methoxide. The resulting anisole was purified through recrystallisation from methanol, m.p. 45°C (lit. 54°C)[87] (Found: C, 42·0; H, 2·9; N, 10·7%. Required: C, 42·1; H, 3·1; N, 10·9%).

<u>4-Trifluoromethyl-2,6-dinitroanisole</u>: was prepared from commercial 4-trifluoromethyl-2,6-dinitrochlorobenzene. The substrate was dissolved in hot methanol and a little over one equivalent of conc. methanolic sodium methoxide was added with stirring. The reaction mixture was refluxed for an hour and allowed to cool, then neutralised with dilute hydrochloric acid when anisole separates as solid. The product was purified by recrystallisation from methanol, m.p. 60°C (lit. 60°C).[88]

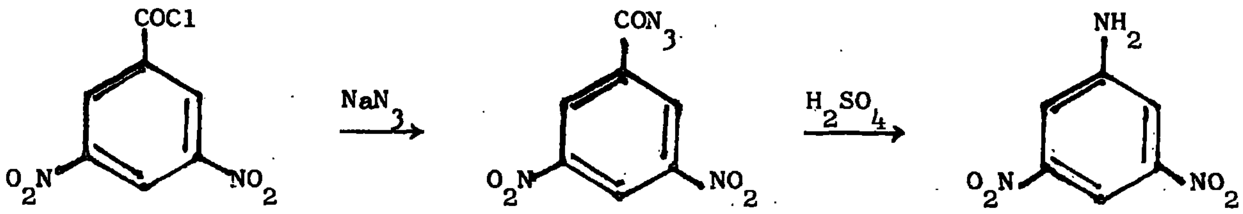
<u>2-Fluoro-4,6-dinitroanisole</u>: was prepared as a yellow oil by the method of Schiemann.[89] The clear mixture from 31·5 g. of o-fluoroanisole and

40 mls. of conc. sulphuric acid was added dropwise with stirring to a nitrating mixture of 30 mls. conc. sulphuric acid and 27 mls. of conc. nitric acid (d = 1·51) at -5 to 0°C. After four hours standing, the mixture was poured onto ice, when an oil separated. This was extracted with ether, then washed with ice cold solution of sodium bicarbonate. The ethereal solution was dried with calcium chloride, and the ether was evaporated off. The resulting oil was purified by distilling under reduced pressure.

3,5-Dinitroaniline: was prepared by the method of Banksma and Verberg[90] in two stages.

(a) 20 g. of 3,5-dinitrobenzoyl chloride was suspended in 60 mls. of glacial acetic acid and 6 g. of sodium azide was added in small portions with shaking. The mixture was allowed to stand for half an hour, then water was added when 3,5-dinitrobenzazide separated as white needles, m.p. 107°C. Yield 70%.

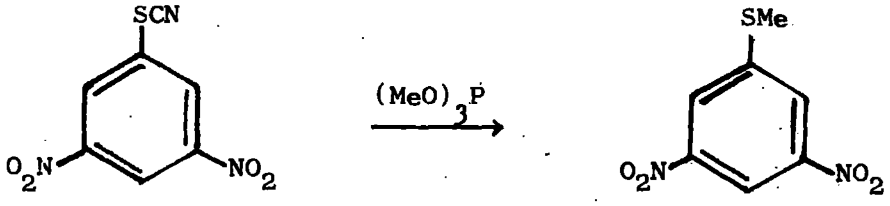
(b) 10 g. of 3,5-dinitrobenzazide was introduced into 40 mls. of conc. sulphuric acid and the mixture was gently warmed on a water bath; the solid dissolved with evolution of gas. Gradually the water bath was heated up to boiling point. The reaction mixture was then allowed to cool and poured into water, then neutralized with ammonia when 3,5-dinitroaniline separated as a bright yellow solid, m.p. 163°C (lit. 163°C).[83]



3,5-Dinitrothiocyanobenzene: was prepared by the method of Gatterman and Hausnecht.[91] 30 g. of 3,5-dinitroaniline was dissolved in a mixture of 1:2 proportion concentrated sulphuric acid and water, and diazotised with 12 g. of sodium nitrite at 5°C. To the diazotised solution was added (at 0°C) a concentrated aqueous solution of 18 g. KSCN and then gradually a paste of cuprous thiocyanate prepared thus: a mixture of 40 g. copper sulphate and 75 g. ferrous sulphated was dissolved in water, then 18 g. KSCN was added and the precipitate was filtered off.

The reaction mixture was stirred for three hours to complete the reaction, it was then neutralised with sodium carbonate and filtered. The solid mass which contains the desired product was washed with water and extracted with benzene several times. All the benzene extracts were mixed and dried over anhydrous sodium sulphate. The solvent was then distilled off using a rotary pump. The residue, which consists of 3,5-dinitrothiocyanobenzene together with some impurities, was dissolved in hot methanol when the desired component dissolves while the impurity remains insoluble. After filtration the methanol was distilled off and the residue recrystallised from methanol, m.p. 100-105°C (lit. 102°C).[92]

3,5-Dinitrothioanisole:



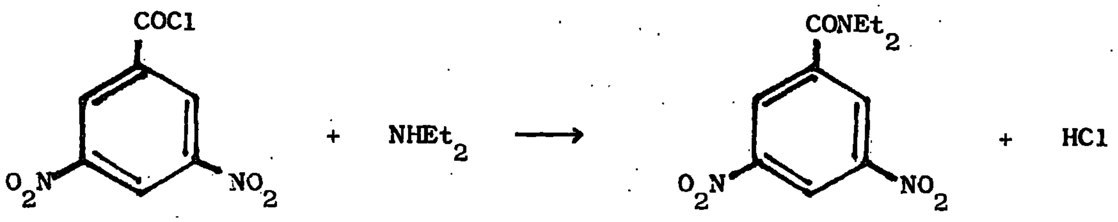
was prepared by the method of Pilgram and Korte;[92] in a round bottomed flask fitted with reflux condenser, dropping funnel and a stirrer, was placed 0·1 mole of 3,5-dinitrothiocyanobenzene and 0·2 moles of trimethylphosphate was added dropwise with stirring, the temperature being kept down by keeping the flask in crushed ice. The reaction mixture was allowed to stand for one hour and then methanol was added and the thio ether crystallised, m.p. 121°C (lit. 121°C).[92]

1-Methylsulphonyl-3,5-dinitrobenzene: was prepared by dissolving 3,5-dinitrothioanisole in the minimum quantity of acetic acid and adding a slight excess of peracetic acid. The resulting mixture was evaporated until about one fifth of the reaction mixture was left. On cooling the desired product crystallised out, m.p. 238°C (lit. 240°C).[92]

1-Trifluoromethyl-3,5-dinitrobenzene:[93] was prepared by the nitration of 3-nitrobenzotrifluoride. To a stirred mixture of 450 g. of fuming nitric acid (d = 1·50) and 900 g. of fuming sulphuric acid (20% SO_3) was added slowly 57 g. of 3-nitrobenzotrifluoride. The temperature was controlled so as not to exceed 100°C for the first ninety minutes. After this period the temperature was raised and maintained at 115°C for the next four to five hours. The reaction mixture was then poured onto crushed ice and the crude product separated as a white solid.

The product was filtered at a water pump, washed with water, and dried. Yield 43 g. (50%), recrystallised twice from methanol, m.p. 50°C (lit. 49-50°C).[93]

N,N-diethyl-3,5-dinitrobenzamide:[94]



was prepared from 3,5-dinitrobenzoylchloride. To 25 mls. of diethylamine (excess) in 100 mls. of heated benzene was slowly added 23 g. of 3,5-dinitrobenzoylchloride. The resulting mixture was poured into water. The benzene layer was separated and washed thrice with water. The solvent was then distilled off and a solid precipitated on addition of petroleum ether. This was recrystallised from ethanol-petroleum ether to give white crystals, m.p. 92°C (lit. 92°C).[94]

3,5-Dinitrobenzenesulphonic acid:[95] This was prepared by the direct sulphonation of m-dinitrobenzene. A mixture of 50 g. of m-dinitrobenzene and 150 mls. of 18% oleum was heated with 4·5 g. of mercury at 150-160°C for eight to nine hours. Reaction mixture was allowed to cool and then poured onto ice and neutralized with milk of lime (calcium carbonate). The deep purple coloured filtrate turned orange as the liquid evaporated. The potassium salt was obtained by adding the calculated quantity of K_2CO_3 and evaporating the solution until crystallisation begins. Yield 35% (40 g.).

In all cases the ^1H n.m.r. spectra of these nitro-compounds in dimethyl sulphoxide as solvent, gave bands consistent with the required structures and showed that the products were $>$95% pure.

IV. Spectroscopic Measurements

Visible Spectra: Visible spectroscopy has been found very useful in the kinetic and equilibrium studies of Meisenheimer complexes. Thus this technique was used in the present work for this purpose. The general shape of the visible spectra were recorded on Unicam SP800 and SP8000 instruments at room temperature 20±2°C. However for quantitative purposes the accurate values of the optical density at suitable wavelengths were measured on an SP500 spectrophotometer, fitted with a thermostatted cell compartment (25°C).

Stock solutions were prepared as near the time of use as possible and the test solutions were made up from stock solutions immediately before the measurements were made. In some cases complete conversion of the parent substrate to complex could be achieved in the basic media used. In these cases the extinction coefficient ϵ_M of the complex M could be found directly using Beer's law.

$$\text{Optical density} = \text{Log}_{10} \frac{I_o}{I} = \epsilon_M . C_M . 1$$

where C_M is the concentration of complex and 1 the pathlength of the cell used (1 cm. in this work). The concentration of complex in less basic media could then be determined.

If however the extinction coefficient of the complex could not be directly determined then the Bensi-Hildebrand[96] expression:

$$\frac{a}{O{\cdot}D} = \frac{1}{\epsilon_M{\cdot}K} \cdot \frac{1}{NU} + \frac{1}{\epsilon_M}$$

was used, where a is the stoichiometric concentration of the parent compound. Thus from a linear plot of $\frac{a}{O{\cdot}D}$ versus $\frac{1}{NU}$, the extinction coefficient ϵ_M and equilibrium constant K could be determined.

Proton Nuclear Magnetic Resonance Spectroscopy:

A Varian A60 spectrometer was used for this purpose. Measurements were usually made at ambient probe temperature. Test solutions were of concentration from 0·2 to 0·5 mole 1^{-1} and tetramethylsilane was used as internal reference.

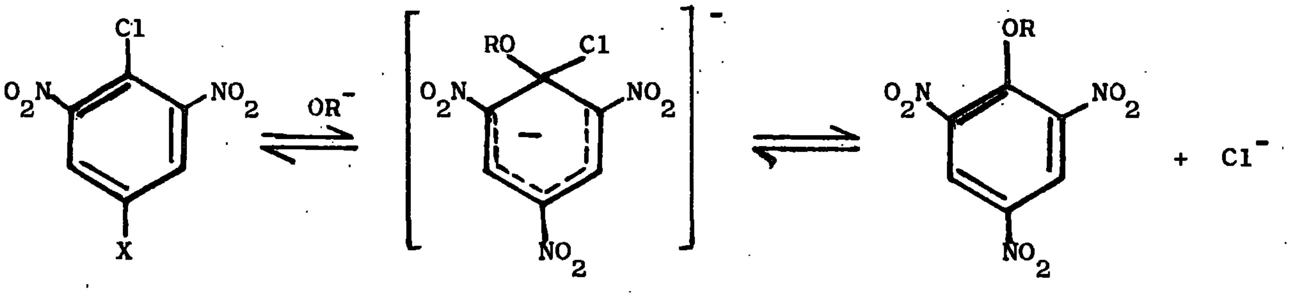
CHAPTER 3

A SPECTROSCOPIC STUDY OF THE INTERACTION OF 2,6-DINITRO-4-X-CHLOROBENZENES AND RELATED ANISOLES WITH NUCLEOPHILES

Introduction

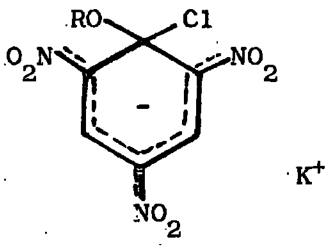
The initial formation of a 1,3-Meisenheimer complex by methoxide ion addition at an unsubstituted carbon atom in 2,4,6-trinitroanisole, was observed by Service.[20] However this species although kinetically favoured is not stable and isomerises to the thermodynamically more stable classical 1,1-Meisenheimer complex[18,20] where addition occurs at a ring carbon carrying methoxyl group. Since then similar results have been obtained with a variety of substituted anisoles including 4-cyano-2,6-dinitroanisole and 3,5-dinitro-4-methoxpyridine.[4,24,30,33,46,97] The initial addition at an unsubstituted carbon has been rationalised in terms of steric factors.[30] In the present work complex formation from 1-chloro-2,6-dinitro-4-X-benzenes has been investigated. In this case because of the established S_N2 mechanism one would expect the nucleophilic substitution of halide ion by incoming nucleophile to occur through Scheme 3.1.

SCHEME 3.1

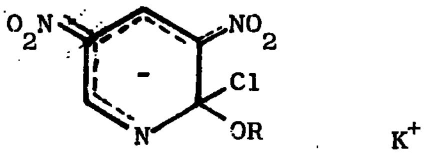


And indeed methyl picrate can be produced from picryl chloride and methanolic sodium methoxide in quantitative yields.

Very recently Syper and Barycki[98] (1972) reported to have isolated coloured solids by reacting picryl chloride and 2-chloro-3,5-dinitropyridine with various potassium alcoholates in hydrocarbon solvents. The reaction is reported to have been reversible and the parent substrates can be obtained by treating the solid adduct with trifluoroacetic acid. Structure (3.1) has been suggested for the complex formed, similarly by analogy structure (3.2) is given to the adduct of 2-chloro-3,5-dinitropyridine with alkoxides.

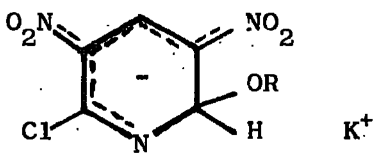


(3.1)

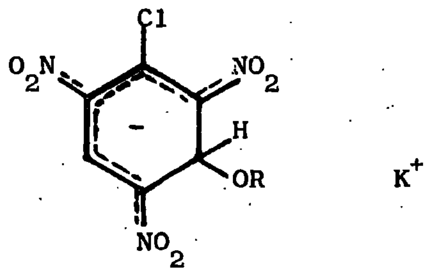


(3.2)

The authors while not discarding the possibility of the formation of Meisenheimer type adducts (3.3) and (3.4) argued that because of the



(3.3)



(3.4)

substantial differences between polynitroaromatic ethers and polynitroaromatic halides, analogies in reaction mechanism of the two types of polynitroaromatics with nucleophiles have limited application. It is further argued that because of the difference inductive effects of chlorine and an alkoxy group, one would expect a greater difference in electron density at C_1 and C_3 in picryl chloride than in picryl ether. This decreased electron density at C_1 compared with C_3 in picryl chloride coupled with the smaller steric requirements of chlorine atom than that of alkoxyl group, can favour kinetically and thermodynamically the addition to the 1-position of picryl chloride and to the 2-position of 2-chloro-3,5-dinitropyridine compared to picryl ether. These observations are contrary to the results which will be presented here, and some of the results published earlier[99,100] which show that in dimethyl sulphoxide (3.4) is more appropriate for the brightly coloured species formed from picryl chloride and methanolic sodium methoxide. Due to the instability with respect to the loss of chloride ion of adducts of the type (3.1) rearrangement will lead to nucleophilic substitution rather than a stable adduct.

For the sake of completion some spectroscopic results with corresponding 2,6-dinitro-4-X-anisoles have also been included and are compared with those of the corresponding substituted chlorobenzenes.

Experimental

Proton Magnetic Resonance Measurements

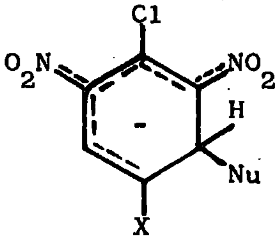
^1H n.m.r. spectra were obtained with a Varian A56/60 instrument either at probe temperature (~ 37°C) or in some cases in order to study more easily the initial interactions, solutions were cooled to 10°C. T.M.S. was used as an internal standard. Solutions of substrate (0·5 - 0·2M) were made just before recording spectra and complexes were generated in situ by the addition of methanolic sodium methoxide (~ 5·0M) with a syringe so as to give a molar ratio of substrate to base of about 1:0·5. The spectrum was recorded as rapidly as possible after mixing the solutions.

Visible Measurements

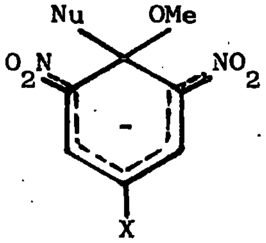
Visible spectra were recorded with a Unicam SP800 instrument on samples with concentrations of 10^{-4} - 10^{-5}<u>M</u>.

Structural Studies

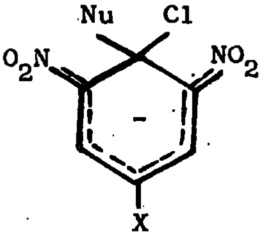
<u>1-Chloro-2,6-dinitro-4-methoxycarbonylbenzene</u>: The ^{1}H n.m.r. spectrum of the parent chlorobenzene in dimethyl sulphoxide gives a single resonance at 8·83 p.p.m. (relative to internal T.M.S.) due to the two equivalent ring protons at C_3 and C_5. The protons of the methoxycarbonyl group resonate at 3·96 p.p.m. and give a single band. On addition of a concentrated solution of methanolic sodium methoxide the ^{1}H n.m.r. spectrum shows in addition to solvent bands, an AX pattern for the two ring protons of the coloured species obtained. Thus two spin coupled doublets of equal intensity are observed at 5·87 and 8·15 p.p.m. A singlet (relative intensity three) at 3·07 p.p.m. is attributed to the methoxyl protons in the adduct while the protons of methoxycarbonyl group gave a sharp single band at 3·70 p.p.m. The large upfield shift of one ring proton relative to parent molecule is consistent with the covalent addition of nucleophile at this position, to form complex of structure (3.5) (X = COOMe, Nu = OMe). The assignments of observed ^{1}H n.m.r. bands are made on the basis of the chemical shifts previously reported by Servis[20], for the analogous 1,3 complex of 2,4,6-trinitroanisole and methoxide



(3.5)

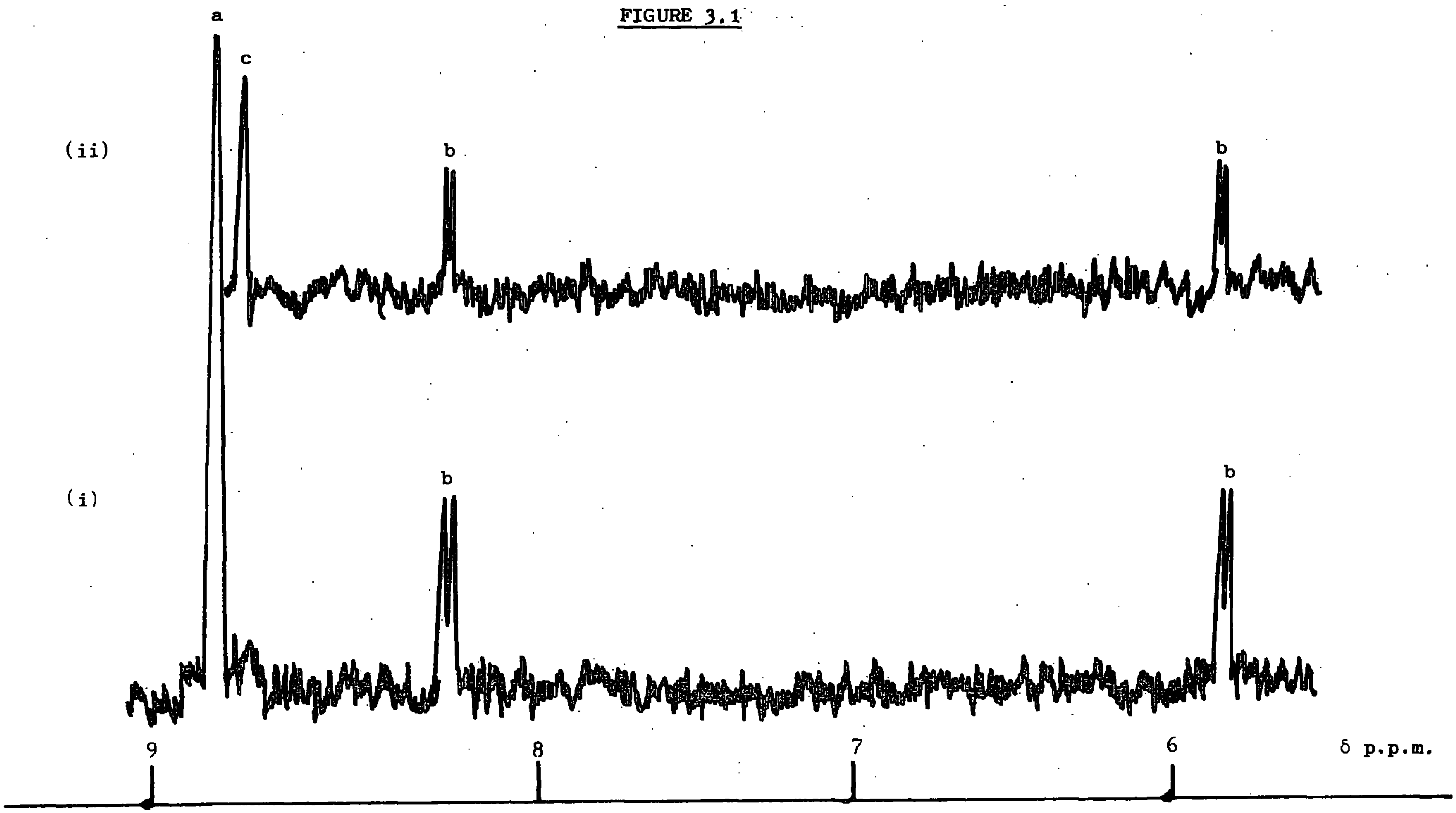


(3.6)



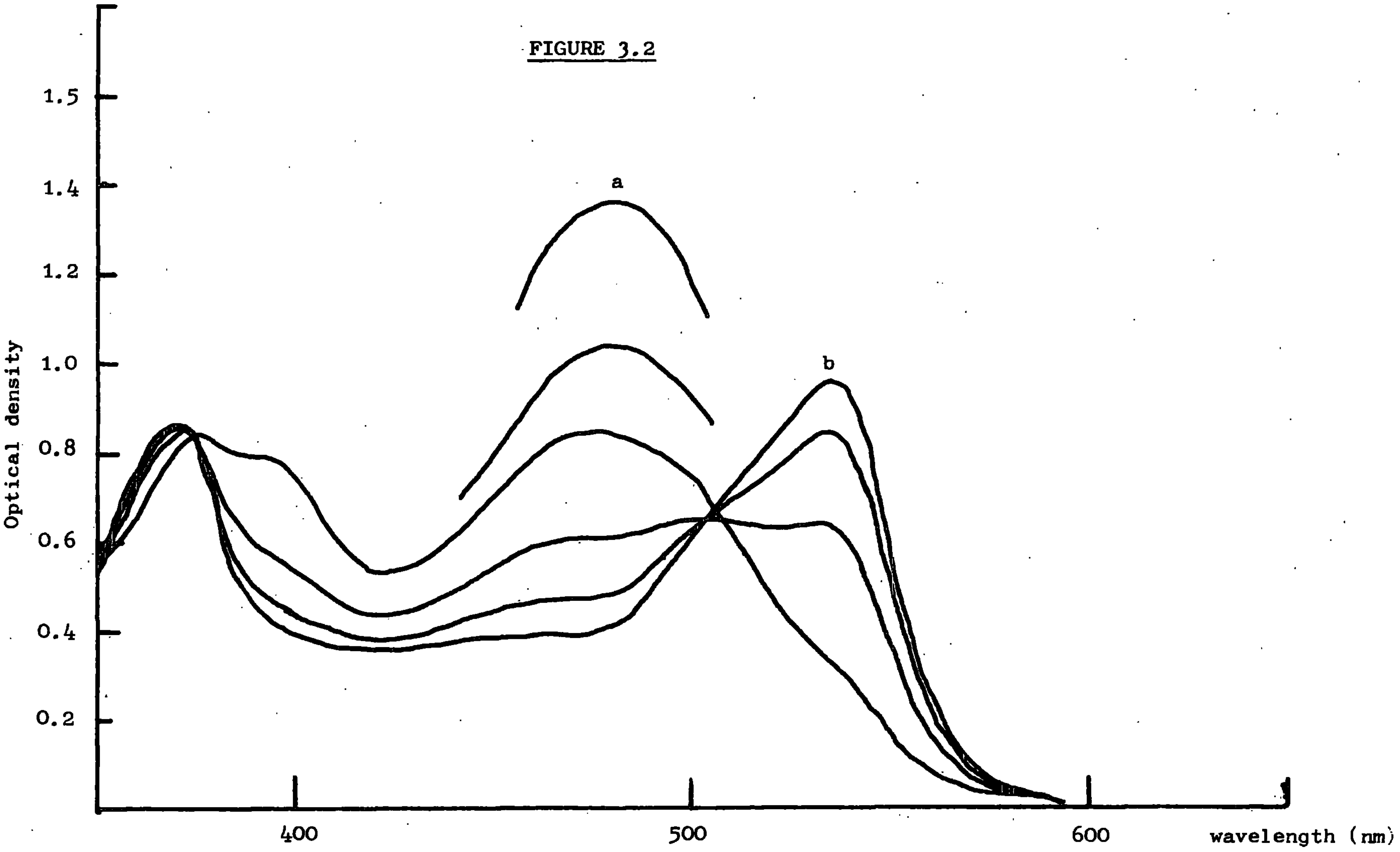
(3.7)

FIGURE 3.1



^{1}H n.m.r. spectra of 1-chloro-2,6-dinitro-4-methoxycarbonylbenzene and sodium methoxide in methanolic dimethyl sulphoxide, (i) initially after mixing reagents, (ii) after about two minutes. Bands labelled 'a' are due to unchanged chloro compound, 'b' to the ring protons of complex (3.5), 'c' to the ring protons of corresponding anisole.

FIGURE 3.2



Visible absorption spectra of 4-methoxycarbonyl-2,6-dinitrochlorobenzene (~ 10^{-4}M) in dimethyl sulphoxide methanol mixture (95:5 v/v) containing sodium methoxide (~ 10^{-3}M). (a) Immediately after mixing reagents, (b) time stable spectra.

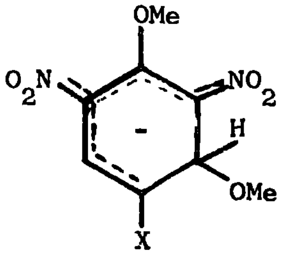
ion. However with time the doublets at 5·87 and 8·15 p.p.m. decrease in intensity and a new band emerges at 8·71 p.p.m. This is at the position expected for the ring protons of 4-methoxycarbonyl-2,6-dinitroanisole indicating the eventual nucleophilic displacement of chlorine by methoxide. In addition a small band appears at 8·42 p.p.m. which is probably due to formation of small amount of (3.6) (Nu = OMe, X = COOMe). No bands were observed which could be assigned to the adduct of structure (3.7) (Nu = OMe, X = COOMe).

Attempts were also made to observe the analogous behaviour with sulphite ion, using aqueous sodium sulphite, but due to the poor solubility of this base in dimethyl sulphoxide, the solvent used, the spectrum observed were not very conclusive.

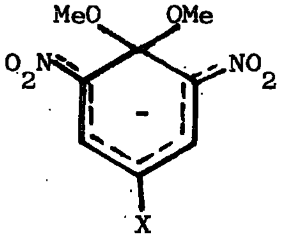
The visible spectra were recorded in more dilute solutions. Thus addition of methanolic sodium methoxide to a dimethyl sulphoxide solution of the parent compound, caused an initial yellow colour which changed to red. The initial spectrum showed bands with absorption maximum at 485 nm. However the spectrum changed rapidly with time to give new bands with maximum at 533 nm, this no doubt is the spectrum of complex (3.6) (Nu = OMe, X = COOMe) which will be formed in the presence of excess of sodium methoxide.

The shift to longer wavelength is due to the fact that the group para to the position of addition is less electron-withdrawing in the adduct of structure (3.6) (X = COOMe, Nu = OMe) than of structure (3.5) (Nu = OMe, X = COOMe).

4-Methoxycarbonyl-2,6-dinitroanisole: The parent anisole in dimethyl sulphoxide gives a resonance due to ring protons at 8·72 p.p.m. The methoxyl group gives a band at 4·03 and the methoxycarbonyl group a band at 3·95 p.p.m. On the addition of a concentrated solution of methanolic sodium methoxide a deep red colour is produced and the ^{1}H n.m.r. spectrum shows the emergence of two spin coupled doublets at 8·07 and 5·80 p.p.m. depicting the attack of nucleophile at unsubstituted ring carbon forming the complex of structure (3.8) (X = COOMe). However as expected these bands fade away with time giving way to single sharp band at 8·43 p.p.m. due to ring protons of 1,1-complex of structure (3.9) (X = COOMe). In addition two bands also emerge at 2·98 p.p.m. ascribed to methoxyl group protons and at 3·70 p.p.m. due to the methoxy carbonyl group in the complex.



(3.8)

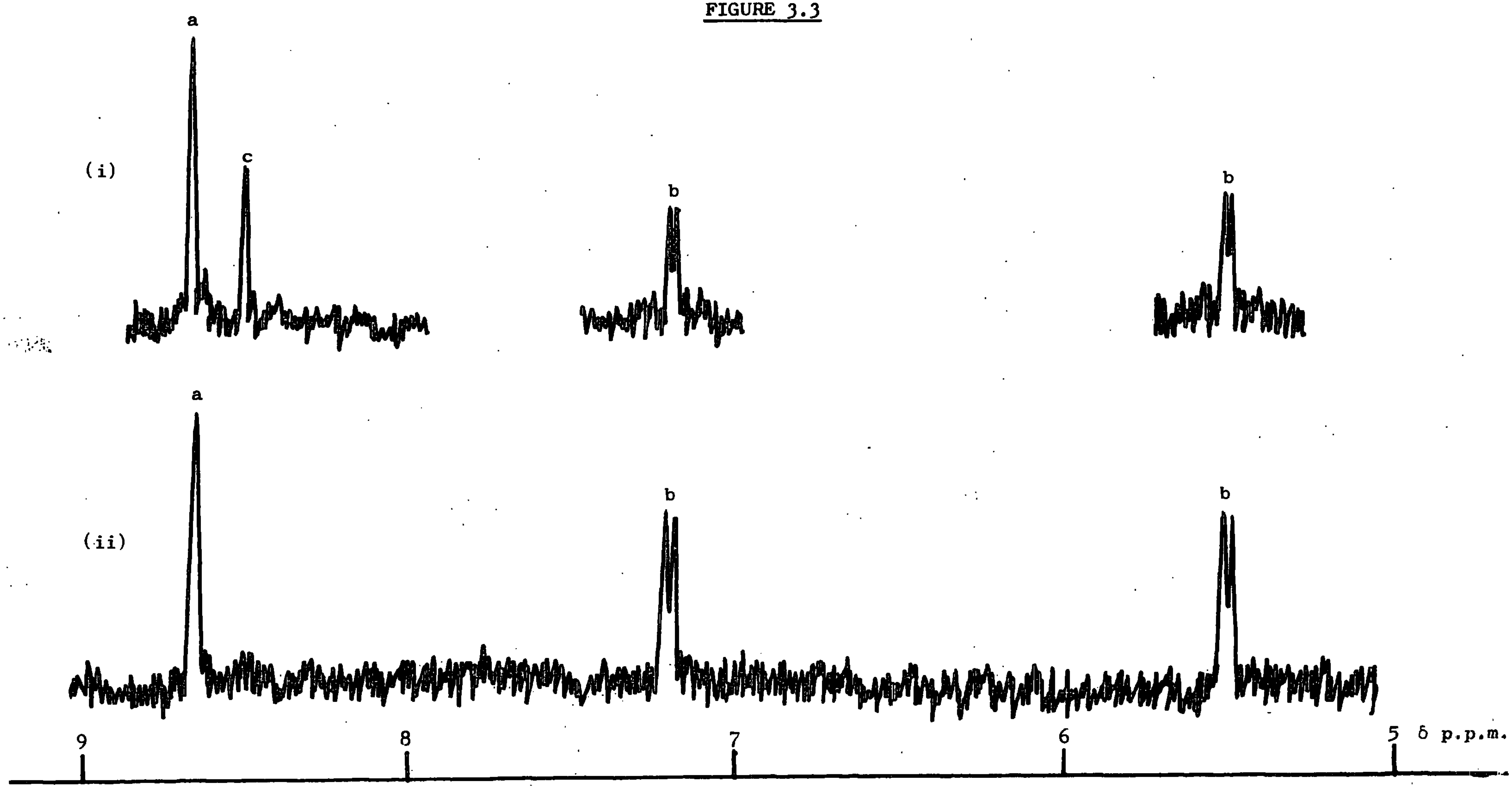


(3.9)

The visible spectrum taken with dilute solutions of substrate in dimethyl sulphoxide rich media shows a colour change from yellow to pink. The initial spectrum due to yellow species gives an absorption maximum at 470 nm which decreases rapidly with time to give new bands with maximum at 533 nm. This change is attributed to the initial formation of kinetically favoured C_3 complex (3.8) (X = COOMe) which rearranges to thermodynamically more stable 1,1-complex (3.9) (X = COOMe).

<u>1,4-Dichloro-2,6-dinitrobenzene</u>: The parent dichlorobenzene gives a sharp resonance at 8·65 p.p.m. in dimethyl sulphoxide. The single band indicates the similar environment of the two ring protons in the molecule. Addition of less than one equivalent of a concentrated solution of methanolic sodium methoxide gives a deep red solution which starts turning blue then finishes orange. The initial spectrum of the red coloured solution shows in addition to solvent bands, and a band for parent molecule at 8·65 p.p.m.,

FIGURE 3.3



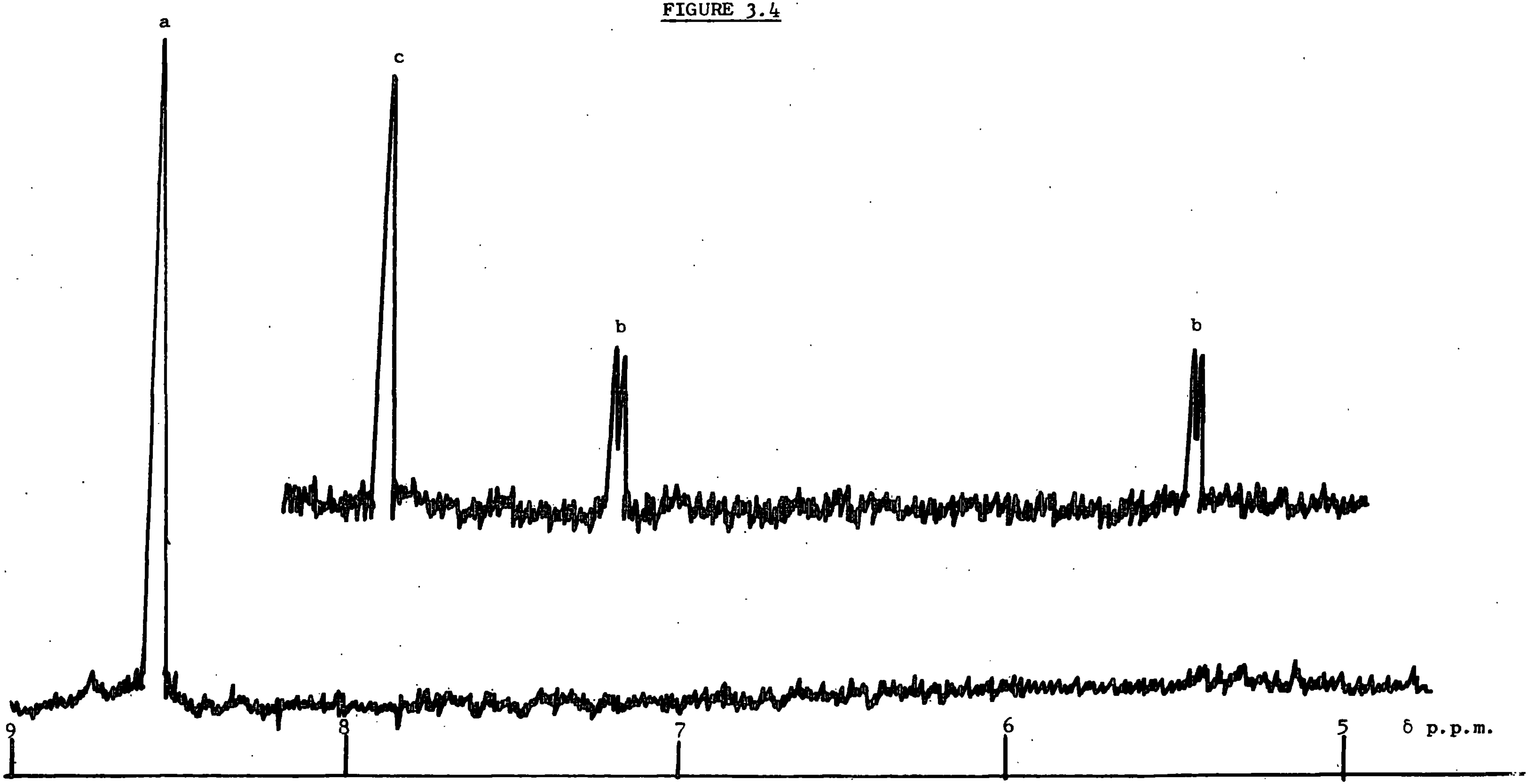
^{1}H n.m.r. spectra of 1,4-dichloro-2,6-dinitrobenzene and sodium methoxide in methanolic dimethyl sulphoxide (i) initially after mixing reagents, (ii) after about two minutes. Bands labelled 'a' are due to unchanged chloro compound, 'b' to the ring protons of complex (3.5), 'c' to the ring protons of corresponding anisole.

two doublets of equal intensity situated at 7·22 and 5·52 p.p.m. due to ring protons and a band at 3·11 p.p.m. assigned to the methoxyl protons of the adduct formed. The large shift to high field of one ring proton resonance can be explained by the change in hybridisation at this position from sp^2 to sp^3, indicating the covalent addition at this position forming a C_3 adduct of structure (3,5) (Nu = OMe, X = Cl). However with time the two doublets fade away and a new band develops at 8·53 p.p.m. ascribed to the ring protons of substitution product, anisole. A band is observed at 3·98 p.p.m. due to the methoxyl protons of anisole. In addition a small band appears with time at 7·9 p.p.m. due to the ring protons of the corresponding phenol probably formed by the nucleophilic substitution of chlorine in the parent dichlorobenzene by hydroxide ions present as traces of water molecules in the solvent used. There was no indication of the formation of adduct of the type (3.7) (Nu = OMe, X = Cl).

The visible spectrum supports the ^1H n.m.r. conclusion, thus in much more dilute solutions than used for ^1H n.m.r. studies, the addition of sodium methoxide to a solution of substrate in dimethyl sulphoxide produces an intense red colour which turns blue. The initial spectrum shows bands with absorption maximum at 504 nm, changing rapidly with time to bands with maximum at 610 nm the former being assigned to complex (3.5) (Nu = OMe, X = Cl) and the latter to adduct (3.6) (Nu = OMe, X = Cl) formed by an excess of methoxide and product anisole.

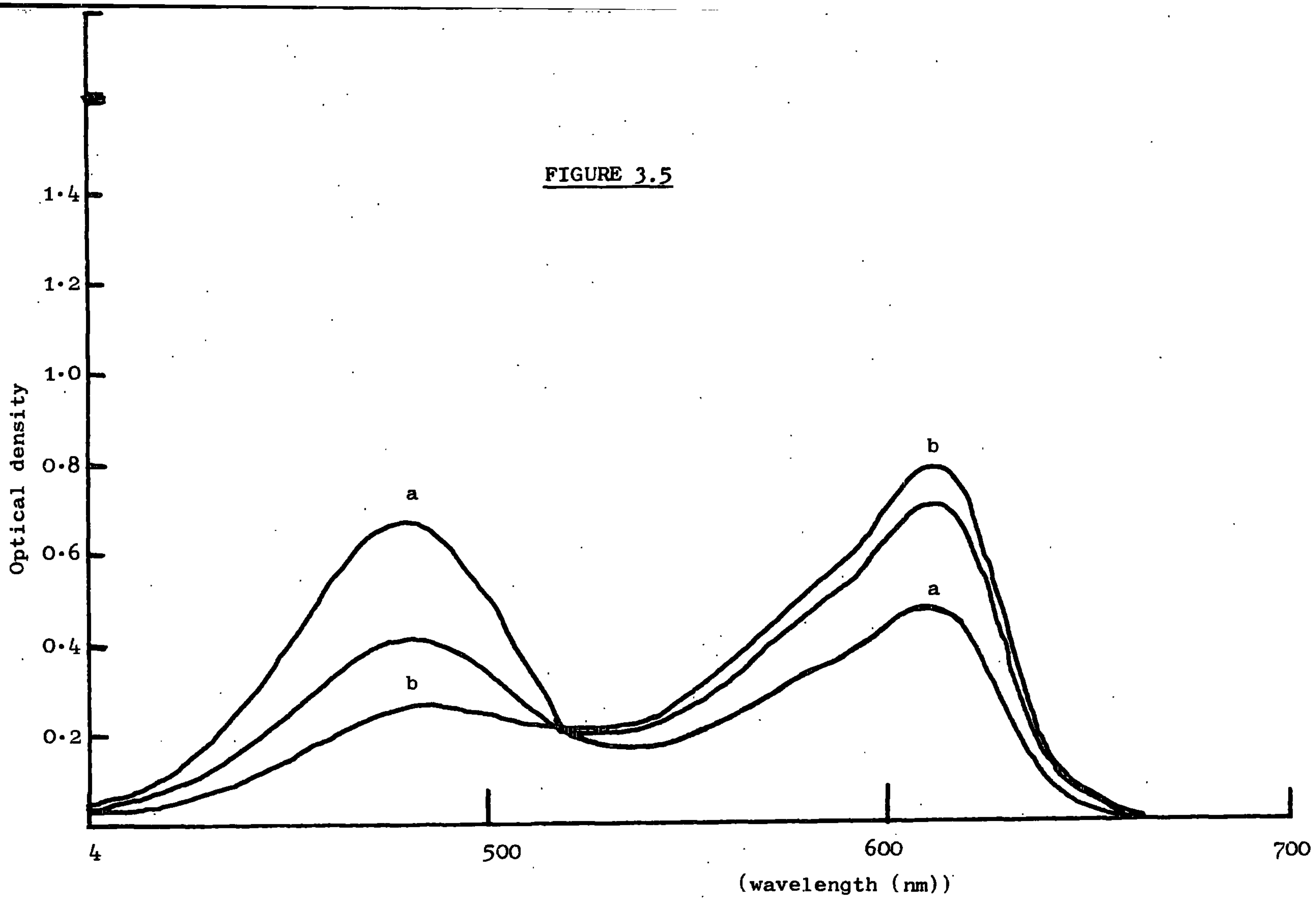
4-Chloro-2,6-dinitroanisole: The parent 4-chloro-2,6-dinitroanisole in dimethyl sulphoxide gives a single sharp resonance at 8·53 p.p.m. due to two symmetrical ring protons. While methoxyl protons resonate at 3·98 p.p.m. on the addition of concentrated solution of methanolic sodium methoxide a red colour is produced and the initial ^1H n.m.r. spectrum shows two doublets at

FIGURE 3.4



^{1}H n.m.r. spectra of 4-chloro-2,6-dinitroanisole and sodium methoxide in methanolic dimethyl sulphoxide, (a) bands due to parent anisole, (b) due to complex (3.8), (c) due to complex (3.9).

FIGURE 3.5



Visible absorption spectra of 4-chloro-2,6-dinitroanisole (4×10^{-5} $\underline{\underline{M}}$) in dimethyl sulphoxide methanol mixture (90:10 v/v) containing sodium methoxide (10^{-3} $\underline{\underline{M}}$). (a) Initially after mixing reagents, (b) time stable spectra.

5·45 and 7·17 p.p.m. due to the ring protons of C_3 complex of structure (3.8) (X = Cl). While two singlets of equal intensity at 3·10 and 3·81 p.p.m. are assigned to the two methoxyl group protons in the adduct. With time the bands due to C_3 adduct fade away and new bands appear, at 7·85 and 3·00 p.p.m. the former being attributed to the ring protons of 1,1-complex and the latter band which is twice the intensity compared with intensity of methoxyl proton resonance in C_3 adduct is due to the two equivalent methoxyl group protons in the 1,1-adduct (3.9) (X = Cl).

The visible spectrum observed in dilute solutions then used in ^1H n.m.r. studies gives an initial absorption maximum at 480 nm. With time this band shifts to longer wavelength with maximum at 610 nm, indicating the initial formation of the C_3 adduct rearranging to thermodynamically more stable 1,1-adduct (3.9) (X = Cl).

1-Chloro-2,6-dinitro-4-trifluoromethylbenzene: The ^1H n.m.r. spectrum of the parent compound in dimethyl sulphoxide gives a single band due to ring protons at 8·90 p.p.m. On the addition of concentrated solution of methanolic sodium methoxide two spin coupled doublets of equal intensity appear at 5·77 and 7·78 p.p.m. with the subsequent decrease in the intensity of parent molecule band at 8·90. This pattern is consistent with the expected spectrum of the C_3 adduct formation, the methoxyl protons of the complex resonate at 3·07 p.p.m. Thus structure (3.5) (Nu = OMe, X = CF_3) can be assigned to the kinetically favoured complex. With time the spectrum changes with the fading of the two doublets and development of a new band at 8·75 p.p.m. indicating the eventual replacement of chlorine by methoxide ion, forming the corresponding anisole. A single band at 4·05 p.p.m. is assigned to the methoxyl protons of the product anisole. In addition a singlet appears at 8·1 p.p.m. and is assigned to the formation of phenol through the replacement of chlorine by hydroxide ions present as an impurity. This observation is consistent with the results obtained by picryl chloride when similar formation of phenol is observed.[99,100] Again no bands were observed which could be attributed to the adduct of structure (3.7) (Nu = OMe, X = CF_3).

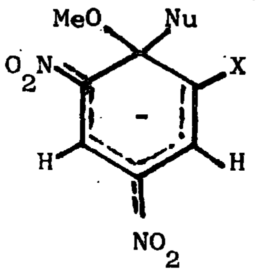
The visible spectrum observed with dilute solutions show the initial formation of an orange coloured species with absorption maximum at 460 nm. The spectrum changes rapidly with time to give new bands with maximum at 545 nm, and a red colour to the solution. This can be rationalised as the initial formation of C_3 adduct of structure (3.5), changing to a 1,1-complex of the product anisole (3.9) (X = CF_3) formed due to the excess of methoxide ions present in the reacting mixture.

Attempts to observe analogous behaviour with sulphite ions using aqueous sodium sulphite failed to give any conclusive results due to the poor solubility of sulphite in dimethyl sulphoxide.

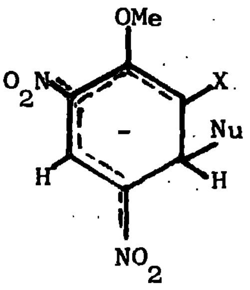
<u>4-Trifluoromethyl-2,6-dinitroanisole</u>: The parent 4-trifluoromethyl-2,6-dinitroanisole gives a single sharp band in dimethyl sulphoxide due to ring protons, at 8·75 p.p.m. and a band at 4·05 p.p.m. due to methoxyl group protons. On addition of concentration solution of methanolic sodium methoxide the initial spectrum gives an AX pattern for the ring protons with two doublets of equal intensity at 7·65 and 5·64 p.p.m. indicating the covalent addition at an unsubstituted carbon and thus giving it an sp^3 character, this could be rationalised in terms of structure (3.8) (X = CF_3). However with time new bands develop, on the expense of the initial bands, giving rise to a single sharp resonance at 8·07 p.p.m., assigned to ring protons in structure (3.9) (X = CF_3). The methoxyl group protons of (3.9) give a single peak at 3·02 p.p.m.

The visible spectrum of the substrate with sodium methoxide in dimethyl sulphoxide rich media also shows the initial absorption at a maximum of 465 nm, shifting with time to longer wavelength at 545 nm. Thus depicting the initial formation of the kinetically favoured C_3 complex (3.8), rearranging to thermodynamically more stable 1,1-complex (3.9).

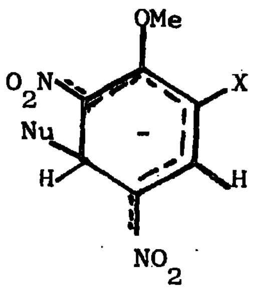
4,6-Dinitro-2-substituted anisoles: The substituted anisoles discussed so far in this chapter included molecules where 2 and 6 positions of the aromatic ring were occupied by nitro groups thus making the unsubstituted 3 and 5 ring carbon atoms equivalent as far as the nucleophilic attack to give σ-complex is concerned. On the other hand in 2-X-4,6-dinitroanisoles the 2-substituent renders the molecule unsymmetrical with respect to nucleophilic attack at unsubstituted 3 and 5 ring positions. Thus such anisoles could form three isomeric adducts, of structures (3.10), (3.11) and (3.12).



(3.10)



(3.11)



(3.12)

Millot and Terrier[101] reported the visible spectral evidence for the formation of all three isomers from 4,6-dinitro-2-X-anisoles (X = CN, Cl; Nu = OMe). The isomers (3.11) and (3.12) being formed as kinetically favoured adducts but rearranging to adduct of structure (3.10). However visible spectrum cannot provide conclusive evidence for the structural pattern of Meisenheimer complexes, thus Fendler et al[24] studied the ^1H n.m.r. spectrum of 4,6-dinitro-2-cyano anisole with methoxide ion. They found that the initial spectrum shows bands due to adduct of structure (3.11), however this rearranges to give thermodynamically more stable 1,1-adduct of structure (3.10). There was no indication for the formation of (3.12) (X = CN, Nu = OMe), which although is expected to have very similar spectrum as (3.11) but because of the less deshielding effect of cyano group than nitro group would be expected to give bands at higher field than were observed and assigned to structure (3.11). This then again stresses the importance of strongly electronegative group as a stabilising factor in Meisenheimer complexes, when present para to the site of addition. This factor has been discussed by many workers including Zollinger et al[102] and Dyall et al.[26]

<u>2-Methoxycarbonyl-4,6-dinitroanisole</u>: The ^1H n.m.r. spectrum of the parent compound in dimethyl sulphoxide shows an AB pattern, with ring protons giving two spin coupled bands of equal intensity at 8·76 and 9·06 p.p.m. (J = 3 Hz). The methoxyl and methoxycarbonyl group protons resonate at 4·02 and 3·98 p.p.m. respectively. On the addition of methanolic sodium methoxide a deep red colour is produced and the spectrum shows two spin coupled doublets at 8·32 and 8·71 p.p.m. These are ascribed to the ring protons of the 1,1-adduct of structure (3.10) (Nu = OMe, X = CO_2Me). The methoxyl protons of the adduct resonate at 2·93 p.p.m. and the band is doubled in intensity compared to the parent anisole, the methoxycarbonyl protons gives a peak at 3·07 p.p.m. No bands were observed which could be assigned to the adduct of the type (3.11) or (3.12). (These assignments are made on the basis of the chemical shifts previously reported by Fendler et al[24] for the analogues 1,1-complex (3.10), X = CN).

The visible spectrum of the substrate with methanolic sodium methoxide gave absorption with two maxima at 384 nm and 472 nm, this being ascribed as due to 1,1-complex of structure (3.10) (X = CO_2Me, Nu = OMe).

On the timescale of these experiments the C_3 complex which will probably be initially formed rearranges quickly to the thermodynamically more stable 1,1-complex.

2-Chloro-4,6-dinitroanisole: The ring protons of the parent in dimethyl sulphoxide gives an AB quartet with chemical shift of 8·74 p.p.m. and 8·80 p.p.m. (J = 3 Hz), the methoxyl protons resonate at 4·08 p.p.m. On the addition of concentrated solution of methanolic sodium methoxide two doublets of equal intensity emerged at 7·50 and 8·73 p.p.m., (J = 3 Hz) ascribed to the two ring protons of the 1,1-adduct (3.10) (X = Cl, Nu = OMe). A single band at 2·95 p.p.m. is due to methoxyl protons in the 1,1 adduct, with an intensity of twice that compared to the parent molecule. No bands were observed which could be assigned to the complex formed by addition at either unsubstituted 3 or 5 ring positions of the parent molecule.

The visible spectrum shows bands with absorption maximum at 352, 364 and 492 nm ascribed to the 1,1-complex.

Conclusion

The results presented show that in dimethyl sulphoxide addition of nucleophiles to unsubstituted ring carbon of the parent chloro compounds is kinetically favoured relative to addition at the chloro substituted position. In this respect the chloro compounds are similar to substituted anisoles,[20,24,103] 1,2,3,5-tetranitrobenzene[104] and 2,4,6-trinitroanilines[30] where in each case addition occurs first at a ring carbon carrying hydrogen. The faster addition at the unsubstituted positions in these compounds have been rationalised in terms of steric factors[30] which inhibit addition at the substituted ring position. Spectral data are summarised in Table 3.1 - 3.3. The ^{1}H n.m.r. shifts for the ring protons of adducts produced by methoxide addition at C_3 to the parent chloro compounds are in similar position but at slightly lower field than the analogous bands from the methoxide adducts of similarly substituted anisoles. To make absolutely sure that the doublets observed from the chloro compounds do not result from prior formation of anisole and subsequent reaction of anisole with methoxide an experiment has

TABLE 3.1

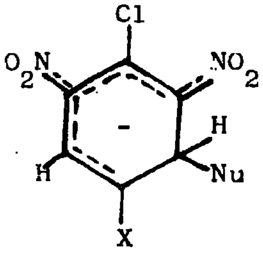
Chemical shifts (downfield from internal tetramethylsilane) for parent compounds in dimethyl sulphoxide

	Ring Protons		Methoxyl (p.p.m.)	Methoxycarbonyl
1-Chloro-2,6-dinitro-4-X-benzenes				
X = NO_2	9·25			
X = CO_2Me	8·83			3·96
X = CF_3	8·90			
X = Cl	8·65			
1-Methoxy-2,6-dinitro-4-X-benzenes				
X = NO_2	9·07		4·05	
X = CO_2Me	8·72		4·03	3·95
X = CF_3	8·75		4·05	
X = Cl	8·53		3·98	
1-Methoxy-4,6-dinitro-2-X-benzenes				
X = CO_2Me	8·76	9·06*	4·02	3·98
X = Cl	8·74	8·80*	4·08	

*Ring proton give an AB quartet, J = 3Hz.

TABLE 3.2

Spectral Data for Complexes[a]



	Chemical Shifts (δ)		
	Ring Protons[b]	Methoxyl Protons	Visible Spectrum λ_{max} (nm)
X = CF_3, Nu = OMe	5·77, 7·78	3·07	460
X = CO_2Me, Nu = OMe	5·87, 8·15	3·07[c]	485
X = Cl, Nu = OMe	5·52, 7·22	3·11	504
X = NO_2, Nu = OMe	6·27, 8·57[d]	3·12	424
X = NO_2, Nu = OH	6·2, 8·4 [d]		
X = NO_2, Nu = SO_3^-	6·1, 8·45[d]		470

[a] The solvent is dimethyl sulphoxide, containing a little methanol when Nu = OMe, or a little water when Nu = OH or SO_3^-.

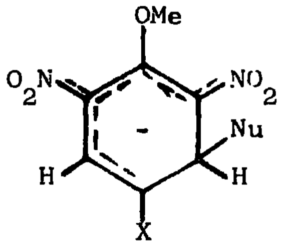
[b] The ring protons in complexes formed by addition at C_3 give spin-coupled bands, J ~ 2 Hz.

[c] CO_2Me protons give a singlet at 3·70 p.p.m.

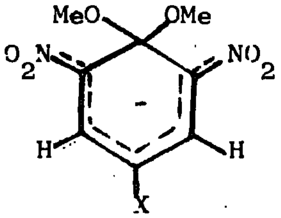
[d] Reference 99.

TABLE 3.3

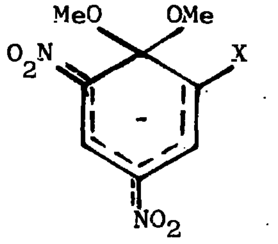
Spectral Data for Complexes[a]



	Chemical Shifts (δ)		
	Ring Protons[b]	Methoxyl Protons	Visible Spectrum λ_{max} (nm)
X = CF_3, Nu = OMe	5·64, 7·65		465
X = CO_2Me, Nu = OMe	5·80, 8·07		470
X = Cl, Nu = OMe	5·45, 7·17	3·10, 3·81	480
X = NO_2, Nu = OMe	6·15, 8·48[c]	3·17, 3·83	418



X = NO_2	8·70	3·02	422
X = CF_3	8·07	3·02	545
X = CO_2Me	8·43	2·98[d]	533
X = Cl	7·85	3·00	610



X = CO_2Me	8·32, 8·71[e]	2·93	472
X = Cl	7·50, 8·73[e]	2·95	492

[a] The solvent is dimethyl sulphoxide, containing a little methanol when Nu = OMe

[b] The ring proton in complex formed by addition at C_3 give spin-coupled bands J = 2 Hz.

[c] Reference 100. [d] CO_2Me protons give a singlet at 3·70 p.p.m.

[e] Ring protons give an Ab quartet J = 3 Hz.

been carried out[99] in which sodium methoxide was added to a mixture of picryl chloride and 2,4,6-trinitroanisole. The resultant spectrum showed four doublets at the positions expected for the ring protons of the adducts from both the chloro compound and the anisole. The argument put forward by Syper and Barycki in their recent publication[98] that the coloured solids obtained by them from reacting picryl chloride and 2-chloro-3,5-dinitro pyridine with different alkoxides are adducts of structure (3.1) and (3.2) (R = Et) on the grounds that the solids obtained give back parent substrate on treating with acid is very doubtful as the adduct of structure (3.4) and (3.3) (R = Et) would also be expected to yield parent substrate by treating with acid. Moreover their argument that because of the difference between polynitroaromatic ethers and polynitroaromatic halides, analogies in reaction mechanism of the two types of polynitroaromatics with nucleophiles have limited application, is not supported by quantitative proof. On the other hand the spectroscopic evidences in favour of analogous behaviour of polynitro-chlorobenzenes and corresponding aromatic ethers is substantial.

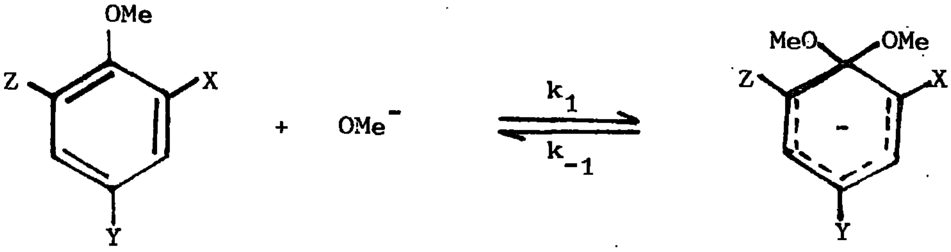
The results presented here were obtained in media rich in dimethyl sulphoxide. In hydroxylic media transient colours have sometimes been observed during nucleophilic substitutions. Thus Gaboriauel and Schaal[105] described the coloured species observed by the reaction of picryl chloride with aqueous sodium hydroxide as having structure (3.7) (Nu = OH, X = NO_2). It looks now more probable that here too the coloured species results from hydroxide addition at an unsubstituted position to give (3.5) (Nu = OH, X = NO_2). Similarly Bowden and Cook[106] in a kinetic study of the reactions of 1-substituted 2,4-dinitrobenzenes with base in aqueous dimethyl sulphoxide have observed coloured species which were thought to result from hydroxide addition at a ring-carbon carrying hydrogen. The results of this work add to the likelihood of this possibility.

CHAPTER 4

EQUILIBRIUM AND KINETICS FOR REACTION OF REACTIVE ANISOLES WITH SODIUM METHOXIDE IN METHANOL

Introduction

Kinetic and equilibrium studies of Meisenheimer complexes have been the subject of investigation in many laboratories around the world.[3,7] One aspect of this interest is in the relative stabilities of these adducts. Although some measurements have been made with other nucleophiles (e.g. sulphite,[62] cyanide[74]) the bulk of the data now available relates to reaction with sodium methoxide in methanol and equilibrium constants for the formation of some twenty compounds have been reported. In the present work which extends these measurements, equilibria of the following type has been studied:-



(4.1)

where methoxide addition occurs at the methoxyl substituted position. However as shown in the preceding chapter there is considerable evidence,[3,20] particularly for the reaction in dimethyl sulphoxide, that the formation of stable adducts of structure (4.1) is preceded by addition at unsubstituted ring positions. In this chapter however these transient adducts will not be the prime concern.

The best known example of a reaction of the type shown is that of 2,4,6-trinitroanisole and the equilibrium constant for methoxide addition has been determined in several laboratories.[12,24,46] In addition Fendler and

and co-workers[24,70,107] have made careful studies of a number of compounds in which the nitro-groups have been variously replaced by cyano-groups. Terrier[88] has made measurements on a number of dinitro compounds containing chloro-, fluoro- or trifluoro-methyl substituents. In favourable cases the approach to equilibrium is sufficiently slow to enable its rate to be measured which leads to values for the individual rate constants k_1 and k_{-1}. Surprisingly some reports[46,88] have indicated variations in values of the equilibrium constant with sodium methoxide concentration even in dilute solutions where ideal behaviour would be expected.

This chapter includes values of equilibrium constant, K_1, and in three cases rate constants, k_1 and k_{-1}, for four relatively reactive compounds whose complex formation occurs in dilute sodium methoxide solutions: 2-methoxycarbonyl-4,6-dinitroanisole, 4-methoxycarbonyl-2,6-dinitroanisole, 2-chloro-4,6-dinitroanisole and 4-trifluoromethyl-2,6-dinitroanisole. In addition the variation of these parameters with sodium methoxide concentration is confirmed by this work and an explanation has been given.

Experimental

Visible spectral measurements were made at 25°C using a Unicam SP500 instrument fitted with a thermostatted cell compartment. Solutions containing the required concentrations of reagents were prepared immediately before measurements by suitable dilution of stock solutions. It was found convenient to make kinetic measurements by the addition from a syringe of a small quantity of a concentrated solution of parent anisole to a solution of methanolic sodium methoxide which had previously been brought to 25°C in the measuring cell. Measurement of optical densities was begun 10 secs. after mixing and continued until completion of reaction. A typical data set with calculated first order rate constant for the reaction of 2-methoxycarbonyl-

4,6-dinitroanisole ($3{\cdot}84 \times 10^{-5}$M) with sodium methoxide (0·04M) is given in Table 4.1. Rate constants were in all cases reproducible within 5%.

TABLE 4.1

Time (seconds)	Optical Density (472 nm)	$10^2\ k_{obs}$ (sec^{-1})
19	0·140	1·95
25	0·177	1·94
32	0·211	1·95
46	0·270	1·95
63	0·320	1·96
76	0·350	1·96
91	0·376	1·97
100	0·387	1·95
127	0·413	1·96
∞	0·450	

Results

Spectral and Structural Studies

Solutions in methanol of each of the four compounds under investigation are colourless. In dilute methanolic sodium methoxide colours are produced. In each case, increasing the concentration of sodium methoxide caused an increase in visible ansorption without however changing the shape of the spectrum or positions of the absorption maxima. Eventually at sodium methoxide concentrations near 1·0M (the exact value depending upon the compound) complete conversion to complex was achieved so that further increase in base concentration caused no further spectral change. The spectra at much higher base concentrations were not examined when higher complexes may be formed. Spectral details are in Table 4.2 and are in good agreement with previous reports.[21,88]

TABLE 4.2

Visible Spectral Data for Complex (4.1) in Methanol

Structure (4.1)	λ_{max} (nm)	$10^{-4}\ \epsilon$ $l.mol^{-1}cm^{-1}$	λ_{max} (nm)	$10^{-4}\ \epsilon$ $l.mol^{-1}cm^{-1}$
$X=CO_2Me$, $Y=Z=NO_2$	384	2·1	472	1·9
$X=Cl$, $Y=Z=NO_2$	352,364	1·6	492	2·3
$Y=CO_2Me$, $X=Z=NO_2$	361	1·3	525	2·1
$Y=CF_3$, $X=Z=NO_2$			540	2·5

The results of the ^1H n.m.r. spectra given in the preceding chapter confirm that the ionisation studies given in this chapter involve methoxide addition at the methoxyl substituted ring position to give adducts of structure (4.1). These spectra were recorded in dimethyl sulphoxide where the visible spectra are similar but shifted slightly to longer wavelength to those recorded in methanol.

Kinetics and Equilibria

The rate of attainment of equilibrium for the formation of complex (4.1) was sufficiently slow in the case of 2-methoxycarbonyl-4,6-dinitroanisole, 4-methoxycarbonyl-2,6-dinitroanisole and 2-chloro-4,6-dinitroanisole at low methoxide ion concentration (10^{-3} - 10^{-1}M). Thus measurements of optical density at the absorption maxima in solutions where the sodium methoxide concentration was in considerable excess (> 100) yielded first order rate constants expressed by equation 4.1

$$k_{obs} = k_1[\text{NaOMe}] + k_{-1} \qquad 4.1$$

where k_1 is the second-order rate constant for the formation of complex (4.1) and k_{-1} is the first-order rate constant for its decomposition. The equilibrium optical densities were used in conjunction with the known extinction coefficient of the complex to obtain values of the stoichiometric equilibrium constant K_C (= k_1/k_{-1}). Individual values for the rate constants k_1 and k_{-1} were then calculated. Measurements were made in solutions containing various concentrations of sodium methoxide some of which contained added electrolyte (sodium perchlorate, sodium chloride or lithium chloride). The results are given in Tables 4.3 - 4.6.

Discussion

^{1}H n.m.r. spectral measurements show clearly that for each of the four compounds studied base addition occurs at substituted ring carbon to give an adduct of structure (4.1). Higher complexes were not formed in the sodium methoxide concentration range used here. In each case the results show that the values of the stoichiometric equilibrium constant K_C (=[Complex]/[Parent]-[NaOMe]) increase with increasing sodium methoxide concentration. Thermodynamic equilibrium constants are found by extrapolation to zero base concentration and are collected in Table 4.7 together with some relevant data from the literature.

As expected the substitution of a methoxycarbonyl group for the more strongly electron withdrawing nitro group causes a considerable decrease in complex stability. In general it has been found that substitution of a nitro group by a less strongly electron withdrawing group para to the position of addition reduces complex stability considerably more than equivalent substitution in the ortho position. Thus the equilibrium constant for 1,1-dimethoxy-2,4,6-trinitrocyclohexadienate is 500 times greater than that of 1,1-dimethoxy-2,6-dicyano-4-nitrocyclohexadienate and 1700 times greater than 1,1-dimethoxy-4,6-dicyano-2-nitrocyclohexadienate. However the effects of methoxycarbonyl substitution are fairly similar at these two positions. It may well be that the stability of the complex from 2-methoxycarbonyl-4,6-dinitroanisole is reduced by steric interactions in the complex. It is seen from Table 4.7 that overall change in complex stability results from changes both in the values of k_1 and k_{-1}.

The large variations of K_C values with sodium methoxide concentration even in very dilute solutions ($< 10^{-2}$ $\underline{\underline{M}}$) is surprising. This effect has been noted previously by Terrier[88] and also, though in more concentrated sodium methoxide solutions, by Bernasconi[108] using 2,4-dinitroanisole. Calculation of the individual rate constants (Tables 4.3 - 4.5) indicates that the overall variations in K_C values are due mainly to large decreases in the apparent values of k_{-1} and much smaller increases in the corresponding k_1 values. It is noteworthy that the variations of the equilibrium constants with sodium methoxide concentration are not identical for the four compounds studied. Thus for 2-methoxycarbonyl-4,6-dinitroanisole the value of the equilibrium constant at 0·05$\underline{\underline{M}}$ sodium methoxide is 4·5 times greater than the thermodynamic value while the corresponding ratios for 4-methoxycarbonyl-2,6-dinitroanisole, 2-chloro-4,6-dinitroanisole and 4-trifluoromethyl-2,6-dinitroanisole are 3·1, 2·1 and 2·3 respectively. Clearly no single J_M acidity function can adequately represent the behaviour of these four compounds.

The increase in K_C values with sodium methoxide concentration was attributed by Terrier[88] to a decrease in the activity coefficient ratio $f_{\text{complex}^-}/f_{\text{parent}} \times f_{\text{OMe}^-}$. However H_M indicators which ionise by proton loss and also 1,3,5-trinitrobenzene[63], where base addition occurs at a ring carbon carrying hydrogen, behave ideally up to at least $0{\cdot}1\underline{M}$ sodium methoxide concentration so that no variation in the value of K_C is observed. In all these reactions a large polarisable anion is produced from methoxide ion and a neutral substrate, so it is hard to see why the adducts (4.1) from the anisoles should behave anomalously. It seems probable that the variation of equilibrium constants with concentration observed in the present case may be in part due to the effects of ion association. Thus the following scheme is suggested to explain this phenomenon:

$$\begin{tikzcd}
\mathrm{P} + \mathrm{OMe}^- + \mathrm{M}^+ \arrow[r, shift left, "k_1"] \arrow[d, shift left, "K_3"] & \mathrm{POMe}^- + \mathrm{M}^+ \arrow[l, shift left, "k_{-1}"] \arrow[r, shift left, "K_2"] & \mathrm{POMe}^-,\mathrm{M}^+ \arrow[l, shift left] \\
\mathrm{M}^+,\mathrm{OMe}^- \arrow[u, shift left] & &
\end{tikzcd}$$

Qualitatively the value of the measured equilibrium constant would be expected to increase with sodium methoxide concentration (as observed) if ion pair formation stabilised the addition complex to a greater extent than the methoxide ion. It is suggested that this is the case when sodium is used as the cation. The results (Table 4.3) where added lithium chloride causes a decrease in K_C indicates that relative to sodium, lithium has a greater stabilising effect on methoxide than on the adduct. It is known that the equilibrium constant for adduct formation of 4-cyano-2,6-dinitroanisole with lithium methoxide[26] is considerably smaller than the value with sodium methoxide.[24]

TABLE 4.3

Kinetic and Equilibrium Measurements at 25°C for 2-Methoxycarbonyl-4,6-dinitroanisole and Sodium Methoxide in Methanol

[NaOMe] (M)	Optical density at equilibrium [a] (472 nm)	K_C ($l.mol^{-1}$)	$10^2\ k_{obs}$ (sec^{-1})	$10\ k_1$ ($l.mol^{-1}sec^{-1}$)	$10^3\ k_{-1}$ (sec^{-1})
0·0039	0·036[b]	13·2	1·85±0·10	2·3	17·5
0·0069	0·074[b]	16·0	1·70	2·4	15·3
0·0098	0·118[b]	19·5	1·55	2·5	13·0
0·0096	0·116	19·5	1·60	2·6	13·5
0·0192	0·254	27·2	1·54	2·8	10·1
0·0288	0·365	33·8	1·82	3·1	9·3
0·0384	0·450	40·5	1·97	3·1	7·4
0·0625	0·575	56	3·05	3·8	6·8
0·077	0·61	61	3·60	3·8	6·3
0·3	0·73				
0·7	0·74				
1·0	0·74				
0·0048[c]	0·120	40·5	0·93	3·1	7·8
0·0096[c]	0·215	43	1·12	3·4	7·9
0·0192[c]	0·330	42	1·45	3·4	8·0
0·0288[c]	0·412	44	1·70	3·3	7·5
0·0384[c]	0·476	44·5	2·00	3·3	7·4
0·0480[c]	0·500	43·5	2·37	3·3	7·7
0·0096[d]	0·220	44	1·12	3·4	7·9
0·0096[e]	0·090	14·5	2·14	2·7	18·5

[a] Concentration of 2-methoxycarbonyl-4,6-dinitroanisole in $3{\cdot}84 \times 10^{-5}$M except where otherwise stated.

[b] For greater accuracy measurements were made with $1{\cdot}94 \times 10^{-4}$M 2-methoxycarbonyl-4,6-dinitroanisole. The values quoted are the actual values divided by 5.

[c] Solutions made up to constant ionic strength (0·05M) with sodium perchlorate.

[d] Containing 0·04M sodium chloride.

[e] Containing 0·04M lithium chloride.

TABLE 4.4

Kinetic and Equilibrium Measurements at 25°C for 4-Methoxycarbonyl-2,6-dinitroanisole (5 x 10^{-5}M) and Sodium Methoxide in Methanol

[NaOMe] (M)	Optical density (525 nm)	K_C ($l.mol^{-1}$)	10^2 k_{obs} (sec^{-1})	k_1 ($l.mol^{-1}sec^{-1}$)	10^2 k_{-1} (sec^{-1})
0·0040	0·028[a]	7·0			
0·0080	0·065[a]	8·4	4·9 ±0·5	0·38	4·6
0·0120	0·108[a]	9·8	4·4 ±0·3	0·39	3·9
0·020	0·203	12·2	4·15±0·3	0·41	3·3
0·030	0·315	14·7	4·15±0·3	0·42	2·9
0·040	0·410	16·5	4·3 ±0·3	0·43	2·6
0·050	0·496	18·7	4·65±0·3	0·45	2·4
0·060	0·584	21·8	5·25±0·4	0·49	2·3
0·080	0·706	27·0	6·6 ±0·5	0·56	2·1
0·10	0·77	29			
0·15	0·86	32			
0·2	0·93	42			
0·25	0·96	45			
0·60	1·01				
1·0	1·03				
1·5	1·04				

[a] For greater accuracy measurements were made with 2·0 x 10^{-4}M 4-methoxycarbonyl-2,6-dinitroanisole. Values quoted are these values divided by 4.

TABLE 4.5

Kinetic and Equilibrium Measurements at 25^{o}C for 2-Chloro-4,6-dinitroanisole and Sodium Methoxide in Methanol

[NaOMe] (M)	Optical density[a] (492 nm)	K_C (l.mol^{-1})	10^2 k_{obs} (sec^{-1})	k_1 (l.mol^{-1}sec^{-1})	10^2 k_{-1} (sec^{-1})
0·0048	0·015[b]	3·5	5·3 ±0·3	0·18	5·2
0·0096	0·034[b]	4·0	5·1 ±0·3	0·19	4·9
0·0144	0·055[b]	4·3	4·7 ±0·3	0·19	4·4
0·0192	0·076[b]	4·6	4·6 ±0·2	0·19	4·2
0·029	0·119	5·1			
0·0385	0·166	5·6	4·25±0·2	0·20	3·5
0·048	0·216	6·3	4·25±0·3	0·21	3·3
0·0625	0·276	6·8	4·3 ±0·3	0·21	3·0
0·077	0·340	7·5	4·4 ±0·3	0·21	2·8
0·096	0·400	8·0	4·8 ±0·4	0·22	2·7
0·15	0·565	10·4			
0·20	0·67	12·9			
0·25	0·735	15·4			
0·30	0·79	18·8			
0·40	0·85	26·5			
0·50	0·875	35			
1·0	0·92				
1·7	0·93				

[a] For 4 x 10^{-5}M 2-chloro-4,6-dinitroanisole.

[b] Measured with indicator concentration of 4 x 10^{-4}M.

TABLE 4.6

Equilibrium Measurements with 4-Trifluoromethyl-2,6-dinitroanisole (4×10^{-5} M) in Methanolic Sodium Methoxide at 25°C

[NaOMe] (M)	Optical density (540 nm)	K_C ($1.mol^{-1}$)
0·010	0·024	2·5
0·020	0·056	3·0
0·030	0·095	3·5
0·040	0·14	4·1
0·060	0·232	5·0
0·080	0·325	6·0
0·10	0·40	6·7
0·15	0·57	8·9
0·20	0·69	11·1
0·25	0·775	13·7
0·30	0·83	16·3
0·40	0·90	22·5
0·60	0·96	
1·0	1·00	

TABLE 4.7

Thermodynamic Constants for Reaction in Methanol at 25°C

Substituents			K_1	k_1	k_{-1}
X	Y	Z	($1.mole^{-1}$)	($1.mol^{-1}sec^{-1}$)	(sec^{-1})
CO_2Me	NO_2	NO_2	10	0·22	$2{\cdot}2 \times 10^{-2}$
NO_2	CO_2Me	NO_2	6	0·36	$6{\cdot}0 \times 10^{-2}$
Cl	NO_2	NO_2	3(2·5)[a]	0·18	$6{\cdot}0 \times 10^{-2}$
NO_2	CF_3	NO_2	2(2·0)[a]		
CF_3	NO_2	NO_2	(14)[a]		
NO_2	NO_2	NO_2	17,000[b]	17·3	$1{\cdot}0 \times 10^{-3}$
CN	NO_2	NO_2	26,000[b]	18·8	$7{\cdot}2 \times 10^{-3}$
NO_2	CN	NO_2	280[b]	6·1	$2{\cdot}2 \times 10^{-2}$
CN	CN	NO_2	10[c]	2·0	$2{\cdot}0 \times 10^{-1}$
CN	NO_2	CN	34[c]	12	$3{\cdot}7 \times 10^{-1}$
NO_2	NO_2	H	5×10^{-5} [d]	$2{\cdot}1 \times 10^{-3}$	42

[a] Ref. 88. [b] Ref. 24. [c] Ref. 70. [d] Ref. 108.

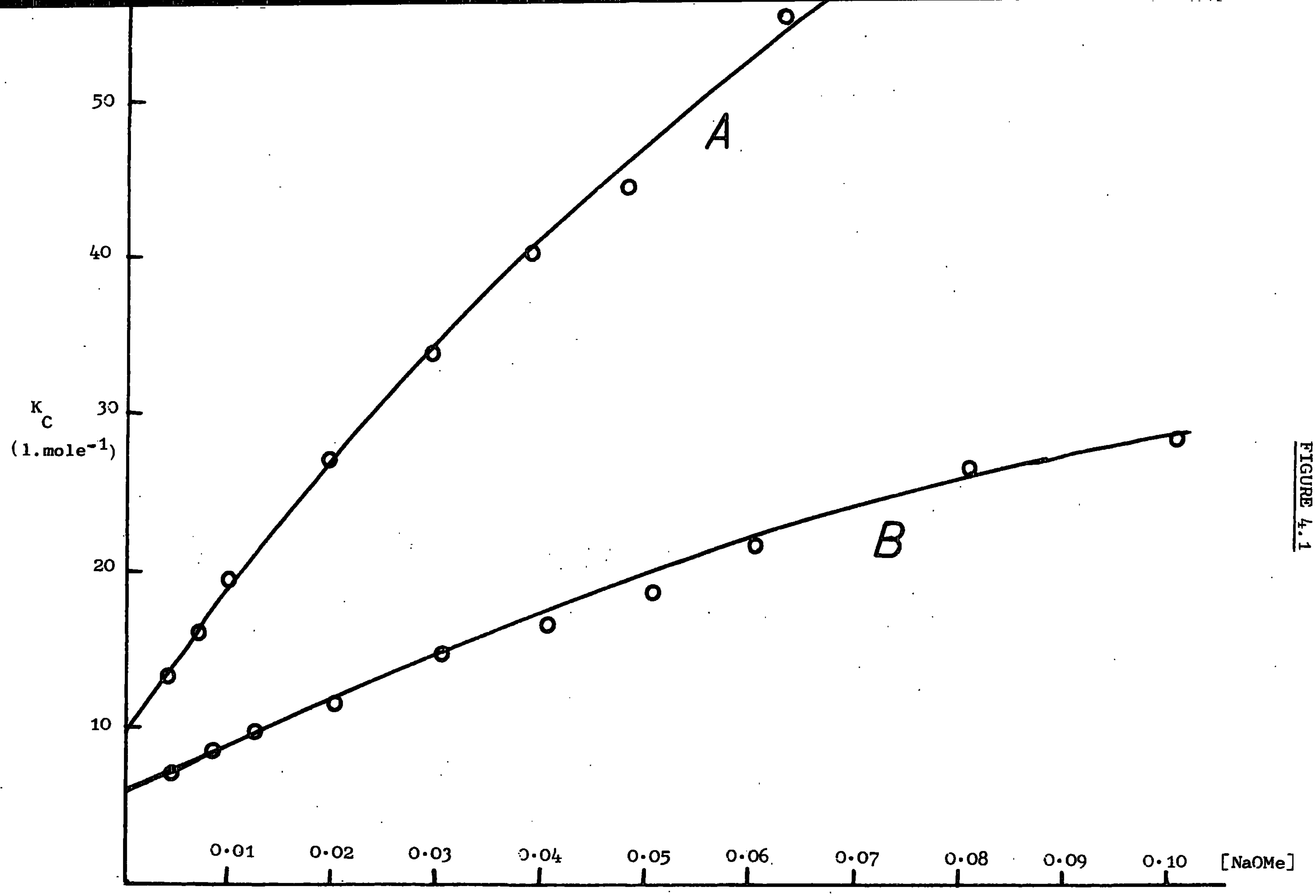
In an attempt to carry out a more quantitative analysis the assumption was made that the free adduct and its ion-pair have identical visible spectra, this seems justified as there is no variation in spectral shape with sodium methoxide concentration when the fraction of ion-pair would be varying. Then the measured equilibrium constant is given by:

$$K_C = \frac{[P.OMe^-] + [P.OMe^-.M^+]}{[P]([OMe^-] + [M^+,OMe^-])} \qquad 4.2$$

$$= K_1 \frac{(1 + K_2[M^+])}{(1 + K_3[M^+])} \qquad 4.3$$

where K_1 is the thermodynamic equilibrium constant in terms of free ions. The precise value of the ion-pair association constant of sodium methoxide is not known but a value close to $10\underline{\underline{M}}^{-1}$ seems likely.[88] In addition ion-pair association with sodium may not substantially reduce the activity of methoxide ions. If then further assumption is made that at low sodium methoxide concentrations most of the sodium methoxide is present as free ions and the $K_2 > K_3$ then we obtain $K_C = K_1 + K_1K_2[NaOMe]_{stoich.}$. Accordingly plots of K_C versus [NaOMe] approach linearity at sufficiently low concentration (Figure 4.1). From the limiting slopes are obtained the following very approximate values for the ion-pair association constants of the sodium salts of the complexes: 2-methoxycarbonyl-4,6-dinitroanisole, $90\underline{\underline{M}}^{-1}$; 4-methoxycarbonyl-2,6-dinitroanisole, $50\underline{\underline{M}}^{-1}$; 2-chloro-4,6-dinitroanisole, $25\underline{\underline{M}}^{-1}$; 4-trifluoromethyl-2,6-dinitroanisole, $25\underline{\underline{M}}^{-1}$. The apparent decrease in k_{-1} with increasing sodium methoxide concentration is predicted by this scheme since neglecting association of the sodium methoxide the observed value is given by $k_{-1}/1 + K_2[M^+])$. The observed value of k_1 would be expected to remain constant, or decrease if ion-pair formation significantly reduces the reactivity of methoxide ions. The observed increase in k_1 values

FIGURE 4.1



Variation of K_C with sodium methoxide concentration for (A) 2-methoxycarbonyl-4,6-dinitroanisole and (B) 4-methoxycarbonyl-2,6-dinitroanisole.

with concentration may be due to a genuine salt effect.[108]

These results suggest then, but of course do not prove, that a major factor affecting the variation of K_C values with sodium methoxide concentration is ion-association in the complex. There also appears to be some correlation between the ion-pair association constants (K_2) and equilibrium constants for adduct formation (K_1). This may be connected with the localisation of charge on specific nitro-groups on complex formation which should favour ion-pair formation. It would then be expected that the ion-pair association constants for more reactive compounds, such as 2,4,6-trinitroanisole, would be large. Additionally the invariance of experimental K_C values for H_M indicators and for 1,3,5-trinitrobenzene would indicate the unimportance of ion-association in these cases.

It is noteworthy that the Fendlers in their careful studies have not noticed variations in K_C values with sodium methoxide concentration. Their work has been mainly with dilute solutions ($< 10^{-2}$ M) where variations will be minimised. However close examination of their results for 1-methoxy-2,4-dinitronaphthalene[34] and 1-(β-hydroxyethoxy)-2,4-dinitronaphthalene[109] indicates significant increases in the values of equilibrium constants with sodium methoxide concentration. Similarly Illuminati and his co-workers[46] found a marked increase in the value of the equilibrium constant for complex formation from 2,4,6-trinitroanisole and sodium methoxide. Their measurements were made in solutions containing less than 10^{-3} M sodium methoxide where carbon dioxide may interfere, however if the increase is genuine then again ion-pair association in the complex is indicated. The Fendlers[24] measured k_{-1} in this latter reaction by direct decomposition of the complex in methanol and combined this value with the constant value of k_1 determined in solutions containing up to 5×10^{-3} M sodium methoxide. They thus found values of the equilibrium constant which were independent of base concentration. Their results no doubt give the thermodynamic value of the equilibrium constant, however since the results do not allow for possible variation of k_{-1} with sodium methoxide concentration they could not be expected to show up variations with the equilibrium constant. Similarly their determinations[24] with 2-cyano-4,6-dinitroanisole and 4-cyano-2,6-dinitroanisole involved the combination of k_{-1} values determined at zero base concentration with k_1 values determined in dilute sodium methoxide solutions. Again the value of the equilibrium constants so determined will be the thermodynamic ones but if, as is suggested here, the main variation is in k_{-1} then their results would not be expected to show up possible variations in equilibrium constant with sodium methoxide concentration.

CHAPTER 5

EFFECTS OF CATIONS

Introduction

The results discussed in Chapter 4 indicate that the value of stoichiometric equilibrium constant $K_C = \frac{[\text{Complex}]}{[\text{Parent}][\text{NaOMe}]}$ increased markedly with base concentration. This was attributed mainly to association of the negatively charged adducts with cations, in this case sodium ions. In order to test this hypothesis, measurements were carried out using a series of different methoxides, where the extent of cation association of the complexes would be expected to vary. Thus measurements similar to those carried out with sodium methoxide were made using lithium methoxide, potassium methoxide and tetra-n-butylammonium methoxide.

It is known that in concentrated solutions of the alkali metal methoxides in methanol the basicity order at a given base concentration, as measured by the H_M acidity function,[110] is KOMe > NaOMe > LiOMe. This order has been attributed[110,111] to ion association in the metal alkoxides which results in a reduction of their activities, the effect being greatest for lithium methoxide and smallest for potassium methoxide. Nevertheless in dilute ($< 0{\cdot}1$ mole l^{-1}) solutions of the three methoxides the H_M basicity has been found to be independent of the cation.[112] In addition the measured ionisation constants, governing proton abstraction from the aniline indicators by base, are independent of base concentration in these dilute solutions.[88,112]

Rate measurements have previously been made by Reinheimer and co-workers[113,114] who determined salt effects on the rates of aromatic nucleophilic substitution reactions in methanol. They found that the rate coefficient for reaction of 2,4-dinitrochlorobenzene with methoxide ions was increased by the addition of potassium salts and decreased by lithium salts. They noted that electrolytes could effect the reaction rate by changing the equilibrium between an ion-paired metal alkoxide and the free alkoxide ion and also considered the possibility of specific interactions of cations with nitro-groups of the substrate in the transition state. Bunton and co-workers[115] and Fendler and co-workers[116] have examined the effect of high salt concentrations on the rate of nucleophilic substitutions in aqueous solutions where ion-association was thought to be unimportant. They were able to separate the overall change in rate into initial state and transition state effects, both of which were important.

Experimental

The same technique as described previously was used for the visible spectral measurements at 25°C, using a Unicam SP500 instrument. In each individual run, the approach to equilibrium was an accurately first-order process and rate constants were reproducible within 5%.

Solubility Measurements

The solubility of 2-methoxycarbonyl-4,6-dinitroanisole in methanol and in methanol solutions containing dissolved salts was determined at 25°C. Excess of the pure substrate was shaken with solvent for 3 hours and then allowed to stand for 1 hour. A sample of the solution was then diluted by a factor of 5000 with pure methanol and the absorption measured at 220 and 275 nm. The extinction coefficients at these wavelengths was measured independently and had values of $1{\cdot}94 \times 10^4$ and $8{\cdot}0 \times 10^3$ mole^{-1} l.cm^{-1} respectively.

TABLE 5.1

Salt in methanol	Solubility (mol. l^{-1})
None	·195
NaCl (0·1 mole l^{-1})	·180
LiCl (0·1 mole l^{-1})	·180
$NaClO_4$ (0·1 mole l^{-1})	·20
Na_2SO_4 (0·1 mole l^{-1})	·19
KCl (saturated)	·19
$(n\text{-}But)_4NCl$ (0·1 mole l^{-1})	·20

The measurements are accurate within 5% so that within experimental error there is little variation in solubility.

Results and Discussion

It has been shown in Chapter 3, that in the presence of methoxide ions, 2-methoxycarbonyl-4,6-dinitroanisole gives a coloured adduct of structure (4.1). For this compound the attainment of equilibrium is sufficiently slow for the rate to be measured by conventional methods, and the absorption at equilibrium allows the determination of the stoichiometric equilibrium constant, K_C. The individual rate coefficients could then be calculated ($k_{obs} = k_1[\text{MOMe}] + k_{-1}$). Data obtained using tetra-n-butylammonium methoxide, potassium methoxide and lithium methoxide are in Tables 5.2, 5.3 and 5.4. The corresponding values for addition of sodium methoxide reported in the previous chapter, Table 4.3, are similar to those for potassium methoxide addition. In addition, equilibrium constants for complex formation with 4-methoxycarbonyl-2,6-dinitroanisole and 2-chloro-4,6-dinitroanisole are given in Tables 5.5 - 5.10. The variance of K_C values with base concentration is also shown graphically in Figures 5.1 and 5.2.

The results show certain similarities for these nitro-compounds. In each case the value of K_C remains constant when lithium methoxide is used, but small increases are observed with tetra-n-butylammonium methoxide and large increases with potassium and sodium methoxide. The changes in K_C values with base concentration will depend on changes in activities of three species; the parent anisoles, the complexes and the base. Bunton's work[115] in aqueous solutions has shown that the activities of neutral substrates may be affected by the presence of high salt concentrations. In order to test whether the activities of the parent anisoles are affected by the presence of dissolved electrolytes in methanol the solubility of 2-methoxycarbonyl-4,6-dinitroanisole in methanol was measured, containing 0·1 mole l^{-1} of various salts. The results indicate (Table 5.1) that within experimental error the solubility, and hence activity,[117] of the substrate is unaffected by the

TABLE 5.2

Kinetic and Equilibrium Measurements at 25°C for 2-Methoxycarbonyl-4,6-dinitroanisole[a] and Tetra-n-butylammonium Methoxide in Methanol

$(n\text{-But})_4$NOMe (mole l^{-1})	Optical density at equilibrium (472 nm)	K_C (l.mole^{-1})	$10^2\ k_{obs}$ (sec^{-1})	$10\ k_1$ (l.mole^{-1}sec^{-1})	$10^3\ k_{-1}$ (sec^{-1})
0·0144	0·091	9·6	2·54$\pm$0·1	2·1	22
0·0217	0·137	10·4	2·68	2·3	22
0·0288	0·180	11·0	2·82	2·4	21
0·0360	0·22	11·6	2·92	2·4	20·5
0·043	0·26	12·5	3·15	2·5	20
0·050	0·30	13·5	3·30	2·6	19·5
0·058	0·33	13·8	3·47	2·7	19
0·50	0·745	-	-	-	-

---

[a] Concentration of substrate is 3·84 x 10^{-5} mole l^{-1}

TABLE 5.3

Kinetic and Equilibrium Measurements at 25°C for 2-Methoxycarbonyl-4,6-dinitroanisole[a] and Lithium Methoxide in Methanol

[LiOMe] (mole l^{-1})	Optical density at equilibrium (472 nm)	K_C (l.mole^{-1})	$10^2\ k_{obs}$ (sec^{-1})	$10\ k_1$ (l.mole^{-1}sec^{-1})	$10^3\ k_{-1}$ (sec^{-1})
0·010	0·054	8·3	2·7±0·3	2·1	25
0·020	0·100	8·3	3·2	2·2	27
0·030	0·134	7·9	3·5	2·2	28
0·040	0·170	8·0	3·6	2·2	27
0·060	0·240	8·7	4·2	2·4	27
0·080	0·285	8·6	-	-	-
0·10	0·31	8·0	-	-	-
0·20	0·45	9·0	-	-	-
0·40	0·57	11·0	-	-	-
1·0	0·7	-	-	-	-

[a] Concentration of substrate is 3·84 x 10^{-5} mole l^{-1}.

TABLE 5.4

Kinetic and Equilibrium Measurements at 25°C for 2-Methoxycarbonyl-4,6-dinitroanisole[a] and Potassium Methoxide in Methanol

[KOMe] (mole l^{-1})	Optical density at equilibrium (472 nm)	K_C (l.mole^{-1})	$10^2\ k_{obs}$ (sec^{-1})	$10\ k_1$ (l.mole^{-1}sec^{-1})	$10^3\ k_{-1}$ (sec^{-1})
0·0044	0·038	12	1·75±0·5	2·0	16·5
0·0070	0·069	14	1·61	2·05	14·5
0·0108	0·121	17·5	1·54	2·3	13
0·0216	0·268	25	1·50	2·5	10
0·0323	0·39	32·5	1·77	2·8	8·5
0·043	0·48	40	1·86	2·8	7
0·054	0·54	45	2·27	3·0	6·5
0·075	0·61	56	3·27	3·5	6·3
0·81	0·76	-	-	-	-

[a] Concentration of substrate is 3·84 x 10^{-5} mole l^{-1}.

TABLE 5.5

Equilibrium Measurements with 4-Methoxycarbonyl-2,4-dinitroanisole (4×10^{-5} mole l^{-1}) in Methanolic Tetra-n-butylammonium Methoxide at 25°C

$[(n\text{-But})_4NOMe]$ (mole l^{-1})	Optical density at equilibrium (522 nm)	K_C (l.mole^{-1})
0·00875	0·044	6·5
0·0175	0·084	6·6
0·0263	0·125	6·9
0·035	0·170	7·5
0·0438	0·210	7·9
0·0525	0·248	8·3
0·0613	0·294	9·2
0·070	0·326	9·5
0·0788	0·358	9·9
0·5	0·763	-
1·0	0·816	-

TABLE 5.6

Equilibrium Measurements with 4-Methoxycarbonyl-2,6-dinitroanisole (4×10^{-5} M) in Methanolic Lithium Methoxide at 25°C

LiOMe (mole l^{-1})	Optical density at equilibrium (524 nm)	K_C (l.mole^{-1})
·01	·040	5·5
·02	·073	5·2
·03	·104	5·2
·04	·133	5·2
·05	·16	5·2
·06	·183	5·2
·07	·206	5·2
·08	·228	5·2
·09	·245	5·2
·0985	·263	5·3
·197	·401	5·5
·296	·493	6·0
·394	·560	6·7
·493	·607	7·5
·788	·690	10·7
1·375	·745	-
2·475	·772	

TABLE 5.7

Kinetic and Equilibrium Data at 25°C for the Addition of Methoxide to 4-Methoxycarbonyl-2,6-dinitroanisole ($3{\cdot}84 \times 10^{-5}$ $\underline{\underline{M}}$) in Methanol

KOMe (mole l^{-1})	Optical density at equilibrium (522 nm)	K_C (l.mole^{-1})	10^2 k_{obs} (sec^{-1})	10 k_1 (l.mole^{-1}sec^{-1})	10^3 k_{-1} (sec^{-1})
·0066	·0418	8·3	4·6±0·2	3·62	43·6
·0088	·0615	9·4	4·4	3·83	40·0
·0108	·079	10·0	4·2	3·79	38·0
·0216	·181	13·31	3·9	4·04	30·3
·0323	·285	16·8	4·0	4·36	25·9
·043	·368	19·35	4·4	4·63	23·9
·054	·441	22·2	4·6	4·65	20·9
·81	·81	-	-	-	-

TABLE 5.8

Equilibrium Measurements with 2-Chloro-4,6-dinitroanisole (4×10^{-5} M) in Methanolic Tetra-n-butylammonium Methoxide at 25°C

$(n\text{-But})_4NOMe$ (mole l^{-1})	Optical density at equilibrium (490 nm)	K_C (l.mole^{-1})
·00875	·033	4·2
·0175	·064	4·3
·0263	·098	4·5
·035	·134	4·9
·0438	·168	5·1
·0525	·208	5·6
·0613	·242	5·8
·070	·285	6·4
·0788	·317	6·7
1·0	·920	-

TABLE 5.9

Equilibrium Measurements with 2-Chloro-4,6-dinitroanisole (4×10^{-5} M) in Methanolic Lithium Methoxide at 25°C

LiOMe (mole l^{-1})	Optical density at equilibrium (492 nm)	K_C (l.mole^{-1})
·01	·029	3·5
·02	·055	3·5
·03	·074	3·2
·04	·094	3·1
·05	·117	3·2
·06	·135	3·2
·07	·153	3·1
·08	·168	3·1
·09	·184	3·1
·096	·189	3·0
·192	·31	3·0
·288	·40	3·1
·384	·472	3·3
·480	·538	3·6
·575	·580	3·7
·768	·665	4·7
1·687	·850	-

TABLE 5.10

Equilibrium Measurements with 2-Chloro-4,6-dinitroanisole (4×10^{-5}M) in Methanolic Potassium Methoxide at 25°C

KOMe (mole l^{-1})	Optical density at equilibrium (492 nm)	K_C (l.mole^{-1})
·0112	·044	4·5
·0224	·091	4·9
·0336	·150	5·8
·0448	·203	6·3
·0560	·259	7·0
·0672	·311	7·6
·0784	·361	8·2
·0896	·410	9·0
·101	·452	9·6
·162	·621	12·8
·243	·757	19·1
·729	·920	-

presence of this concentration of salt. We must then look to changes in the activity of the base or the complex to account for the increases in equilibrium constant.

These results might be interpreted in terms of a general medium effect in which the presence of dissolved electrolyte produces a favourable environment for complex formation. However no such effect is observed in the ionisation of aromatic amines used to determine the H_M acidity function. Neither are increases in value of K_C observed[63] for complex formation of 1,3,5-trinitrobenzene with sodium methoxide. In view of the fairly specific nature of the observed effects these results are rationalised in terms of the stabilisation of the 1,1-complex, (4.1), by association with the cations present. Due to the much lower dielectric constant of methanol the effects of ion-association should be more pronounced in methanol than in water and indeed Fendler et al[116] found that in aqueous solution the Meisenheimer complex from 2,4,6-trinitroanisole is apparently destabilised at high salt concentrations.

In terms of the following scheme:

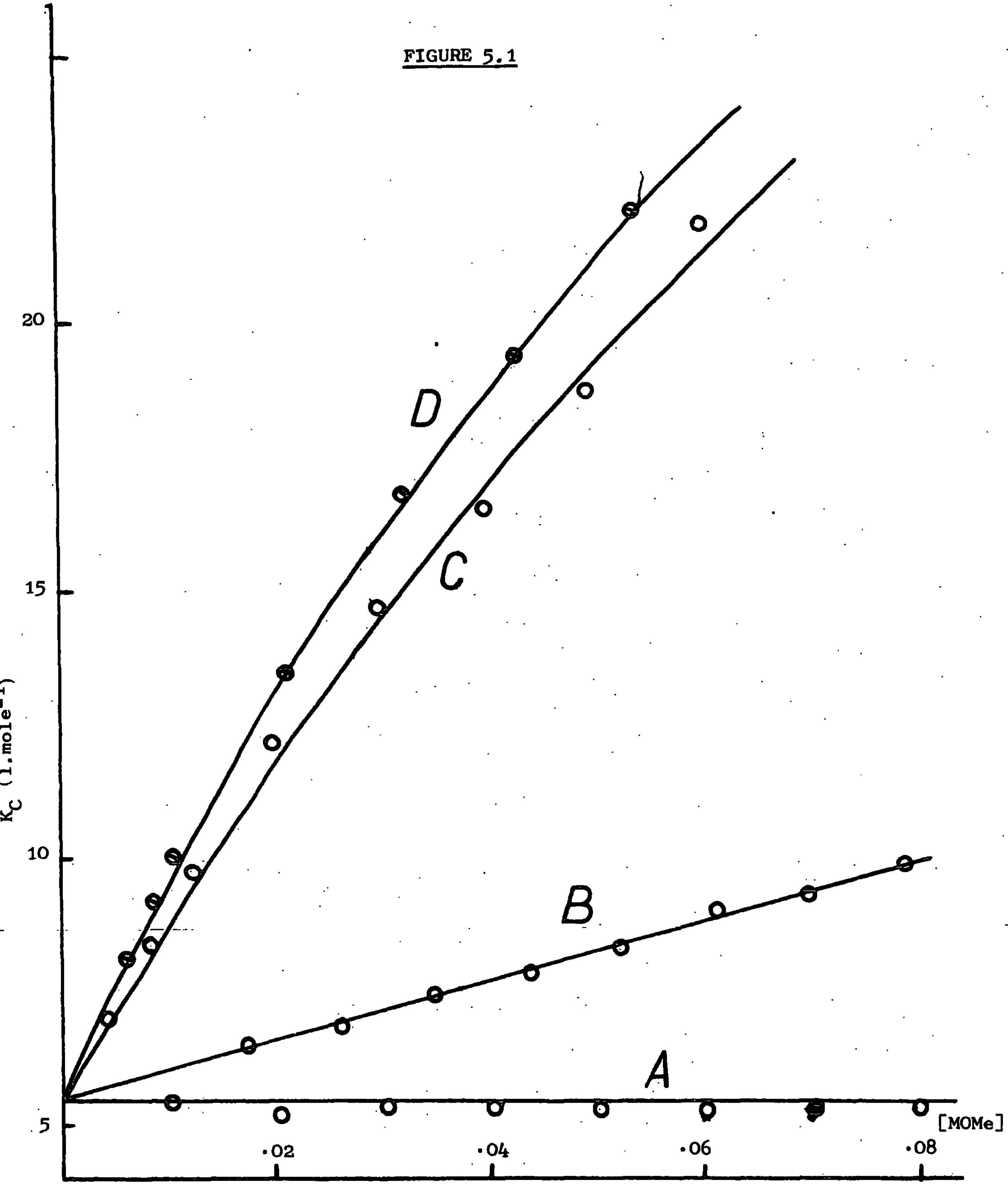
$$\begin{tikzcd}
P + M^+ + OMe^- \arrow[r, shift left, "K_1"] \arrow[d, shift left, "K_3"] & POMe^- + M^+ \arrow[l, shift left] \arrow[r, shift left, "K_2"] & POMe^-,M^+ \arrow[l, shift left] \\
M^+,OMe^- \arrow[u, shift left] & &
\end{tikzcd}$$

ion association will effect the measured equilibrium constant so that $K_C = K_1(1 + K_2[M^+])/(1 + K_3[M^+])$. In accordance with the assumption made in the previous chapter, it can be assumed that in the case of potassium ions, as with sodium ions, there will probably be little association with methoxide ions in dilute solutions so that plots of K_C versus the stoichiometric base concentration, [MOMe], should approach linearity at sufficiently low base concentrations, and that this is the case is indicated by the results in Figures 5.1 and 5.2. In fact ion association may not significantly reduce the reactivity of methoxide ions but may cause curvature in the plots by reducing the concentration of cations available for association with the complexes. The results indicate similar association of the complexes with potassium and sodium ions with association constants decreasing in the order 2-methoxycarbonyl-4,6-dinit oanisole, $K_2 \sim 100$ mole^{-1}l; 4-methoxycarbonyl-2,6-dinitroanisole, $K_2 \sim 60$ mole^{-1}l; 2-chloro-4,6-dinitroanisole, $K_2 \sim 20$ mole^{-1}l.

With tetra-n-butylammonium methoxide the measured values of K_C increase linearly with base concentration. The effect is independent of the particular anisole used and an enhancement in K_C by a factor of 1·5 is observed in the presence of 0·05 mole l^{-1} base over the value at zero base concentration. Association of the large diffusely charge tetra-alkylammonium ions with methoxide ions, containing a localised negative charge, is likely to be small. However tetra-alkylammonium ions are known[115,118] to interact with and stabilise large polarisable anions, such as Meisenheimer complexes. In this case it seems likely that the increase in K_C values result from such interactions, the effect being largely independent of the structure of the complex. The effect is smaller than that observed with sodium or potassium ions and gives a value of ca. 10 mole^{-1}l for K_2.

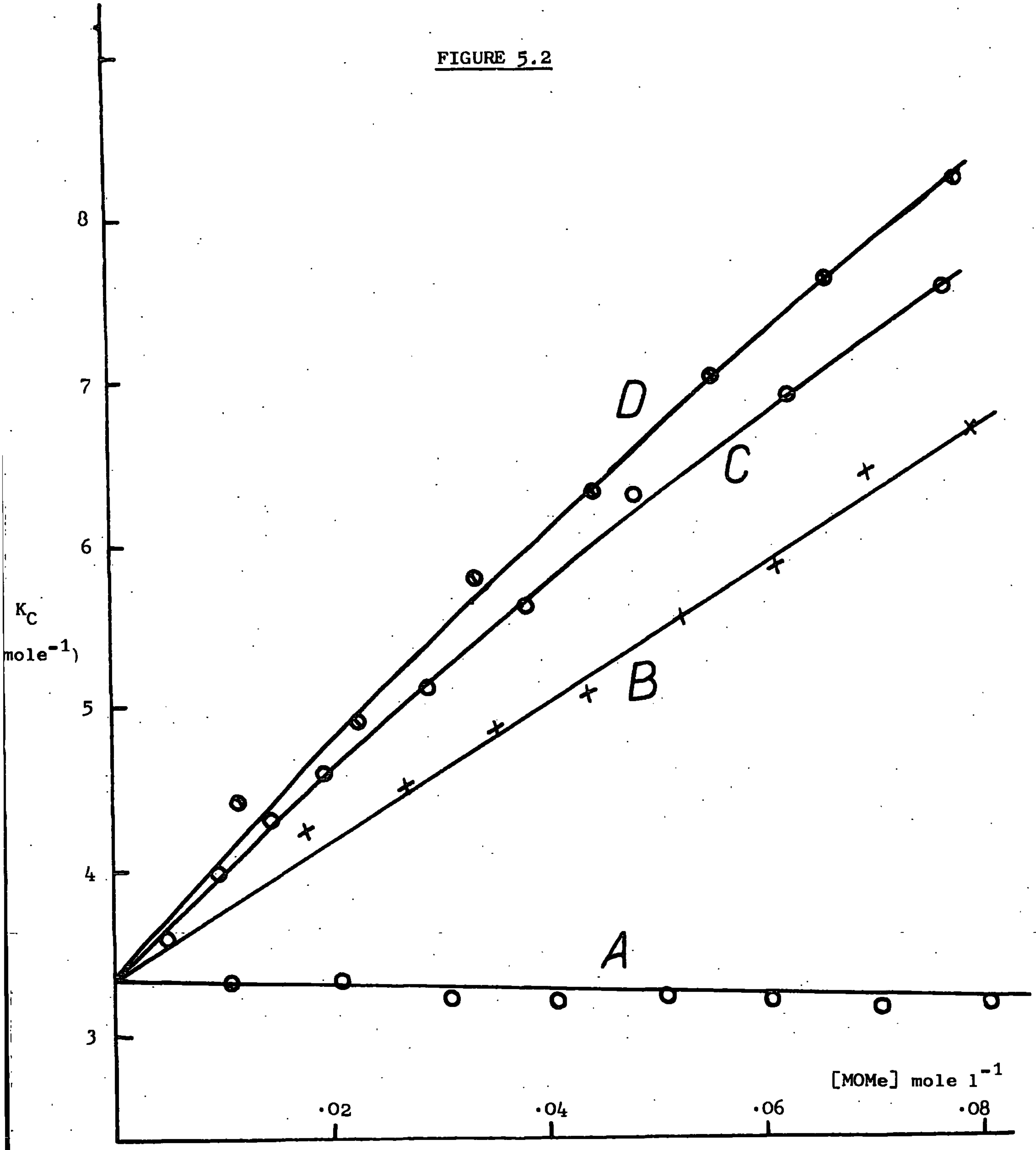
The independence of K_C values on base concentration in the case of lithium methoxide is perhaps surprising. One explanation would be that there is little association of the complexes with lithium ions. The lithium ions will be more strongly solvated than sodium or potassium ions so that their ability to form ion-pairs may be reduced. For example the ion-pair association constant for lithium chloride in alcoholic solvents has been

FIGURE 5.1



Variation of K_C with base concentration for Meisenheimer complex formation from 4-methoxycarbonyl-2,6-dinitroanisole with the following methoxides: (A) lithium; (B) tetra-n-butylammonium; (C) sodium; (D) potassium

FIGURE 5.2



Variation of K_C with base concentration for Meisenheimer complex formation from 2-chloro-4,6-dinitroanisole with the following methoxides: (A) lithium; (B) tetra-n-butylammonium; (C) sodium; (D) potassium found to be smaller than for the potassium or sodium salts.[119] A special argument using the idea of localised solvolysis[120] has been advanced to account for the special stability of the lithium methoxide ion-pair. It might then be expected that increasing association of the lithium and methoxide ions would result in a decrease in equilibrium constant with increasing base concentration. The case is perhaps overstated in that a methoxide ion in a lithium methoxide ion-pair would be expected to have reduced reactivity rather than no reactivity. However small rate decreases (induced by lithium ions) in nucleophilic substitution reactions have been found by Reinheimer.[113] A possible explanation in the present case is that the lithium ions associated to a similar extent with methoxide ions and with complexes so that little overall variation in equilibrium constant is obtained.

In general the results (Tables 5.2 and 5.4) show that change in K_C values result from increase in value of k_1 and decrease in k_{-1} indicating that the interactions of cations with the transition state for methoxide addition are present, but to a smaller extent than with the complex.

As a consequence of this work it would appear to be preferable to use lithium methoxide or tetra-n-butylammonium methoxide in order to measure thermodynamic equilibrium constants for Meisenheimer complex formation. The results given in this chapter give the following values at 25°C: 2-methoxycarbonyl-4,6-dinitroanisole, 8·3(10) $l.mole^{-1}$; 4-methoxycarbonyl-2,6-dinitroanisole, 5·5(6) $l.mole^{-1}$ and 2-chloro-4,6-dinitroanisole, 3·4(3) $l.mole^{-1}$. The values in parentheses are those (Table 4.7) obtained using sodium methoxide where the extrapolation to zero base concentration is less accurate.

As a further example kinetic and equilibrium studies for the Meisenheimer complex formation of 1-methoxy-2,4-dinitronaphthalene using lithium methoxide (Table 5.11) were carried out. They indicate a value of 205 $l.mole^{-1}$ for the

TABLE 5.11

Kinetic and Equilibrium Data for Lithium Methoxide Addition to 1-Methoxy-2,4-dinitronaphthalene ($3{\cdot}84 \times 10^{-5}$ mole l^{-1}) in Methanol at 25°C

LiOMe (mole l^{-1})	Optical density at equilibrium (498 nm)	K_C (l.mole^{-1})	10^2 k_{obs} (sec^{-1})	k_1 (l.mole^{-1}sec^{-1})	10^3 k_{-1} (sec^{-1})
·0038	·39	202	0·81±·02	·93	4·6
·0077	·55	204	1·13	·90	4·4
·0096	·60	208	1·34	·93	4·5
·0192	·72	208	2·30	·95	4·6
·029	·77	204	3·20	·94	4·6
·96	·90	-	-	-	-

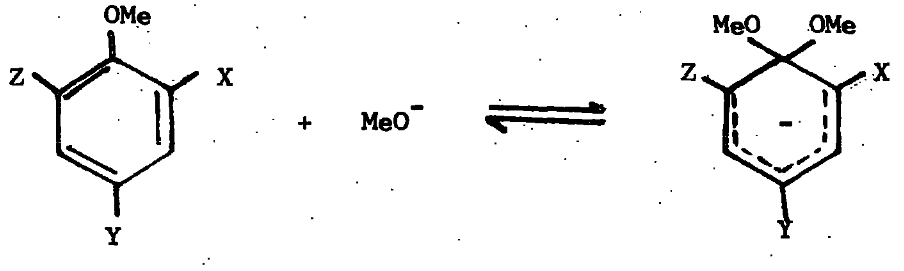
thermodynamic equilibrium constant, compared to the previously quoted value of 240 l.mole^{-1} obtained[34] using sodium methoxide.

CHAPTER 6

EFFECTS OF ADDED BARIUM AND CALCIUM IONS

Introduction

It has been shown in the last two chapters that for several anisoles the measured stoichiometric equilibrium constant K_C (= [Complex]/[Parent][NaOMe]) for the equilibrium of the type:



(4.1)

increased markedly with increasing sodium or potassium methoxide concentration even in dilute solutions. This is in contrast with the behaviour of anilines (used to measure the H_M acidity function[110] in this medium) where little variation in ionisation constant is observed at base concentration below $0{\cdot}1\underline{\underline{M}}$. This effect has been rationalised in terms of stabilisation of the Meisenheimer complexes by association with sodium or potassium ions. The results discussed in chapter 5 indicated that the magnitude of this effect varied with the nature of the substituents X, Y, Z and the following approximate values for association with sodium ions were found: $X = CO_2Me$, $Y = Z = NO_2$, 90 l.mole^{-1}; $Y = CO_2Me$, $X = Z = NO_2$, 50 l.mole^{-1}; $X = Cl$, $Y = Z = NO_2$, 25 l.mole^{-1}. Similar results were obtained using potassium as the counter ion. However with tetra-n-butylammonium ions a small non-specific stabilising effect was observed while lithium ions gave no evidence for association.

In the present chapter are reported the large effects produced by the bivalent barium and calcium ions on the stabilities of Meisenheimer complexes.

Results and Discussion

2-Methoxycarbonyl-4,6-dinitroanisole: The 1,1-complex formed in the presence of methoxide ions has the thermodynamic equilibrium constant, K_1, value of 8·3 l.mole^{-1} (chapter 5). Obtained by extrapolation to zero base concentration, using lithium methoxide. The results in Tables 6.1 and 6.2 show the enormous increase in stoichiometric equilibrium constant K_C (= [Complex]/[Parent][NaOMe]) produced on the addition of small concentrations of barium salts.

Several points are of interest: (i) similar effects are observed on the addition of either barium chloride or barium perchlorate; (ii) the K_C value at a given concentration of barium salt decreases slightly as the sodium methoxide concentration is increased - this may be attributed to loss of barium ions by association with methoxide ions; (iii) the measured K_C values approach a limiting value at high concentration of added salt. Full analysis of the data is complicated and only a semi-quantitative treatment has been made. The cation present will associate with Meisenheimer complexes, equilibrium constant K_2, and with methoxide ions, equilibrium constant K_3, giving the following scheme:

$$\begin{tikzcd}
\mathrm{P} + \mathrm{OMe}^- + \mathrm{M}^{n+} \arrow[r, shift left, "K_1"] \arrow[r, leftarrow, shift right] \arrow[d, shift left, "K_3"] \arrow[d, leftarrow, shift right] & \mathrm{P.OMe}^- + \mathrm{M}^{n+} \arrow[r, shift left, "K_2"] \arrow[r, leftarrow, shift right] & \mathrm{P.OMe}^-,\mathrm{M}^{n+} \\
\mathrm{M}^{n+},\mathrm{OMe}^-
\end{tikzcd}$$

In the presence of both sodium and barium ions the stoichiometric equilibrium constant K_C will be related to the thermodynamic constant K_1 by:

$$K_C = K_1 \frac{(1 + K_2^{Na}[\mathrm{Na}^+] + K_2^{Ba}[\mathrm{Ba}^{++}]}{(1 + K_3^{Na}[\mathrm{Na}^+] + K_3^{Ba}[\mathrm{Ba}^{++}]} \qquad 6.1$$

TABLE 6.1

The Effect of Barium Ions on the Reaction of 2-Methoxycarbonyl-4,6-dinitroanisole with Sodium Methoxide at 25°C

NaOMe (mole l^{-1})	$BaCl_2$ (mole l^{-1})	Optical density at equilibrium[a] (472 nm)	K_C (l.mole^{-1})	10^2 k_{obs} (sec^{-1})	k_1 (l.mole^{-1}sec^{-1})	10^3 k_{-1} (sec^{-1})
0·0096	-	0·117	20	1·47	0·24	12·5
0·0096	0·0010	0·313	93	2·5	1·2	12·5
0·0096	0·0019	0·39	150	3·4	2·1	14
0·0096	0·0038	0·46	240	4·8	3·5	14
0·0096	0·0067	0·51	350	6·4	5·0	14·5
0·0096	0·017	0·55	520	-	-	-
0·0048	-	0·43	13	1·85	0·23	17·5
0·0048	0·0010	0·23	95	2·3	1·6	16
0·0048	0·0019	0·31	185	2·9	2·8	15
0·0048	0·0038	0·39	300	3·5	4·3	14
0·0048	0·0080	0·45	440	4·1	5·8	13

[a] The concentration of parent anisole is 3·84 x 10^{-5} $\underline{\underline{M}}$. The extinction coefficient of the complex is decreased by association with barium ions so that the optical density for complete conversion to ion-paired complex is 0·66.

TABLE 6.2

The Effect of Barium Ions on the Reaction of 2-Methoxycarbonyl-4,6-dinitroanisole with Sodium Methoxide at 25°C

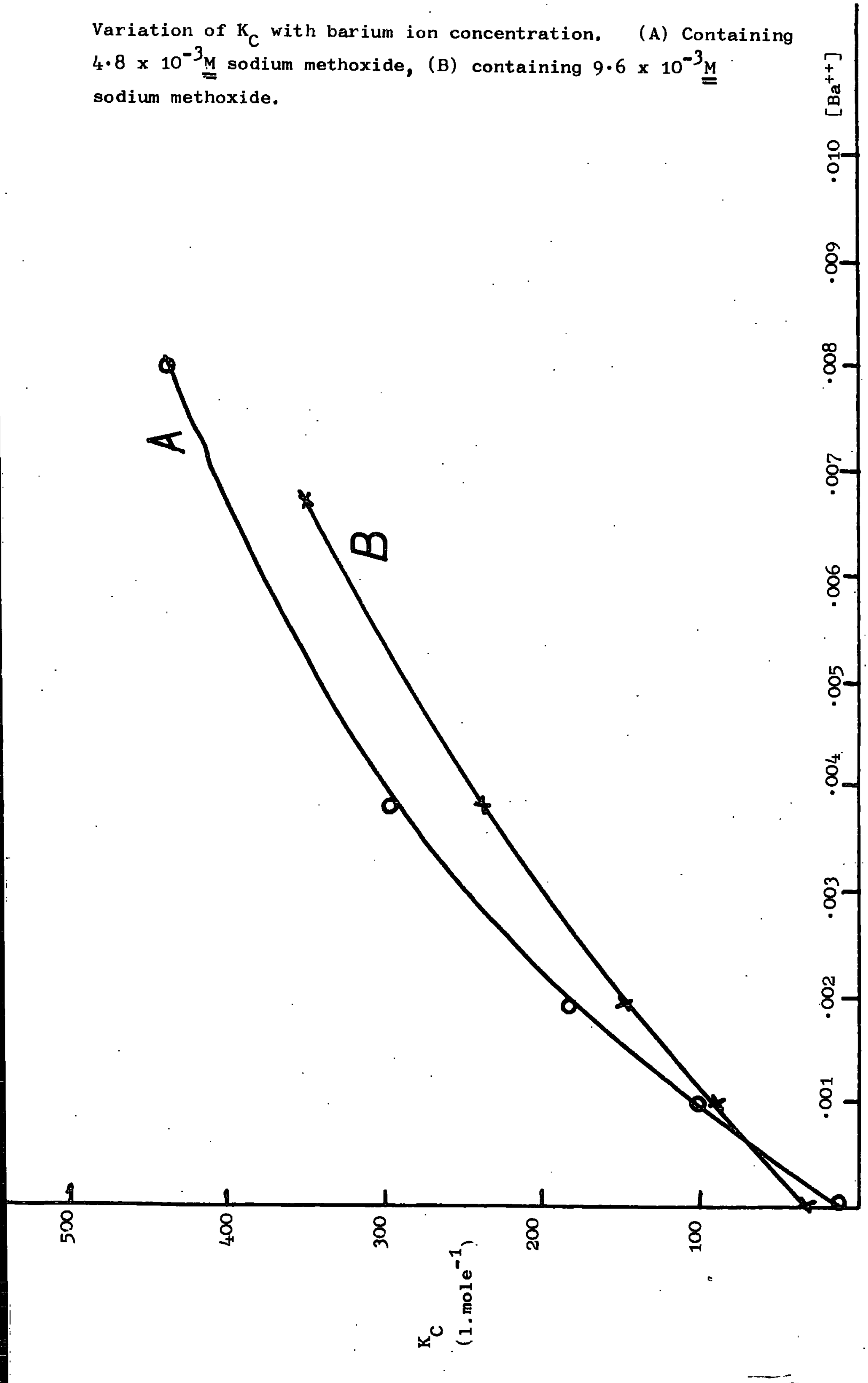
NaOMe (mole l^{-1})	$Ba(ClO_4)_2$ (mole l^{-1})	Optical density at equilibrium[a] (472 nm)	K_C (l.mole^{-1})	$10^2\ k_{obs}$ (sec^{-1})	k_1 (l.mole^{-1}sec^{-1})	$10^3\ k_{-1}$ (sec^{-1})
0·0096	-	0·117	20	1·47	0·24	12·5
0·0096	0·0038	0·47	260	4·5	3·3	13
0·0096	0·0067	0·51	350	6·0	4·8	13·5
0·0096	0·030	0·58	750	-	-	-
0·0096	0·060	0·60	<u>ca</u>.1000	-	-	-
0·0096	0·090	0·61	<u>ca</u>.1200	-	-	-
0·0048	-	0·043	13	1·85	0·23	17·5
0·0048	0·090	0·57	<u>ca</u>.1300	-	-	-
0·019	0·060	0·63	-	-	-	-
0·019	0·090	0·63	-	-	-	-
0·038	0·090	0·65	-	-	-	-
0·50	-	0·73	-	-	-	-

[a] The concentration of parent anisole is $3{\cdot}84 \times 10^{-5}$<u>M</u>. The extinction coefficient of the complex is decreased by association with barium ions so that the optical density for complete conversion to ion-paired complex is 0·66

It is assumed that for a given cation the value of K_3 is small compared with K_2, i.e. association of cations with methoxide ions is considerably weaker than with the Meisenheimer complex, then the denominator may be neglected. Then at constant sodium ion concentration a plot of K_C versus barium ion concentration should be linear with slope $K_1.K_2^{Ba}$. From the limiting slopes of such plots at low barium ion concentrations a value of ca. 10^4 $l.mole^{-1}$ for K_2^{Ba} is estimated (Figure 6.1). However this procedure gives only a minimum value for K_2^{Ba} since account should also be taken of the association of barium and methoxide ions. This will introduce a term in the denominator of equation 6.1 and will reduce the concentration of free barium ions. A value for the ion-pair association constant of barium methoxide could not be found in literature, however the association constants of bivalent cations with hydroxide ions in water[121] have values of ca. 10 $l.mole^{-1}$ and it seems likely that in methanol values will be larger. If a value of 10^2 $l.mole^{-1}$ is assumed for K_3^{Ba} then in the presence of 10^{-2}M methoxide ions, considerable amounts of the ion-pair Ba^{++}, OMe^- will be formed so that the concentration of free barium ions will be considerably reduced from the stoichiometric concentration of barium salt added. Taking a value of 10^2 $l.mole^{-1}$ for K_3^{Ba} results in a value of $1{\cdot}6 \times 10^4$ $l.mole^{-1}$ for K_2^{Ba}. Equation 6.1 predicts that at high barium ion concentrations the value of K_C should approach a limit of $K_1.K_2^{Ba}/K_3^{Ba}$. The experimentally obtained limiting value of ca. 1200 is in reasonable agreement with that predicted from values of $K_2^{Ba} \sim 1{\cdot}6 \times 10^4$ and $K_3^{Ba} \sim 1 \times 10^2$ $l.mole^{-1}$. These are, of course, only very approximate values but demonstrate the very strong association of barium ions with this Meisenheimer complex. In a more quantitative treatment it would be necessary to consider association of barium ions with chloride or perchlorate ions and also variations in the activity coefficient of barium ions with concentration.

<u>FIGURE 6.1</u>

Variation of K_C with barium ion concentration. (A) Containing $4 \cdot 8 \times 10^{-3}\underline{\underline{M}}$ sodium methoxide, (B) containing $9 \cdot 6 \times 10^{-3}\underline{\underline{M}}$ sodium methoxide.



Measurement of the rate of attainment of equilibrium as described in the previous chapters, allows the determination of the individual rate coefficients for complex formation ($k_{obs} = k_1[NaOMe] + k_{-1}$). The results in Tables 6.1 and 6.2 show that the major effect of added barium ions is to increase the value of k_1 indicating that the interaction of cation with substrate is present to a considerable extent in the transition state for complex formation.

In the presence of added calcium ions results following a similar general pattern to those described with barium ions were obtained and give a value for K_2^{Ca} of circa $8 \times 10^3 \underline{\underline{M}}^{-1}$, Table 6.3.

<u>4-Methoxycarbonyl-2,6-dinitroanisole</u>: The thermodynamic equilibrium constant, K_1, for the formation of 1,1-complex in this case has a value of 5·5 l.mole^{-1} (chapter 5). The results in Table 6.4 show that the presence of small concentration of barium ions results in increased complex formation. By use of equation 6.1, taking K_3^{Ba} as 10^2 l.mole^{-1} a value of <u>ca</u>. 5×10^3 for the ion-pair association constant K_2, of the Meisenheimer complex with barium ions is calculated.

<u>2-Chloro-4,6-dinitroanisole</u>: The results in Table 6.5 indicate that for this anisole methoxide addition is enhanced in the presence of barium ions. They yield a value of <u>ca</u>. 1×10^3 l.mole^{-1} for the ion-pair association constant of the complex with barium ions.

<u>2,4,6-Trinitroanisole</u>: Sodium methoxide addition to 2,4,6-trinitroanisole to give a Meisenheimer complex of structure (4.1) has been studied by several groups of workers.[12,24,46] The value of the equilibrium constant, K_1, is high (17,000 l.mole^{-1})[24] so that in solutions containing $1 \times 10^{-2}\underline{\underline{M}}$ methoxide conversion of the anisole to complex is virtually complete. The visible spectrum in the presence of $1 \times 10^{-2}\underline{\underline{M}}$ tetra-n-butylammonium methoxide

TABLE 6.3

The Effect of Calcium Ions on the Reaction of 2-Methoxycarbonyl-4,6-dinitroanisole with Sodium Methoxide at 25°C

NaOMe (mole l^{-1})	$Ca(ClO_4)_2$ (mole l^{-1})	$CaCl_2$ (mole l^{-1})	Optical density at equilibrium[a] (472 nm)	K_C ($l.mole^{-1}$)	10^2 k_{obs} (sec^{-1})	k_1 ($l.mole^{-1}sec^{-1}$)	10^3 k_{-1} (sec^{-1})
0·0096	-	-	0·116	20	1·58	0·26	13
0·0096	0·00096	-	0·175	38	5·6	1·55	41
0·0096	0·0019	-	0·232	56	8·3	3·0	54
0·0096	0·0038	-	0·308	91	10·5	5·1	56
0·0096	0·0058	-	0·345	114	-	-	-
0·0096	0·0096	-	0·383	144	-	-	-
0·0096	0·0192	-	0·435	200	-	-	-
0·0096	0·0288	-	0·44	-	-	-	-
0·0096	0·048	-	0·45	-	-	-	-
0·0096	0·087	-	0·45	-	-	-	-
0·0096	-	0·00096	0·183	40	6·0	-	-
0·0096	-	0·00192	0·240	59	7·8	-	-
0·0096	-	0·0058	0·338	110	-	-	-
1·00	-	-	0·72	-	-	-	-
0·0048	-	0·00096	0·118	45	7·0	2·5	57
0·0048	-	0·00192	0·185	81	8·4	-	-
0·0048	-	0·0038	0·246	125	10·4	-	-
0·0048	-	0·0077	0·29	163	-	-	-
0·0048	-	0·0135	0·31	185	-	-	-

[a] The concentration of parent anisole is $3{\cdot}84 \times 10^{-5}\underline{\underline{M}}$. The extinction coefficient of the complex is decreased by association with clacium ions so that the optical density for complete conversion to ion-paired complex is 0·66

TABLE 6.4

The Effect of Barium Ions on the Complex Formation of 4-Methoxycarbonyl-2,6-dinitroanisole[a] with Sodium Methoxide at 25°C

NaOMe (mole l^{-1})	$BaCl_2$ (mole l^{-1})	Optical density at equilibrium (525 nm)	K_C (l.mole^{-1})
0·0096	-	0·064	9
0·0096	0·0010	0·141	23
0·0096	0·0019	0·196	34
0·0096	0·0038	0·26	50
0·0096	0·0058	0·30	63
0·0096	0·0110	0·36	86
1·0	-	0·80	-

[a] Concentration is $3{\cdot}84 \times 10^{-5}$ mole l^{-1}

TABLE 6.5

The Effect of Barium Ions on Complex Formation of 2-Chloro-4,6-dinitroanisole ($3{\cdot}84 \times 10^{-5}$ M) with Sodium Methoxide at 25°C

NaOMe (mole l^{-1})	$BaCl_2$ (mole l^{-1})	$Ba(ClO_4)_2$ (mole l^{-1})	Optical density at equilibrium (500 nm)	K_C (l.mole^{-1})
0·0096	-	-	0·034	4·0
0·0096	0·0019	-	0·056	6·8
0·0096	0·0038	-	0·072	8·9
0·0096	0·0058	-	0·084	10·6
0·0096	0·017	-	0·115	15
0·019	-	-	0·075	4·6
0·019	-	0·0048	0·12	8·0
0·019	-	0·0096	0·15	10·2
0·019	-	0·019	0·19	13·2
0·019	-	0·029	0·21	16
1·0	-	-	0·92	-

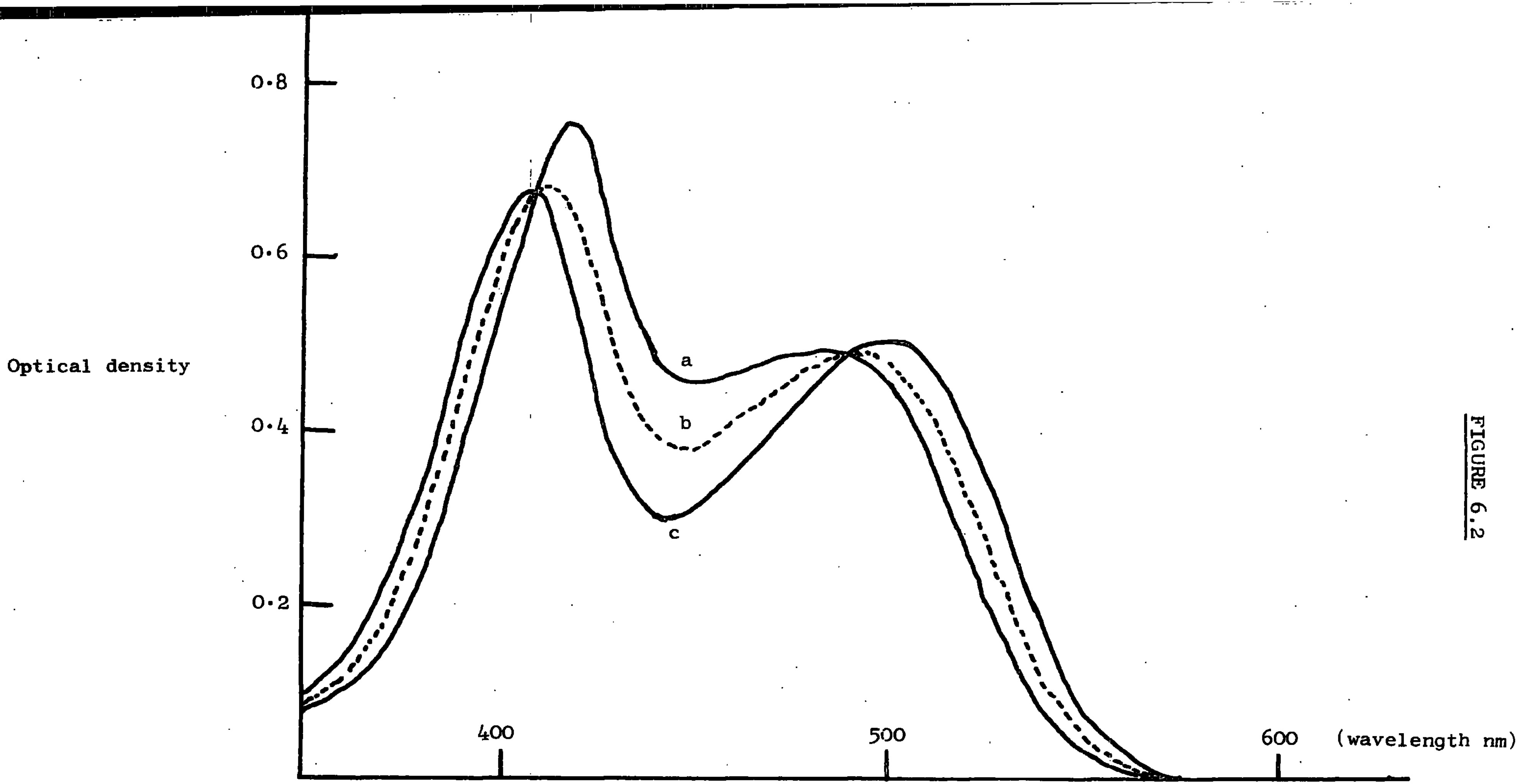
is shown in Figure 6.2 By analogy with previous results the tetra-n-butylammonium cation would not be expected to associate strongly with the trinitrocyclohexadienate anion so that this spectrum will correspond to the unassociated anion. The changes in visible spectrum produced in the presence of barium ions are shown in Figure 6.2. On increasing the barium chloride concentration to $1{\cdot}4 \times 10^{-2}$M the short wavelength maximum shifts from 418 to 405 nm and decreases in intensity, while the long wavelength band shifts from 480 to 500 nm with little change in intensity. These changes are interpreted as showing the formation of an ion-associate of the methoxide adduct with barium ions:

$$\mathrm{P.OMe^{-}} + \mathrm{Ba^{++}} \xrightleftharpoons{K_2} \mathrm{P.OMe^{-},Ba^{++}}$$

The change in spectral shape results no doubt from changes in charge distribution on ion-association. Similarly the addition of calcium chloride or sodium chloride produced marked changes in visible spectrum of the adduct, details in Table 6.6. However the addition of lithium chloride in concentrations up to $0{\cdot}2$M produced no spectral changes indicating little association of the adduct with lithium ions.

Using the variation in visible spectrum with cation concentration it was possible to calculate very approximate values for the ion-pair association constants, K_2. Values are collected in Table 6.8 and should be regarded as giving the order of magnitude of the association constants rather than precise values. The values of ca. 70 $\mathrm{l.mole^{-1}}$ for association with sodium ions indicates that in methanolic sodium methoxide solutions the effect of ion-pairing will be small at base concentrations below 10^{-3}M. Hence the variation of measured equilibrium constant with base concentration observed by Illuminati and co-workers[46] is unlikely to result from this source.

FIGURE 6.2



The effect of barium ions on the visible spectrum of the Meisenheimer complex from 2,4,6-trinitroanisole. Each sample was made up with $2{\cdot}94 \times 10^{-5}$ $\underline{\underline{M}}$ 2,4,6-trinitroanisole and 1×10^{-2} $\underline{\underline{M}}$ tetra-n-butylammonium methoxide. The barium chloride concentrations are:
(a) 0; (b) 2×10^{-3} $\underline{\underline{M}}$; (c) $1{\cdot}4 \times 10^{-2}$ $\underline{\underline{M}}$.

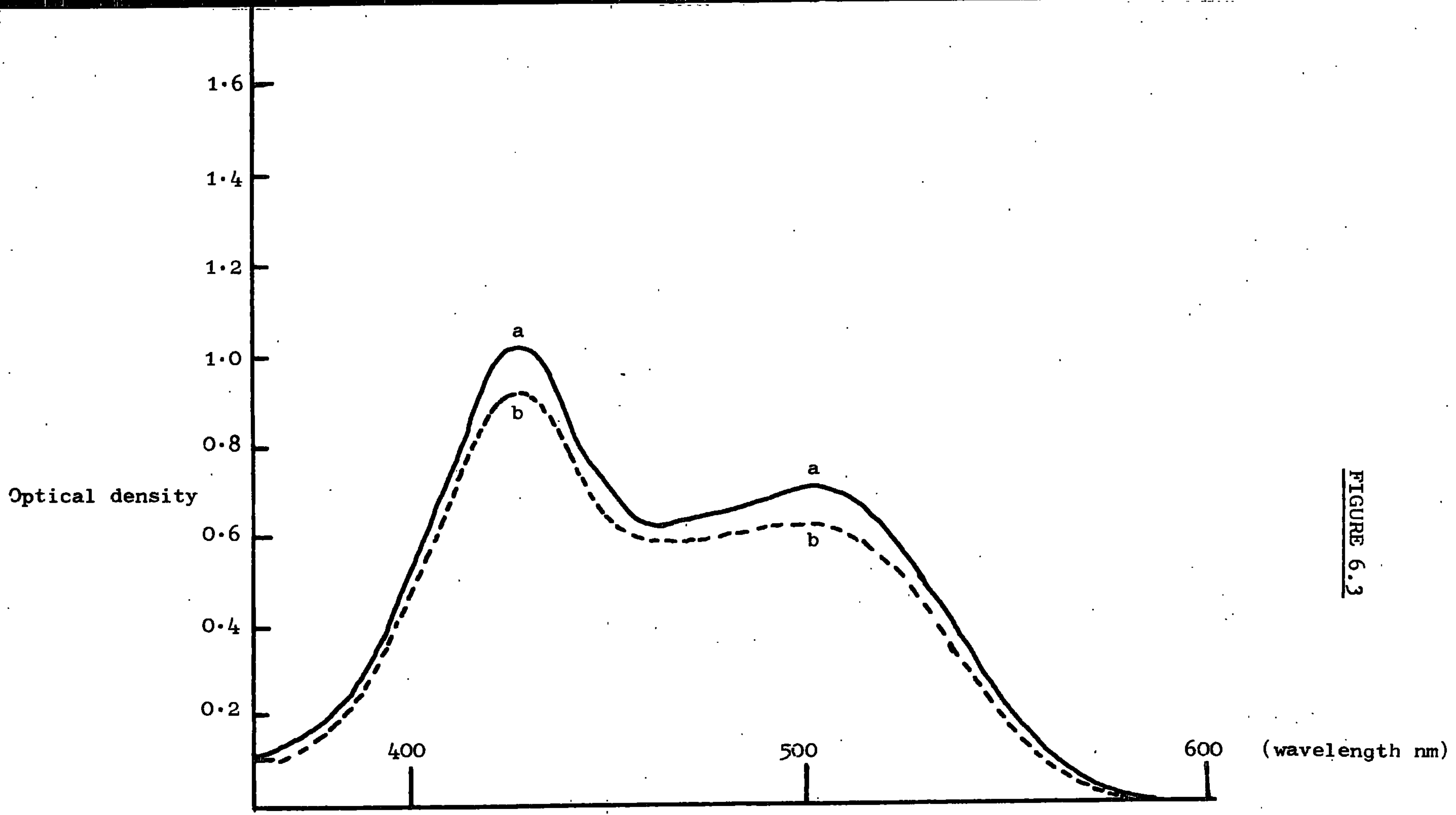
TABLE 6.6

The Effect of Counter-Ion on the Visible Spectrum of 2,4,6-Trinitro-1,1-dimethoxycyclohexadienate ion in Methanol

Cation	λ_{max} (nm)	Extinction Coefficient ($l.mole^{-1}cm^{-1}$)	λ_{max} (nm)	Extinction Coefficient ($l.mole^{-1}cm^{-1}$)
$(n\text{-}But)_4N^+$	418	$2{\cdot}55 \times 10^4$	480	$1{\cdot}67 \times 10^4$
Na^+	412	$2{\cdot}42 \times 10^4$	490	$1{\cdot}67 \times 10^4$
Ba^{++}	405	$2{\cdot}20 \times 10^4$	500	$1{\cdot}66 \times 10^4$
Ca^{++}	404	$2{\cdot}05 \times 10^4$	490	$1{\cdot}62 \times 10^4$

1,3,5-Trinitrobenzene: As an example of a compound where methoxide addition occurs at a ring carbon carrying hydrogen 1,3,5-trinitrobenzene was chosen. Using methanolic sodium methoxide Gold and Rochester[63] determined a value of 15·4 $l.mole^{-1}$ for the equilibrium constant K_1, while Bernansconi[66] found a value of 23 $l.mole^{-1}$ in solutions made up to constant ionic strength (0·2M) with sodium perchlorate. The results obtained, Table 6.7, indicate that with sodium methoxide there is a very slight increase in measured equilibrium constant, K_C, with increasing base concentration. However the addition of small concentrations of barium or calcium ions causes a reduction in optical density without changing the general spectral shape (Figure 6.3). This indicates that there is no strong association between the adduct and calcium or barium ions. The decrease in absorption results from a reduction of the methoxide ion concentration by ion-association with the bivalent cations. In this case, in terms of equation 6.1 the values of the association constants of bivalent cations with methoxide ions, K_3, are larger than those for association with the adduct, K_2.

FIGURE 6.3



Visible absorption spectra of 1,3,5-trinitrobenzene ($1{\cdot}23 \times 10^{-4}$M) in methanol containing (a) $9{\cdot}6 \times 10^{-3}$M NaOMe, (b) $9{\cdot}6 \times 10^{-3}$M NaOMe + $5{\cdot}76 \times 10^{-3}$M $BaCl_2$.

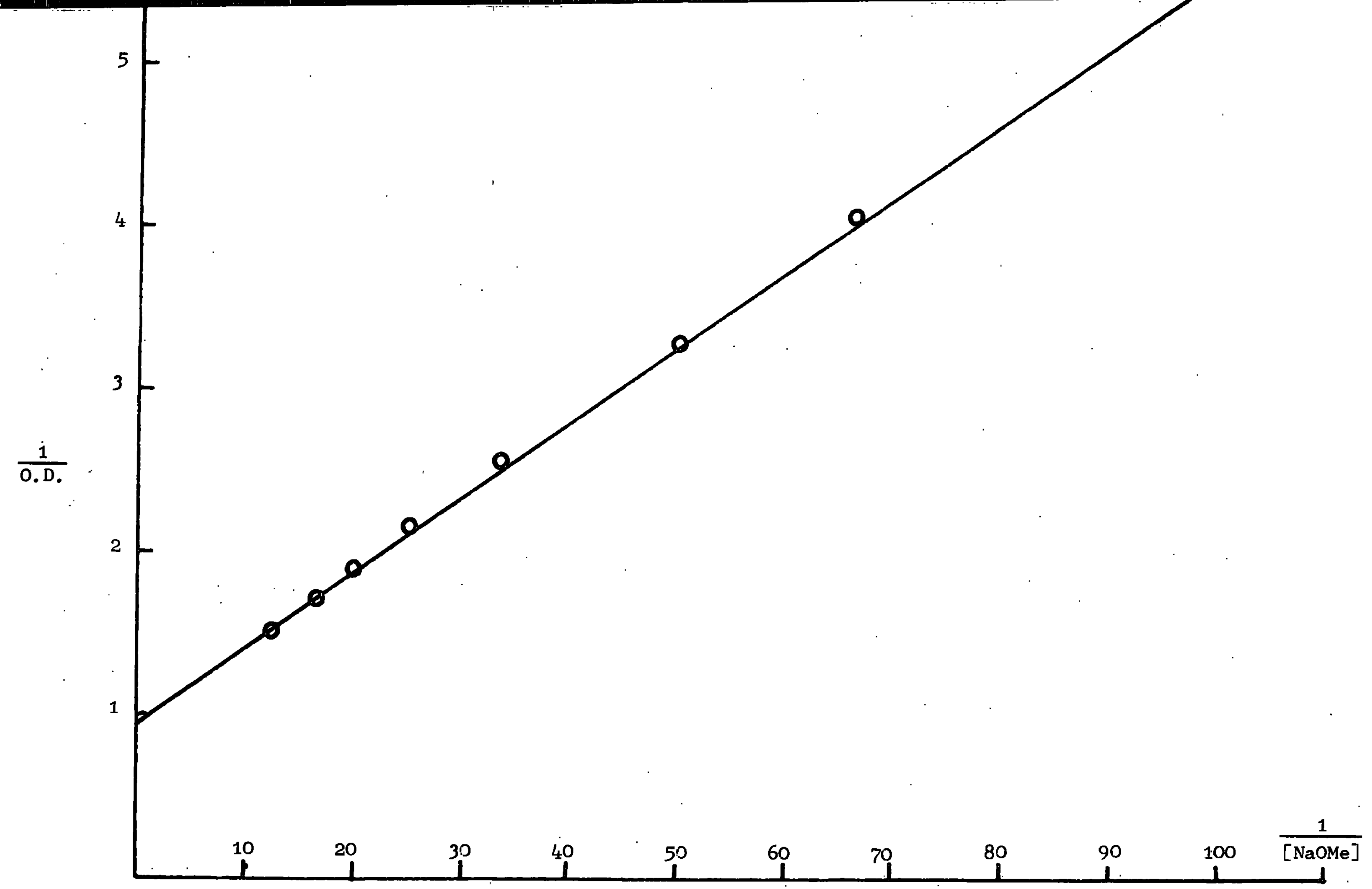
TABLE 6.7

The Effects of Cations on the Interaction of 1,3,5-Trinitrobenzene (4×10^{-5} M) in Methanol with Sodium Methoxide at 25°C

NaOMe (M)	$BaCl_2$ (M)	$CaCl_2$ (M)	Optical density at equilibrium[a] (425 nm)	K_C ($l.mole^{-1}$)
0·01	-	-	0·160	18·1
0·02	-	-	0·282	18·5
0·04	-	-	0·45	19·0
0·06	-	-	0·57	20·2
0·08	-	-	0·65	21·0
0·01	0·001	-	0·155	17·6
0·01	0·002	-	0·153	17·4
0·01	0·008	-	0·147	16·5
0·01	-	0·001	0·150	17·0
0·01	-	0·002	0·140	15·5
0·01	-	0·004	0·123	13·4

[a] The value for complete conversion to complex is 1·04 as determined from the intercept of a linear Benesi-Hildebrand plot in solutions containing constant sodium ion concentration (0·10M) (Figure 6.4).

FIGURE 6.4



Benesi-Hildebrand plot for 1,3,5-trinitrobenzene (4×10^{-5}M) and sodium methoxide in methanol at constant sodium ion concentration of 0·10M with NaCl. Measurements at 25° and 425 nm.

Conclusion

The results discussed in this chapter and the preceding chapters 4 and 5 clearly demonstrate the presence of ion-association of Meisenheimer complexes with cations in methanol. The results with 2,4,6-trisubstituted anisoles show that the stoichiometric equilibrium constants for complex formation are greatly increased by the presence of small concentrations of barium or calcium cations. Previously the stabilising effects of cationic micelles of Meisenheimer complexes have been noted[116]; the results discussed show that simple cations may also be very effective in this respect.

The values for ion-pair association constants of several Meisenheimer complexes with various cations are summarised in Table 6.8. It should however be noted that the values K_2^{Ba} and K_2^{Ca} for association with barium and calcium ions are dependent on the values used for the ion pair association constants of the metal methoxides. Hence they should be regarded as giving the orders of magnitude of the association rather than precise values. This uncertainty will not however affect the relative magnitude of K_2 for the various Meisenheimer complexes.

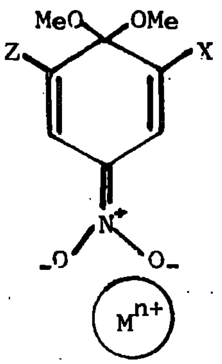
TABLE 6.8

Association Constant of Meisenheimer Complexes with Cations

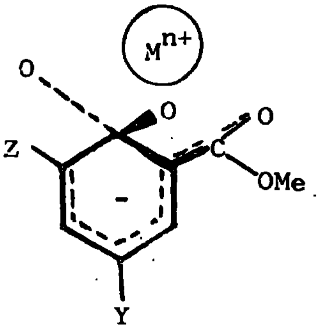
Parent	K_1 (l.mole^{-1})	K_2^{Na} (l.mole^{-1})	K_2^{Ba} (l.mole^{-1})	K_2^{Ca} (l.mole^{-1})
2-Methoxycarbonyl-4,6-dinitroanisole	8·3	90	$1{\cdot}6 \times 10^4$	8×10^3
4-Methoxycarbonyl-2,6-dinitroanisole	5·5	50	5×10^3	-
2,4,6-Trinitoanisole	17,000[a]	70	2×10^3	10^3
2-Chloro-4,6-dinitro-anisole	3·4	25	1×10^3	-
1,3,5-Trinitrobenzene	17	< 10	$< 10^2$	$< 10^2$

[a] Reference 24

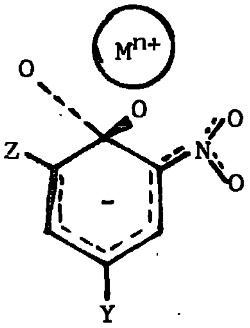
The extent of the association varies with the nature of the cation. From the present work it is found that association decreases in the order $Ba^{2+} > Ca^{2+} >> Na^{+} \sim K^{+} > Li^{+}$. There is apparently little tendency for lithium ions to associate with the Meisenheimer complexes studied possibly due to their strong solvation. The tendency to associate also varies widely with the structure of the parent nitro-compound being greatest with the adduct from 2-methoxycarbonyl-4,6-dinitroanisole. It is of interest to speculate on the structure of the ion-associates produced. One possibility would be (6.1) where a metal ion associates strongly with a nitro-group, or other electronegative substituents such as CO_2Me, at the positions <u>para</u> or <u>ortho</u> to addition. Recent evidence[3,7,122] suggests that more negative charge resides at the <u>para</u> than the <u>ortho</u> position so that this form, as shown in (6.1), would be favoured. Indeed Meisenheimer in his original formulation[2] seventy years ago specifically associated the metal cation with the <u>para</u> nitro-group. However the large variation in association constant K_2 with structure, particularly the small tendency of the 1,3,5-trinitrobenzene adduct to associate, is difficult to rationalise on this basis. It looks more probable that ion associate is formed whereby the cation is held by a



(6.1)



(6.2a)



(6.2b)

cage effect by the oxygen atoms around the position of addition as shown in (6.2). The two methoxyl groups at C_1 are orthogonal to the plane of the benzene ring while the ortho-substituents will be planar, or nearly planar, so that a favourable site for the cation is produced. The data obtained from this work suggests that the ortho-CO_2Me group (6.2a) provides somewhat better stabilisation than an ortho-NO_2 group (6.2b). The necessity for two methoxyl groups at C_1 for strong ion-association is demonstrated by the small association in the case of the adduct from 1,3,5-trinitrobenzene.

CHAPTER 7

LESS REACTIVE ANISOLES - J_M ACIDITY FUNCTION

Introduction

Equilibrium constants of the relatively stable Meisenheimer complexes obtained by the reaction of more reactive substituted anisoles with sodium methoxide in methanol solutions have been dealt with in chapter 4. In those case dilute solutions of sodium methoxide were used, as the complete conversion of anisoles to stable 1,1-Meisenheimer complexes was obtained in such solutions, due to the strong electronegative nature of the substituents on parent anisoles. However it was noted that the variation of the indicator ratio with sodium methoxide concentration was not identical for the four compounds studied. Thus no simple J_M acidity function can be defined which can adequately represent the formation of complex in the medium used for the study of equilibria. In the present chapter results obtained by using much less reactive anisoles are discussed, where appreciable conversion to complex occurs only in more basic media. To achieve this the alternative approach of increasing the basicity of the medium by the addition of dimethyl sulphoxide to methanol solutions containing a fixed concentration (0·1$\underline{\underline{M}}$) of sodium methoxide has been used. Dimethyl sulphoxide is thought to enhance the basicity by desolvation of the methoxide ions which are otherwise solvated by methanol through hydrogen bonding,[71] thus making the methoxide ions more available for nucleophilic attack. The same medium have previously been used[79] to define an acidity function involving the ionisation of substituted anilines (proton loss). Kroeger and Stewart[123] also determined an acidity function for the addition of base to α-cyanostilbenes using the same medium.

Results

Solutions in methanol or dimethyl sulphoxide-methanol mixtures of each of the compounds studied are colourless. In the presence of sodium methoxide coloured species are produced whose structures have been determined previously by use of ^1H n.m.r. spectroscopy. Thus in the cases of 2,4-dinitroanisole[30,33] and 2,6-dinitroanisole[33] these measurements show that methoxide addition occurs at the methoxyl-substituted ring position. The structure of the adduct formed from sodium methoxide and 4-chloro-2,6-dinitroanisole has been discusssed in chapter 3, which shows the initial formation of an adduct by base addition at the unsubstituted 3-carbon atom, however this quickly rearranges to give the thermodynamically more stable 1,1-adduct.[99,124] Methoxide addition to 1,3-dimethoxy-4,6-dinitrobenzene has been studied previously and is shown to give an adduct by base addition at one of the methoxyl-substituted ring positions.[33,125] Structure of adducts from 2-chloro-4,6-dinitroanisole, 4-trifluoromethyl-2,6-dinitroanisole are discussed in chapter 3. 2-Fluoro-4,6-dinitroanisole also forms a stable adduct by methoxide ion addition at the methoxyl-substituted ring carbon atom.

Measurement of Indicator Ratios

The experimental determination of indicator ratios (Log_{10}[Complex]/[Parent]) required the knowledge of the extinction coefficients of the coloured species, in this case complex. By increasing the proportion of dimethyl sulphoxide in the solvent it was possible for each indicator to obtain virtually complete conversion to complex and hence obtain a value for the extinction coefficient in that medium. In order to check whether extinction coefficients varied appreciably with solvent composition a test experiment was carried out with 2,4,6-trinitroanisole. It is known that for this compound conversion to 1,1-complex is complete in methanol containing

10^{-2}M sodium methoxide.[12] The measurements, in Table 7.1 which correspond to the formation of 1,1-complex, were made in mixed solvents containing this concentration of base.

TABLE 7.1

The Effect of Solvent Composition on Extinction Coefficient of 1,1-Dimethoxy-2,4,6-trinitrocyclohexadienate

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density
0	412	·747
10	414	·767
20	415	·788
30	416	·805
40	417	·812
50	418	·816
60	420	·855
70	421	·855
80	421	·859

There is clearly a bathochromic shift as the proportion of dimethyl sulphoxide is increased and this is associated with an increase in extinction coefficient. Examination of the data indicates a linear correlation of extinction coefficient (proportional to optical density since conversion to complex is complete) with absorption maximum. Similar linear correlations were observed for other adducts studied. It was therefore assumed that for other adducts where conversion to complex was complete only in media rich in dimethyl sulphoxide a linear correlation would exist between the extinction coefficient and wavelength of maximum absorption, so that indicator ratios could be accurately determined. The results given in Tables 7.2 - 7.8 are from measurements made in solutions containing 0·1$\underline{\underline{M}}$ sodium methoxide and at 25°C.

Measurements were also made with 2,4-dinitroanisole in 80-20 dimethyl sulphoxide - methanol with various sodium methoxide concentrations, allowing the determination of values of K_C $\left(= \frac{[\text{Complex}]}{[\text{Parent}][\text{NaOMe}]}\right)$. The observed values of K_C increased with base concentration but extrapolation to zero base concentration gave a value of 15$\underline{\underline{M}}^{-1}$ (Figure 7.1). Similar measurements with 1,3-dimethoxy-4,6-dinitrobenzene in 80-20 dimethyl sulphoxide - methanol mixture gave a value of K_C extrapolate to zero base concentration of 1·5$\underline{\underline{M}}^{-1}$.

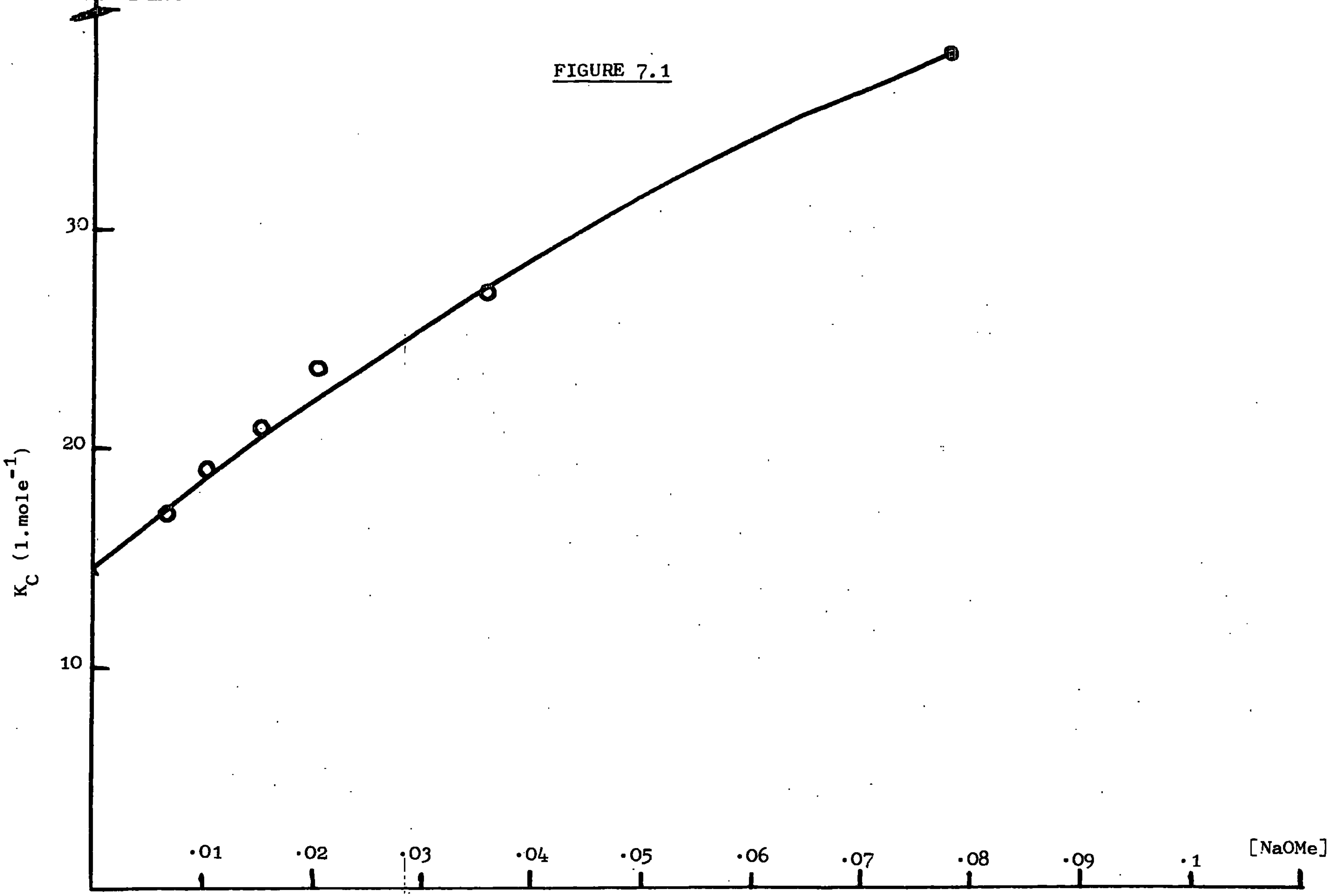
TABLE 7.2

Variation of Indicator (2-Chloro-4,6-dinitroanisole) Ratio With Dimethyl Sulphoxide Composition in 0·1$\underline{\underline{M}}$ Methanolic Sodium Methoxide at 25°C

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density[a]	$\log_{10}$ (Indicator Ratio)
0	492	·41	-0·11
5	492	·54	+0·14
10	492	·68	0·41
15	492	·77	0·65
20	492	·85	-
25	493	·90	-
30	493	·92	-
40	494	·95	-
50	494	·96	-
60	495	·97	-
70	495	·98	-
80	496	·99	-

[a] With 4 x $10^{-5}\underline{\underline{M}}$ indicator. Measurements in methanolic sodium methoxide give an optical density of 0·93 for complete conversion.

FIGURE 7.1



Variation of K_C for the complex formation from 2,4-dinitroanisole in 80:20 (v/v) dimethyl sulphoxide methanol mixture with sodium methoxide concentration.

TABLE 7.3

Variation of Indicator (4-Trifluoromethyl-2,6-dinitroanisole) Ratio With Dimethyl Sulphoxide Composition in 0·1M Methanolic Sodium Methoxide at 25°C

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density[a]	$\log_{10}$ (Indicator Ratio)
0	540	·40	-0·18
5	540	·522	+0·04
10	540	·66	0·28
15	540	·774	0·51
20	540	·872	0·79
25	540	·94	-
30	541	·99	-
40	541	1·03	-
50	542	1·08	-
60	542	1·08	-
70	543	1·10	-
80	543	1·11	-

---

[a] With 4×10^{-5} M indicator. Measurements in methanolic sodium methoxide give a value of 1·00 for complete conversion.

TABLE 7.4

Variation of Indicator (2-Fluoro-4,6-dinitroanisole) Ratio With Dimethyl Sulphoxide Composition in 0·1M Methanolic Sodium Methoxide at 25°C

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density[a]	$\log_{10}$(Indicator Ratio)
5	493	·139	-0·81
10	493	·206	-0·61
15	494	·327	-0·35
20	494	·470	-0·10
25	494	·653	+0·18
30	494	·821	0·46
40	495	1·05	-
50	496	1·10	-
60	497	1·14	-

[a] With 4 x 10^{-5}M indicator. Terrier[88] gives λ_{max} (methanol) 492 nm; ϵ_{max} 25,300

TABLE 7.5

Variation of Indicator (4-Chloro-2,6-dinitroanisole[a]) Ratio With Dimethyl Sulphoxide Composition in 0·1$\underline{\underline{M}}$ Methanolic Sodium Methoxide at 25°C

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density[b]	$\log_{10}$ (Indicator Ratio)
15	601	·0061[c]	-2·14
20	601	·0103[c]	-1·91
25	602	·0177[c]	-1·67
30	602	·0313[c]	-1·41
35	603	·064	-1·11
40	603	·117	-0·80
45	604	·210	-0·49
50	604	·37	-0·15
55	605	·575	+0·23
60	606	·74	0·58
65	607	·89	-
70	608	·93	-
75	608	·94	-

[a] Indicator concentration is 4 x $10^{-5}$$\underline{\underline{M}}$ unless otherwise stated.

[b] In media rich in dimethyl sulphoxide the optical density at the absorption maximum initially increases to a maximum value (due to rearrangement of the 1,3-complex to the thermodynamically more stable 1,1-complex and then gradually decreases. Extrapolation to zero time of the optical densities measured during the fading process gave the reported optical densities which correspond to formation of the 1,1-complex.

[c] Measured with indicator concentration 4 x $10^{-4}$$\underline{\underline{M}}$.

TABLE 7.6

Measurement of Indicator Ratio With Varying Dimethyl Sulphoxide Composition in 0·1$\underline{\underline{M}}$ Methanolic Sodium Methoxide at 25°C

2,6-Dinitroanisole

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$(Indicator Ratio)
50	588	·014[a]	-1·81
55	588	·031[a]	-1·46
60	588	·074	-1·07
65	588	·159	-0·69
70	588	·341	-0·25
75	589	·600	+0·24
80	589	·84	0·85
85	590	·94	-
90	591	·97	-

[a] Measured with indicator concentration x 10.

TABLE 7.7

Measurement of Indicator Ratio With Varying Dimethyl Sulphoxide Composition in 0·1M Methanolic Sodium Methoxide at 25°C

2,4-Dinitroanisole

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
50	498	·0053[a]	-2·14
55	498	·0117[a]	-1·79
60	499	·029[a]	-1·41
65	499	·073	-0·99
70	499	·19	-0·49
75	499	·39	0·00
80	499	·62	0·56
85	500	·75	-
90	500	·80	-

[a] Measured with indicator concentration x 10.

TABLE 7.8

Measurement of Indicator Ratio with Varying Dimethyl Sulphoxide Concentration in 0·1M Methanolic Sodium Methoxide at 25°C

1,3-Dimethoxy-4,6-dinitrobenzene[a]

Dimethyl Sulphoxide % (v/v)	Optical density[b] (492 nm)	$\log_{10}$ (Indicator Ratio)
65	·0066[c]	-2·02
70	·018[c]	-1·58
75	·054[c]	-1·08
80	·155	-0·55
85	·370	+0·05
90	·625	+0·90
95	·703	-
95[d]	·70	-

[a] Indicator concentration is 3×10^{-5}M unless otherwise stated.

[b] The red colour initially produced fades very slowly with time, due to formation of 3-methoxy-4,6-dinitrophenol.[131] Measurements were made at one minute intervals and extrapolated to zero time.

[c] Measured with indicator concentration x 10.

[d] With 0·2M sodium methoxide.

FIGURE 7.2

Variation of $\log_{10}$ indicator ratio with dimethyl sulphoxide concentration

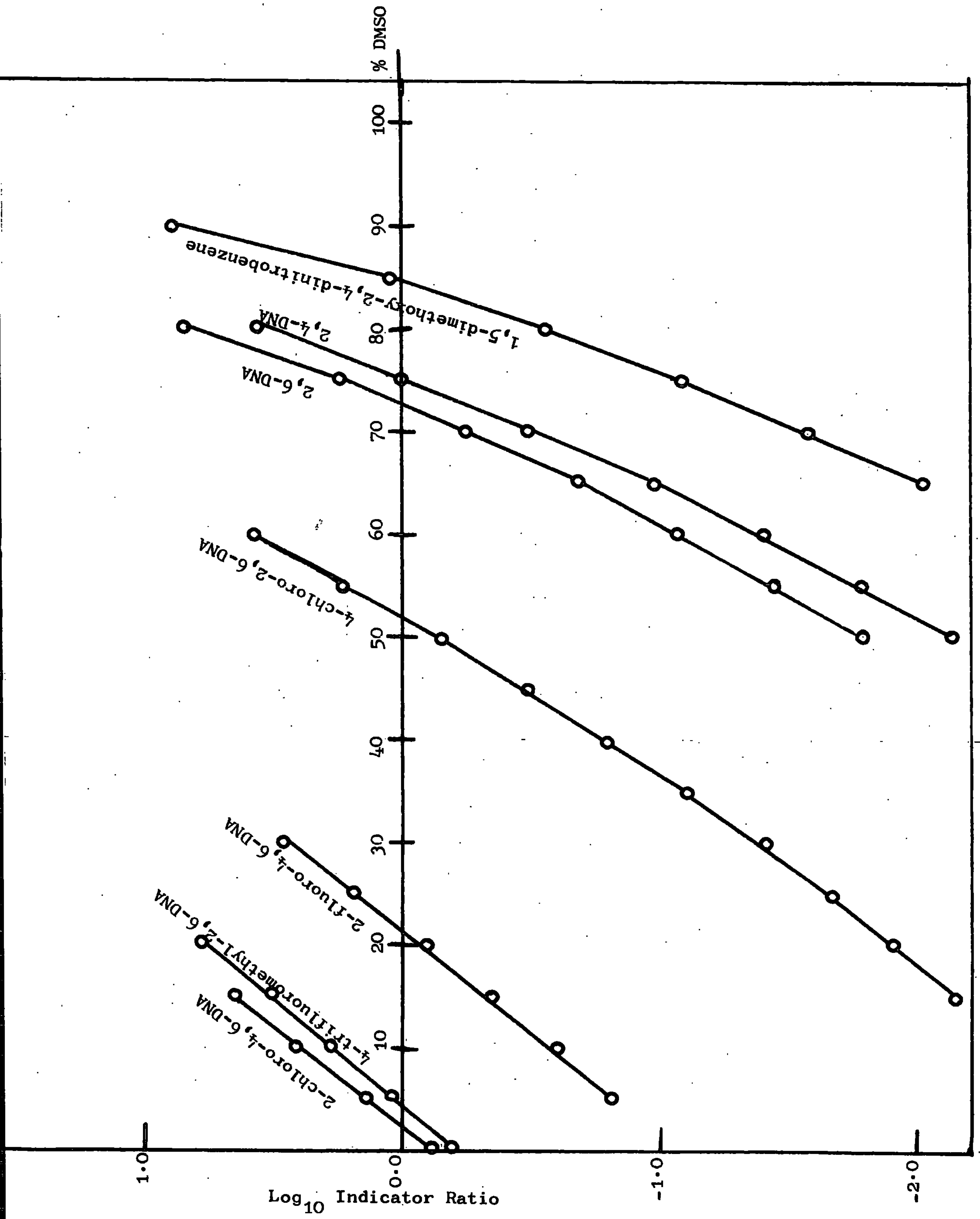


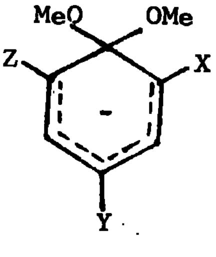
TABLE 7.9

J_M Acidity Scale

Dimethyl Sulphoxide % (v/v)	J_M	Dimethyl Sulphoxide % (v/v)	J_M
0	16·40	55	19·51
5	16·63	60	19·89
10	16·87	65	20·29
15	17·11	70	20·75
20	17·36	75	21·24
25	17·62	80	21·80
30	17·89	85	22·40
35	18·19	90	23·25
40	18·50		
45	18·81		
50	19·51		

Discussion

For each compound studied methoxide addition occurs to give coloured adducts of structure (4.1). Measurements of optical density were made in



(4.1)

methanol-dimethyl sulphoxide mixtures containing 0·1M sodium methoxide and indicator ratios calculated taking account of the variations of extinction coefficient with solvent composition. Examination of the results show that indicator ratios for the different compounds studied vary in parallel fashion with solvent composition (Figure 7.2). For example, on changing the proportion of dimethyl sulphoxide from 65 to 80% (v/v) the indicator ratios for 2,4-dinitroanisole, 2,6-dinitroanisole and 1,3-dimethoxy-4,6-dinitrobenzene increase respectively by 1·55, 1·54 and 1·47 logarithmic units. These results indicate that a single J_M acidity function can adequately describe the behaviour of these particular compounds in these media. This can only be the case if the activity coefficient ratios $f_{parent}/f_{complex^-}$ vary with solvent composition in similar fashion for the anisoles studied. In addition if, as suggested in preceding chapters, ion-pair formation in the complex is important then the effects of dimethyl sulphoxide on the ion-pair equilibria of all the adducts must be similar. The construction of a J_M acidity scale was carried out using the usual stepwise technique.[110] The question arises as to the value of J_M to take for 0·1M sodium methoxide in methanol, the starting point of the scale. It has been shown previously (chapter 4) that for the four compounds studied there are differences in the variation of equilibrium constant with sodium methoxide concentration below 0·1M. From the results for 2-chloro-4,6-dinitroanisole and 4-trifluoromethyl-2,6-dinitroanisole, indicators used in the present study, a J_M value of 16·34 and 16·45 respectively is calculated, for 0·1M methanolic sodium methoxide. The average of these 16·40 is in reasonable agreement with the value of 16·45 found by Terrier.[88]

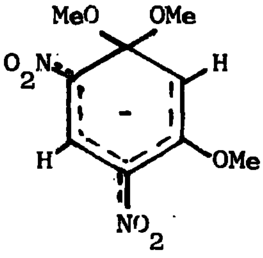
The present J_M scale (Table 7.9) which increases by 6·85 units on going from methanol to 90% (v/v) dimethyl sulphoxide is intermediate in behaviour between that involving proton loss from anilines[79] which increases by 5·80 units for a similar solvent change and that involving methoxide addition to α-cyanostilbenes[123] which increases by 7·85 units. The rather similar general behaviour of these three acidity scales may result from the fact that the major source of increase in basicity in dimethyl sulphoxide is probably the desolvation of the base. This effect will of course be independent of the particular indicator used. It does not necessarily follow that methoxide addition to other aromatic nitro compounds will comply with the J_M acidity function defined here.

The equilibrium constants for complex formation calculated using the J_M acidity function are given below (Table 7.10). Due to the unavoidable inaccuracies resulting from use of an acidity function these values are probably accurate only within a factor of two. The value for 2,4-dinitroanisole can be compared with values of $5{\cdot}0 \times 10^{-5}$ found by Bernasconi[108] and $6{\cdot}8 \times 10^{-5}$ by Terrier.[88]

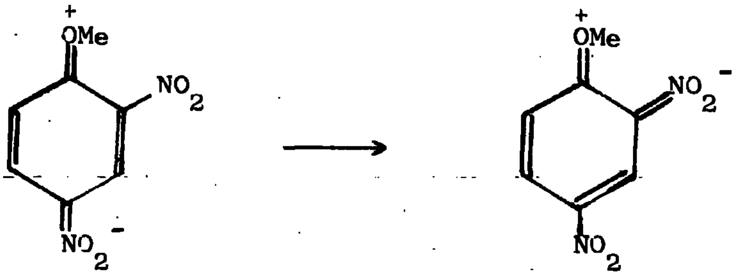
TABLE 7.10

	K_1 l.mole^{-1}
2-Fluoro-4,6-dinitroanisole	0·3
4-Chloro-2,6-dinitroanisole	$4{\cdot}3 \times 10^{-3}$
2,6-Dinitroanisole	$9{\cdot}0 \times 10^{-5}$
2,4-Dinitroanisole	$4{\cdot}6 \times 10^{-5}$
1,3-Dimethoxy-4,6-dinitrobenzene	$3{\cdot}8 \times 10^{-6}$

It is of interest that the complex formed from 1,3-dimethoxy-4,6-dinitrobenzene has a stability roughly ten times smaller than that from 2,4-dinitroanisole. This is evident both from the thermodynamic values in methanol determined via the acidity function and also applies to the equilibrium constants in 80-20 dimethyl sulphoxide-methanol where the values are 1·5 and 15·0 mole^{-1} respectively. On statistical grounds the complex from 1,3-dimethoxy-4,6-dinitrobenzene should be favoured since there are two equivalent positions where methoxide addition can occur. Steric factors at the position of addition should be similar for the two complexes. However the smaller stability of the adduct from the dimethoxy compound may result from steric interaction in the complex between the methoxyl group at C_3 and the nitro group at C_4 (structure (7.1)). This will cause the nitro group to bend from the plane of the aromatic ring and so be less effective in accommodating the negative charge. Bernasconi[66] has argued recently that resonance interaction of the form:



(7.1)



may stabilise the parent anisoles. Comparison of 2,4-dinitroanisole with 1,3-dimethoxy-4,6-dinitrobenzene indicates that the former compound will lose two such resonance forms on complex formation while the latter will lose four. This may be a factor to account for the smaller stability of the adduct from the latter compound.

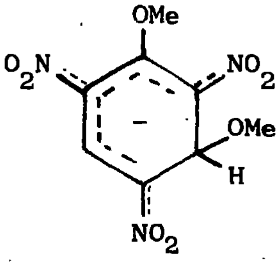
Also of interest is the greater stability of the adduct from 2,6-dinitroanisole. It has frequently been argued that the presence of a strongly electron-withdrawing group para to the position of addition is of considerable importance in determining the stabilities of Meisenheimer complexes. Evidence for this comes from the present study in that the equilibrium constant for complex formation from 2-chloro-4,6-dinitroanisole, 3 mole^{-1} (Table 4.7), is roughly a thousand times greater than that from 4-chloro-2,6-dinitroanisole. However the results for the isomeric dinitroanisoles indicates that this factor is not always of over-riding importance.

CHAPTER 8

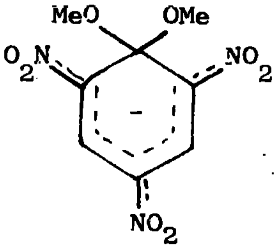
1-X-3,5-DINITROBENZENES

Introduction

The results discussed so far include σ-complexes formed from substituted anisoles. Several examples quoted from the literature,[3,7,20] as well as the work done during this study show that in general addition at an unsubstituted ring position to give a 1,3-complex (8.1) is kinetically favoured but rearrangement occurs to give the thermodynamically more stable 1,1-complex (8.2).

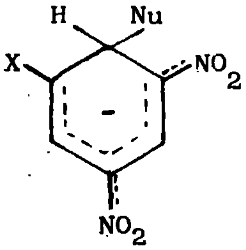


(8.1)



(8.2)

Similarly many examples are known of the formation of Meisenheimer complexes from 1,3,5-trinitrobenzene.[17,126,127] Thus Foster[126] described the visible spectrum of 1,3,5-trinitrobenzene in methanolic sodium methoxide, with maxima at 425 nm and 495 nm as due to complex (8.3) (X = NO_2, Nu = OMe).

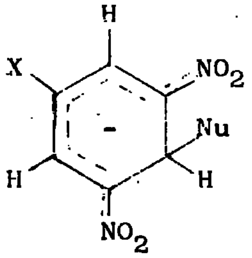


(8.3)

The structure was later supported by the ^{1}H n.m.r. studies of Crampton and Gold.[17] Although Meisenheimer complexes derived from 1,3,5-trinitrobenzene have been studied by many groups of workers, very few complexes derived from

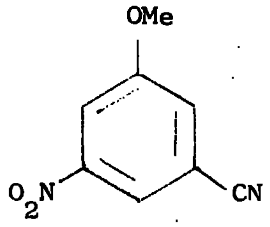
1-X-3,5-dinitrobenzenes, where X is other than nitro-group, have been investigated. If X is an electronegative group then such compounds would be expected to behave in an analogous manner to 1,3,5-trinitrobenzene. However because of the non-equivalence of the three unsubstituted ring positions in such a compound, two isomeric products are possible by attack of a nucleophile. Addition can occur either at a ring position para to substituent X, or at the two equivalent positions para to the nitro-groups.

Pollitt and Saunders[56] attempted to distinguish the possibilities of addition at C_2 (or C_6) from addition at C_4, by visible spectral studies of some 1-X-3,5-dinitrobenzenes. The visible absorption spectra of a number of such compounds in the presence of nucleophile show two maxima not present in the spectra of the parent substituent nitrobenzenes. It was thought that these two maxima correspond to complexes formed by addition at C_4 and C_2 (or C_6) position of the aromatic ring. The C_4 complex having maxima at longer wavelength than the C_2 (or C_6) complex. It was further postulated that the ratio in which the two complexes are formed varies somewhat with the exact conditions used, but usually the complex formed by addition para to nitro-group predominates. The arguments as to the structure of Meisenheimer complexes based on visible spectroscopy, although proved useful cannot be conclusive. However ^1H n.m.r. spectroscopy should give more conclusive results. Thus Foreman and Foster[128] used this technique to study the structure of products formed by the reaction of 1-X(=CN,CF_3)-3,5-dinitrobenzene with methoxide ions in wet dimethyl sulphoxide. The ^1H n.m.r. spectrum obtained corresponds exclusively to adduct (8.3) (X = CF_3,CN; Nu = OMe,OH). However in the presence of carbanions generated from ketones both isomeric adducts (8.3) and (8.4) (X = CN; Nu = CH_2COCH_3) are formed, and the intensities of the ^1H n.m.r. peaks suggest an approximate ratio of 2:1 respectively. However this work does not show whether this is the



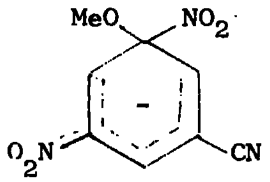
(8.4)

situation at equilibrium. Terrier et al[129] in a kinetic study re-investigated the reaction of 1-cyano-3,5-dinitrobenzene with methoxide and hydroxide ions in dimethyl sulphoxide, their results show that base addition occurs first at C_4 followed by rearrangement to the C_2 adduct which is thermodynamically more stable. Fendler et al[130] isolated crystalline potassium 1-methoxy-2-cyano-4,6-dinitrocyclohexadienate and established its structure by ^1H n.m.r. spectroscopy. The formation of 3-cyano-5-nitroanisole (8.5) from solutions



(8.5)

containing (8.3) (X = CN; Nu = OMe) implies the decomposition, resulting in nucleophilic substitution of a nitro-group by methoxide. This also indicates the formation of a species such as (8.6) either as a short-lived intermediate



(8.6)

or as a transition state. A structure similar to (8.6) was previously considered by Gold and Rochester[63] in the interaction of methoxide ion with 1,3,5-trinitrobenzene.

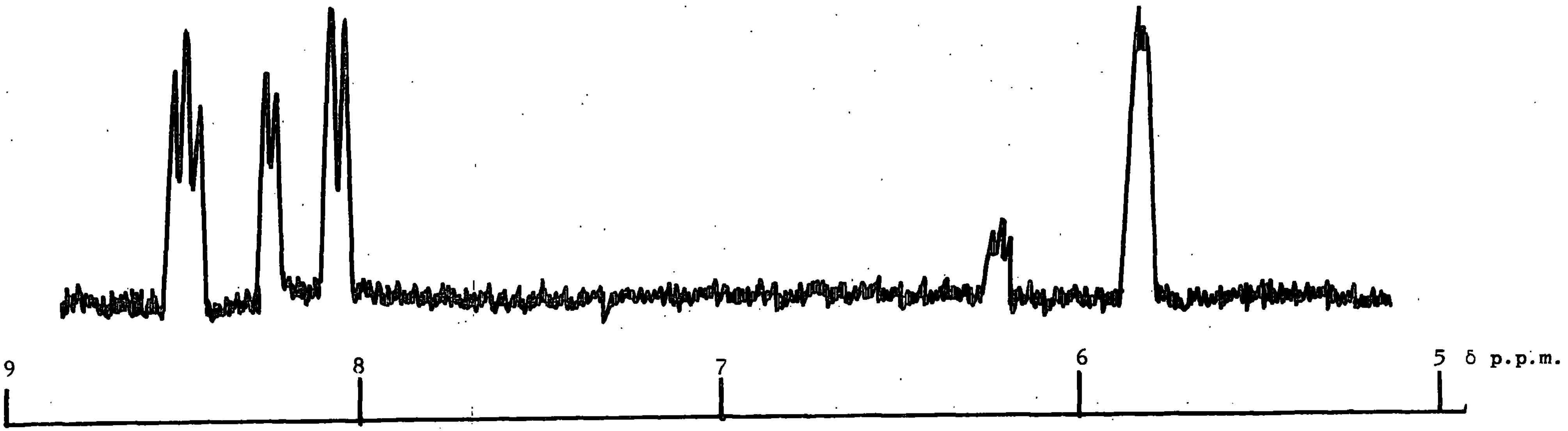
Results

I. Structural Studies

(a) 1-Methoxycarbonyl-3,5-dinitrobenzene and sodium methoxide

^{1}H n.m.r. results: 1-Methoxycarbonyl-3,5-dinitrobenzene was chosen for a detailed study of isomeric addition in the present study of 1-X-3,5-dinitrobenzenes. The spectral analysis is based on standard methods described by Pople et al.[132] The ^{1}H n.m.r. spectrum of this compound in dimethyl sulphoxide gives an AB_2 type spectrum centred at ~9·0 p.p.m. (Table 8.1). On addition of one equivalent of concentrated methanolic sodium methoxide (ca. ~ 5·0M) to a dimethyl sulphoxide solution of the parent compound a deep red colour is produced and the ^{1}H n.m.r. spectrum shows the instantaneous disappearance of the absorption due to parent compound. The resulting ^{1}H n.m.r. spectrum corresponds to the two species of structures (8.3) and (8.4) (X = CO_2Me; Nu = OMe) (Figure 8.1). The ring protons of (8.3) (X = CO_2Me; Nu = OMe) give three spin-coupled bands of equal intensity at 5·83, 8·51 and 8·09 p.p.m. (Table 8.2), while the ring protons of (8.4) (X = CO_2Me; Nu = OMe) give two sets of bands with intensity ratio 2:1 at 8·27 and 6·22 p.p.m. respectively. The bands in the region of 6 p.p.m. correspond to the hydrogen at sp^3 hybridised carbon atom in the isomeric adduct (8.4). The spectrum was scanned between 5 and 60 minutes from the time of mixing and the relative intensities of bands in the two spectra remained the same. This indicates that under the experimental conditions a stable equilibrium mixture of the two

FIGURE 8.1



^{1}H n.m.r. spectrum produced on the addition of 1 equivalent of sodium methoxide in methanol to 1-methoxycarbonyl-3,5-dinitrobenzene in dimethyl sulphoxide.

TABLE 8.1

Chemical Shifts (δ/p.p.m. downfield from internal tetramethylsilane) for 1-X-3,5-Dinitrobenzene in Dimethyl Sulphoxide

X	Ring Protons		Methyl Protons
	2-H and 6-H	4-H	
NO_2 [30]	9·21	9·21	
CN [130]	9·16	9·08	
SO_2Me	9·07	9·14	3·52
CF_3	8·98	9·14	
CO_2Me	8·95	9·08	4·05
I	8·96	8·87	
$CONEt_2$	8·62	8·90	
SMe	8·43	8·58	
SO_3^-	8·70	8·85	

TABLE 8.2

Chemical Shifts[a] (downfield from internal tetramethylsilane) and Coupling Constants[b]

Structure	Ring Protons 2-H	4-H	6-H	CO_2Me	OMe	$J_{2,4}$	$J_{4,6}$	$J_{2,6}$
	(p.p.m.)					(Hz)		
(8.3); X = CO_2Me Nu = OMe	5·83	8·51	8·09	3·72	3·08	1·4	2·0	0·5
(8.3); X = CO_2Me Nu = SO_3^-	5·50	8·22	7·72	3·70	-	1·3	1·9	0·3
(8.3); X = CO_2Me Nu = CH_2COCH_3	4·61	8·31	7·82	-	-	1·0	2·0	0·3[c]
(8.4); X = CO_2Me Nu = OMe	8·27	6·22	8·27	-	-	1·2	1·2	-
(8.4); X = CO_2Me Nu = CH_2COCH_3	8·05	5·07	8·05	-	-	1·0	1·0	-[c]
(8.7); Nu = CH_2COCH_3	8·23	5·10	8·23	-	-	1·0	1·0	-[c]
(8.8); Nu = CH_2COCH_3	4·68	8·35	7·58	-	-	1·0	2·0	0·3[c]

[a] Solvent is dimethyl sulphoxide containing a little methanol or water.

[b] Accurate to ±0·2 Hz.

[c] Coupling J ~ 5·5 Hz is observed between the ring protons at high field and the methylene protons of the acetone.

TABLE 8.3

Visible Spectral Data for Adducts from 1-Methoxycarbonyl-3,5-dinitrobenzene in Dimethyl Sulphoxide

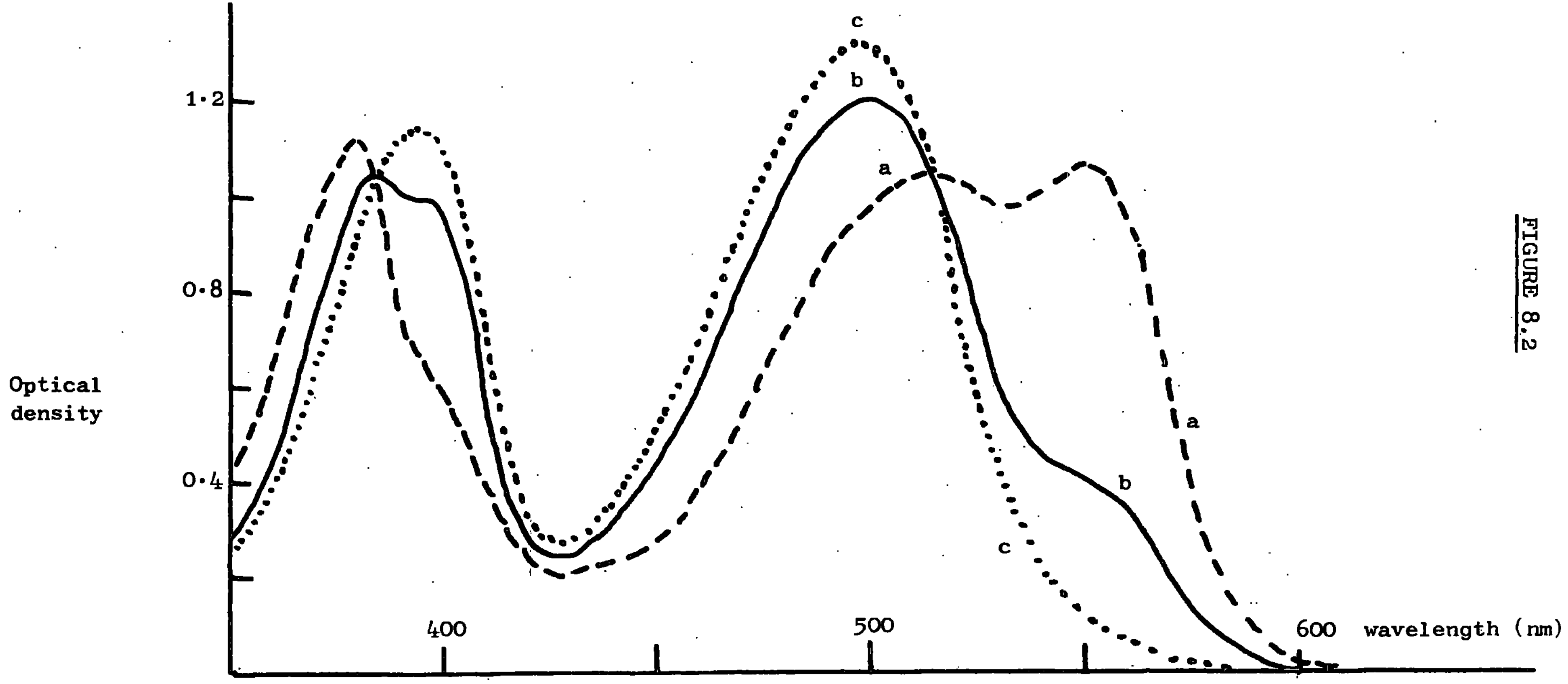
Structure	λ_{max} (nm)	$10^4\epsilon$ ($mole^{-1}l.cm^{-1}$)	λ_{max} (nm)	$10^4\epsilon$ ($mole^{-1}l.cm^{-1}$)	λ_{max} (nm)	$10^4\epsilon$ ($mole^{-1}l.cm^{-1}$)
(8.3); X = CO_2Me Nu = OMe	392	1·85	496	2·20	-	-
(8.3); X = CO_2Me Nu = SO_3^-	414	1·80	538	1·70	-	-
(8.3); X = CO_2Me Nu = CH_2COCH_3	414	-	545	-	-	-
(8.4); X = CO_2Me Nu = OMe	378	1·80	514	1·75	550	1·75
(8.4); X = CO_2Me Nu = SO_3^-	410	1·75	560	1·30	620	1·00
(8.4); X = CO_2Me Nu = CH_2COCH_3	410	-	560	-	630	-

isomeric complexes has been produced. From the intensities of the two sets of bands measured at 25°C an approximate ratio of the two isomers (8.3) and (8.4) in the equilibrium mixture can be calculated as 70:30 respectively.

Visible spectrum: Visible spectrum of 1-methoxycarbonyl-3,5-dinitrobenzene with methoxide ions gives additional independent information as to the formation of both isomeric adducts (8.3) and (8.4) in media rich in dimethyl sulphoxide. Thus initially a red-purple species (λ_{max} = 378, 514 and 550 nm) is formed. However the spectrum changes quickly with time as shown in Figure 8.2. In view of the ^1H n.m.r. results which show the presence of both isomeric adducts it seems rational to assume that both species will be present at equilibrium so that the time stable spectrum will be comprised of two overlapping sets of bands. If it is assumed that the small shoulder at long wavelength in the time stable spectrum (Figure 8.2) is due to initially formed species then at equilibrium approximately 30% of this species will still be present and 70% of the isomer. This observation does not of itself indicate which is the kinetically preferred isomer, however comparison with the spectrum of the adducts formed with sulphite ions (described later, Figure 8.3) shows that structure (8.4) is initially produced. The equilibrium ratio of 70:30 for the two isomers (8.3) and (8.4) respectively is in good agreement with that obtained independently from the ^1H n.m.r. data.

As mentioned above these results correspond to experiments in media rich in dimethyl sulphoxide containing only a small amount of methanol (3% v/v). However the shape of the time stable spectrum obtained in media containing from 3 to 50% methanol was independent of the solvent composition. This indicates that there is no large change in the proportion of the two isomers present at equilibrium with change of the solvent composition. However in more methanolic solvents spectra recorded within one minute of mixing

FIGURE 8.2



Visible spectra of 1-methoxycarbonyl-3,5-dinitrobenzene (6·0 x 10^{-5} M) and sodium methoxide (4·0 x 10^{-4} M) in dimethyl sulphoxide-methanol 97:3 (v/v): (a) initial spectrum - corresponds to (8.4) (Nu = OMe), (b) time stable spectrum recorded after 10 minutes, (c) spectrum calculated for (8.3) (Nu = OMe).

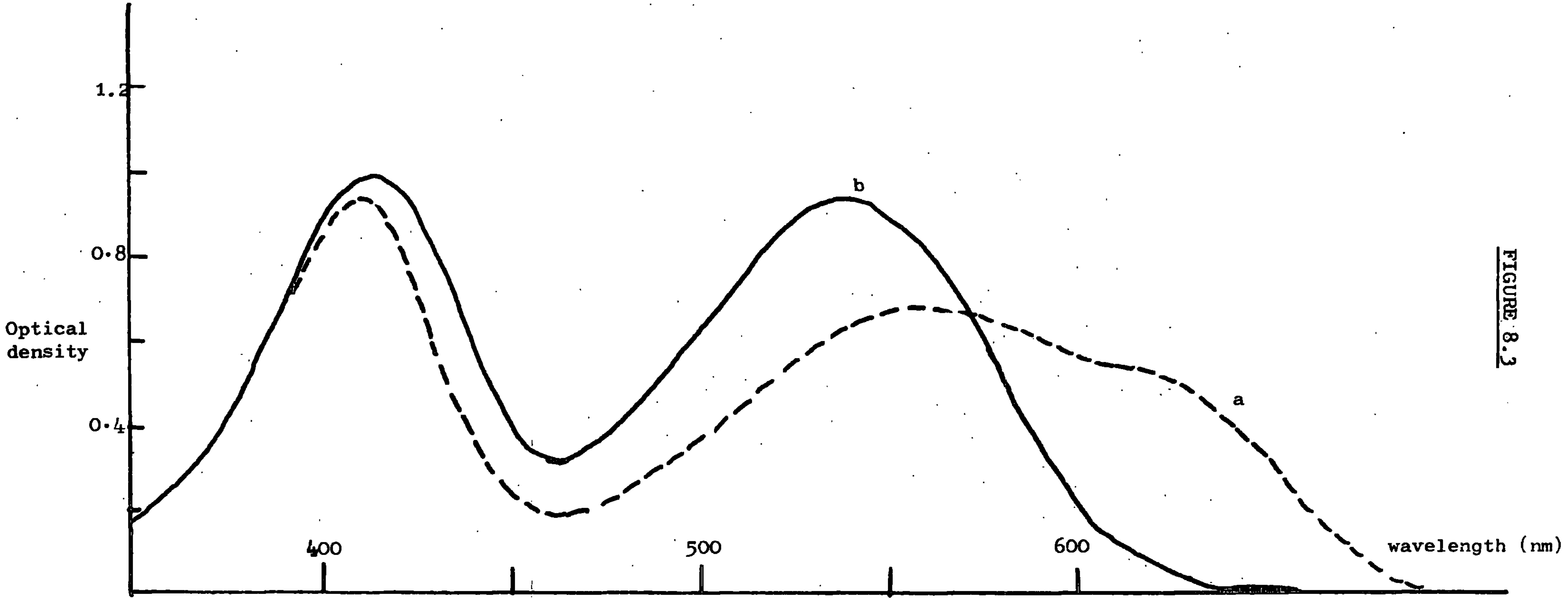
corresponded to the equilibrium mixture of the two isomers, indicating the faster rate of conversion from (8.4) to (8.3) in such media.

With Sulphite Ions

^{1}H n.m.r. results: An intense red colour is produced when one equivalent of aqueous sodium sulphite is added to a dimethyl sulphoxide solution of 1-methoxycarbonyl-3,5-dinitrobenzene. The ^{1}H n.m.r. spectrum obtained immediately after mixing the reagents show three spin coupled bands of equal intensity at 5·50, 8·22 and 7·72 p.p.m. The coupling pattern being the same as observed with methoxide ions, described above. The band at 8·22 p.p.m. is a triplet indicating the coupling of C_4-proton with both C_2- and C_6-protons. The high field shift of one of the resonance at 5·5 p.p.m. indicates a covalency change at this position. A doublet at 7·72 p.p.m. assigned to C_6-proton shows little coupling if any with C_2-proton. This pattern of spectrum corresponds to structure (8.3) ($X = CO_2Me$; $Nu = SO_3^-$) which shows that at equilibrium this isomer predominates. It is estimated that 10% of the other isomer (8.4) ($X = CO_2Me$; $Nu = SO_3^-$) would be detectable thus setting an upper limit in its concentration. It was not possible to take ^{1}H n.m.r. spectra in media containing more than 70% dimethyl sulphoxide, due to the poor solubility of sodium sulphite in dimethyl sulphoxide.

Visible spectra: Visible spectra taken in more dilute solutions (10^{-4}M) indicates the initial formation of complex by addition of sulphite ion para to methoxycarbonyl group. In the presence of sodium sulphite (4×10^{-3}M) in dimethyl sulphoxide-water (95:5 v/v) solvent mixture, initially a blue species is produced which rearranges slowly ($t_{\frac{1}{2}}$ = 15 hours) to a red species. The initial spectrum (Figure 8.3) due to the blue species shows three absorption maxima at 410, 560 and 620 nm. (Table 8.3), corresponding to complex formed by the addition at a ring carbon para to carbomethoxy group. The time stable

FIGURE 8.3



Visible spectra of 1-methoxycarbonyl-3,5-dinitrobenzene ($5{\cdot}4 \times 10^{-5}\underline{\underline{M}}$) and sodium sulphite ($4 \times 10^{-3}\underline{\underline{M}}$) in dimethyl sulphoxide-water (90:10 v/v): (a) initial spectrum - corresponds to (8.4) (Nu = SO_3^-), (b) final spectrum recorded after 12 hours - corresponds to (8.3) (Nu = SO_3^-).

spectrum gives two maximum at 414 and 538 nm due to red species of structure (8.3), where addition occurs at a ring carbon para to nitro group. Earlier Pollitt and Saunders[56] in an attempt to identify the two isomers formed from 1-X-3,5-dinitrobenzenes, did postulate that the complex of the type (8.4) would absorb at a longer wavelength than the complex of structure (8.3) where there is a more electronegative group para to the position of addition. Increasing the proportion of water in the solvent causes an increase in the rate of the rearrangement; thus in a solvent containing 15% water $t_{\frac{1}{2}}$ is ca. 5 minutes while with 30% water the spectrum recorded within one minute of mixing the reagents is that of the red species.

Comparison of the results obtained with sulphite ion, with those of methoxide ions show that with sulphite ions structure (8.3) is the thermodynamically favoured isomer, while with methoxide ions both isomers are present at equilibrium.

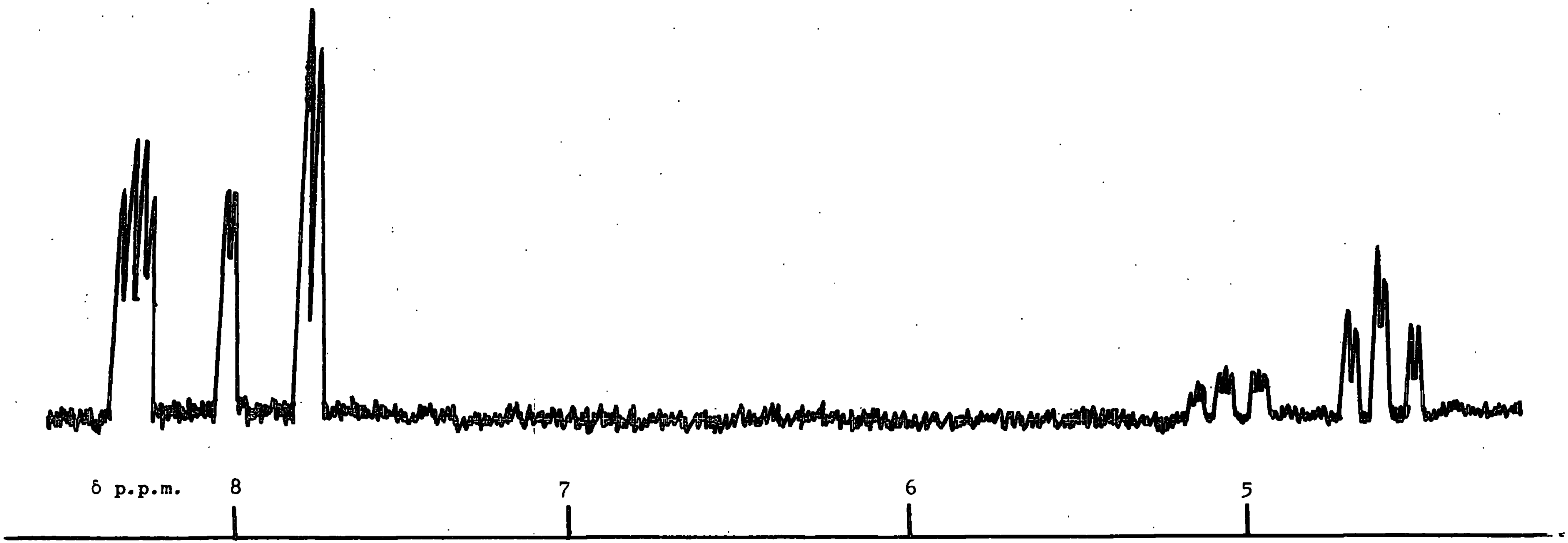
With Acetonate Ions

^{1}H n.m.r. results: A deep blue solution was produced when one equivalent of concentrated methanolic sodium methoxide was added to a dimethyl sulphoxide solution of 1-methoxycarbonyl-3,5-dinitrobenzene containing acetone (0·1 ml of acetone in 0·5 ml of 0·5M substrate solution in dimethyl sulphoxide). Indicating the formation of complex by the addition of acetonate ions generated through the equilibrium:

$$CH_3COCH_3 + {}^{\cdot}OMe^- \rightleftharpoons \bar{C}H_2COCH_3 + MeOH$$

The ^{1}H n.m.r. spectrum scanned immediately after mixing reagents as above shows in addition of solvent bands, two different sets of spin coupled bands (Figure 8.4). A doublet centred at 8·05 p.p.m. is assigned to the two protons para to the nitro groups in structure (8.4) ($X = CO_2Me$; $Nu = CH_2COCH_3$). The splitting results through coupling with the proton para to methoxycarbonyl

FIGURE 8.4



^{1}H n.m.r. spectrum produced on the addition of 1 equivalent of sodium methoxide in methanol to 1-methoxycarbonyl-3,5-dinitrobenzene in dimethyl sulphoxide-acetone (4:1). Bands due to both adducts (8.3) and (8.4) (Nu = CH_2COCH_3) are present.

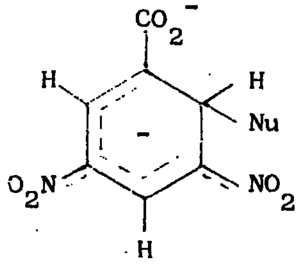
group. The other set of bands is centred at 5·07 p.p.m. and is assigned to the proton para to methoxycarbonyl group, the large upfield shift indicates the covalency change at this position. The coupling pattern observed at 5·07 p.p.m. is due to the coupling of the ring proton at the site of addition with the remaining two ring protons para to the two nitro groups, and with the two methylene protons in the adjacent acetonyl group. However this initial spectrum is not stable and the intensity of the bands fade with time giving way to new spin coupled bands which emerge at 8·31, 7·82 and 4·61 p.p.m. This new pattern of coupling could be rationalised in terms of structure (8.3) (X = CO_2Me; Nu = CH_2COCH_3). The band at 8·31 p.p.m. is assigned to the ring proton para to methoxycarbonyl group (structure (8.3)), the splitting of this band into a quartet results from coupling with the two ring protons para to nitro groups. A doublet at 7·82 p.p.m. is assigned to one of the two ring protons para to nitro groups, the splitting of the band into doublet is due to coupling with the ring proton para to methoxycarbonyl group. The bands due to ring proton at the site of addition is situated at 4·61 p.p.m., the splitting pattern results due to coupling with the ring proton para to methoxycarbonyl group and the two protons of the methylene group in the adjacent acetonyl group (Figure 8.4). It looks as if the coupling between the two ring protons para to nitro groups in structure (8.3) (X = CO_2Me; Nu = CH_2COCH_3) is small if any. This observation is consistent with the earlier observation of Foreman and Foster[128] who described the analogous spectrum of (8.3) (X = CN; Nu = CH_2COCH_3). The time stable spectrum ($t_{\frac{1}{2}} \sim$ several days) shows (Figure 8.4) an equilibrium mixture of the two isomers (8.3) and (8.4) (X = CO_2Me; Nu = CH_2COCH_3) in the ratio of 7:1 respectively. Visible spectra recorded in more dilute solutions indicate similar behaviour, the initial spectrum gives maxima at 410 and 560 nm which changes slowly to give new maxima at 414 and 545 nm (Table 8.3).

(b) 3,5-Dinitrobenzoic acid

As expected the addition of one equivalent of sodium methoxide to the 3,5-dinitrobenzoic acid solution in dimethyl sulphoxide results in the formation of the corresponding carboxylate ion without the production of any coloured species. Further addition of base gave a red coloured solution, but ^1H n.m.r. measurements were not successful probably due to the formation of small quantities of radical anions.[128,132] However visible measurements were more informative with the spectrum showing a maxima at 530 nm and a small shoulder at 600 nm.

With Acetonate Ions

It was possible to obtain the ^1H n.m.r. spectrum of 3,5-dinitrobenzoic acid in dimethyl sulphoxide solution, in the presence of acetonate ions, generated as above. The spectrum obtained immediately after mixing reagents shows a pattern similar to that obtained with methyl ester and acetonate ions (Figure 8.4). The initial spectrum is consistent with a pattern assigned to structure (8.7) (Nu = CH_2COCH_3), however the spectrum changes with time and new bands develop as the bands of the initial spectrum fade with time.



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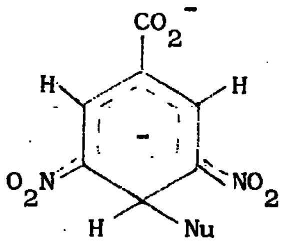


(8.7)

This change is similar to that observed with methyl ester, and indicates the rearrangement of (8.7) to (8.8) (Nu = CH_2COCH_3). The chemical shifts are summarised in Table 8.2.

The visible spectra also indicates the formation of a short lived species with maxima at 580 and 680 nm changing with time to new bands with maxima at

555 nm. This can be explained as the initial formation of (8.7) rearranging with time to (8.8) (Nu = CH_2COCH_3). These spectral changes are similar but shifted to longer wavelength compared to those obtained from the spectra produced from the methyl ester and acetonate ions. It seems probable, therefore, that the visible spectra of the isomeric methoxide adducts of the 3,5-dinitrobenzoate ion will have similar spectral shapes to the methoxide adducts produced from the methyl ester of the acid. The shoulder at 600 nm in the spectrum of the methoxide adduct of 3,5-dinitrobenzoate ion can then be ascribed to the adduct (8.7) (Nu = OMe) and probably about 10% of this isomer is present in the equilibrium mixture.

(c) Other 1-X-3,5-dinitrobenzenes

^{1}H n.m.r. studies: The spectral data obtained with 1-X-3,5-dinitrobenzenes studied during present work has been summarised in Table 8.1. The parent molecule in each case gives an AB_2 type spectrum with spin-coupling constant J_{AB} 2Hz. As with 1-methoxycarbonyl-3,5-dinitrobenzene described above intensely coloured solutions are produced when one equivalent of concentrated methanolic sodium methoxide is added to a dimethyl sulphoxide solution of the different 1-X-3,5-dinitrobenzenes. The ^{1}H n.m.r. spectrum recorded immediately after mixing the reagents show bands characteristic of the methoxide adducts of structure (8.3) (Nu = OMe). The data for the adducts together with some data from the literature is collected in Table 8.4. Apart from the compounds where X = CO_2Me and CN[129] no other substituted dinitrobenzene studied showed ^{1}H n.m.r. bands with sodium methoxide which could be assigned to isomeric adduct (8.4) (Nu = OMe). However this does not eliminate the possibility of their formation, but does set an upper limit on their equilibrium concentrations, as the measurements made in the present study are sufficiently sensitive to detect 10% of these species if present.

TABLE 8.4

Chemical Shifts (δ/p.p.m.) and Coupling Constants for Methoxide Adducts (Nu = OMe) of 1-X-3,5-Dinitrobenzenes (Structure (8.3)) in Dimethyl Sulphoxide

X	Ring Protons 2-H	4-H	6-H	OMe (p.p.m.)	$J_{2,4}$	$J_{4,6}$ (Hz)	$J_{2,6}$
NO_2 [30]	6·14	8·42	8·42	3·10	1·5	-	1·5
CN [130]	5·60	8·48	7·77	3·08	1·2	2·2	0·3
SO_2Me [a]	6·13	8·62	8·05	3·08	1·2	2·0	< 0·5
CF_3	5·83	8·60	7·70	-	-	-	-
CO_2Me	5·83	8·51	8·09	3·06	1·4	2·0	0·5
I	5·65	8·52	7·67	3·05	1·0	2·0	< 0·5
$CONEt_2$	5·92	8·50	7·15	3·08	1·2	2·0	0·3
SMe	5·50	8·45	6·90	3·00	1·0	2·0	< 0·5
H [32]	5·35	8·36	6·96	-	-	-	-

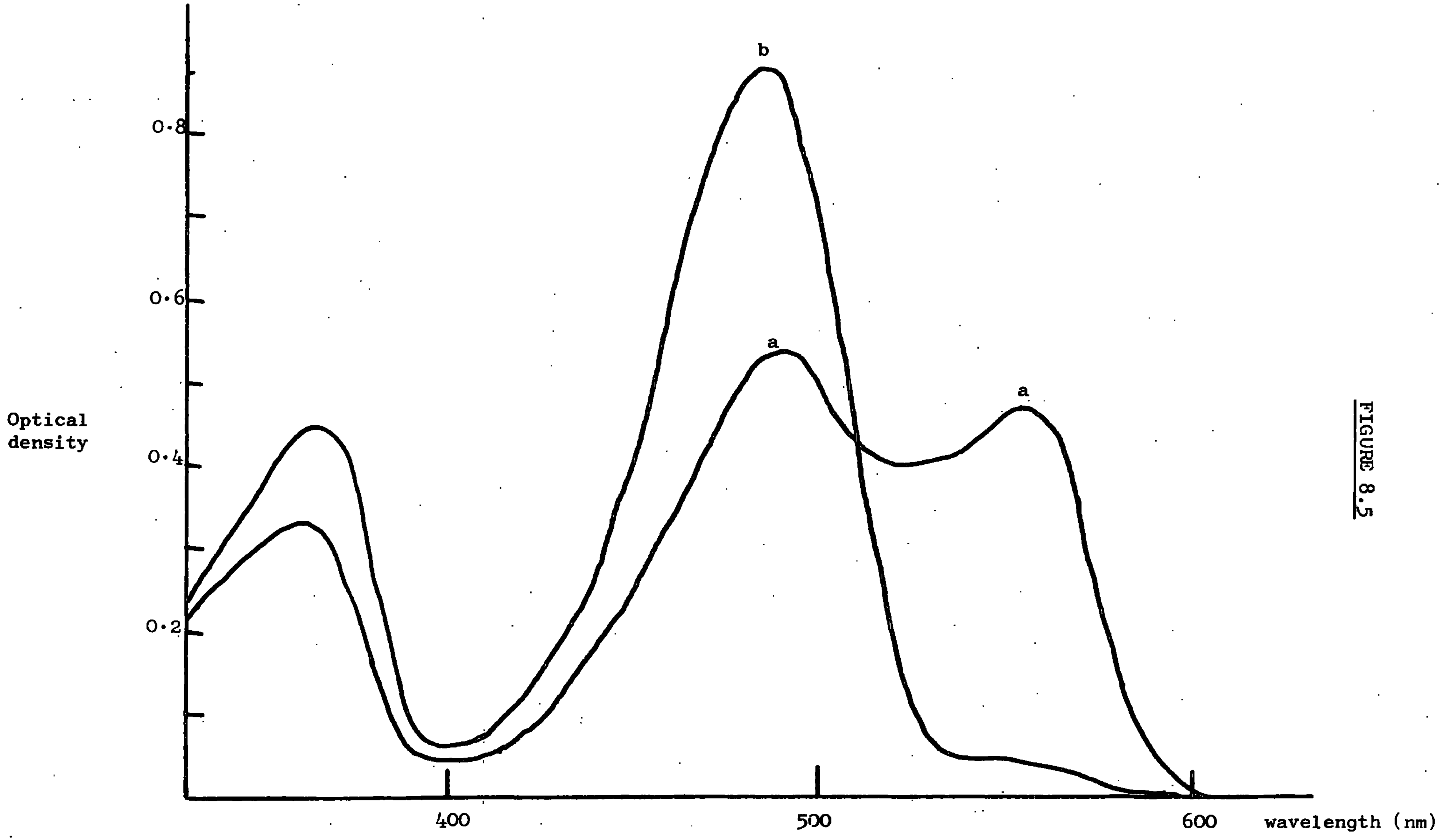
[a] SO_2Me protons absorb at 3·37 p.p.m. in the complex.

Visible spectra: The visible spectra recorded immediately after adding methanolic sodium methoxide to a dimethyl sulphoxide solution of 1-X-3,5-dinitrobenzenes, indicates the initial formation of structure (8.4) (Nu = OMe). The rate of isomerisation from (8.4) to (8.3) increased greatly by increasing the percentage volume of methanol in the solvent mixture. However the final shape of the spectrum remained unchanged in going from 3% to 50% (v/v) methanol.

As a typical example (Figure 8.5), when methanolic sodium methoxide ($10^{-3}\underline{\underline{M}}$) is added to a dimethyl sulphoxide solution of ($10^{-5}\underline{\underline{M}}$) 1-trifluoromethyl-3,5-dinitrobenzene a red colour is produced which changes quickly to orange. The spectrum recorded as soon as possible after mixing the reagents show three absorption maxima at 360, 488 and 555 nm. However the shape of the spectrum changes quickly with time and the final time stable spectrum shows absorption maxima at 362 and 490 nm. In accord with the ^{1}H n.m.r. spectrum of this compound with sodium methoxide which shows bands for adduct (8.3) (X = CF_3; Nu = OMe) only it can be deduced that the initial visible spectrum corresponds to the adduct (8.4) (X = CF_3; Nu = OMe) and the final spectrum to the isomeric adduct (8.3). It seems likely that at least some of the initially formed adduct (8.4), will still be present at equilibrium, and if it is assumed that the absorption beyond 550 nm in the time stable spectrum results from this isomer a ratio of 93:7 is obtained for the two isomers (8.3) and (8.4) respectively at equilibrium.

Other 1-X-3,5-dinitrobenzenes, where X = SO_2Me, $CONEt_2$ or SO_3^- show similar general behaviour as above. With 1-iodo-3,5-dinitrobenzene a change of colour from purple to red is observed by eye when base is added to the substrate solution, but the change is too fast for the spectrum of the initially formed species to be obtained, although the spectrum does show a small shoulder beyond 550 nm. With X = H or SMe no change in spectral shape

FIGURE 8.5

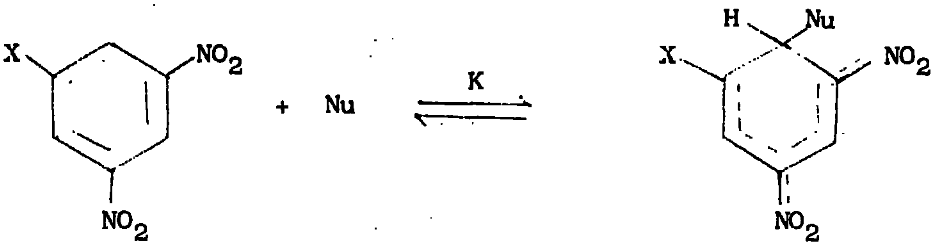


Visible spectra of 1-trifluoromethyl-3,5-dinitrobenzene ($3{\cdot}3 \times 10^{-5}\underline{\underline{M}}$) in dimethyl sulphoxide containing sodium methoxide; (a) initially after mixing, (b) time stable spectrum.

is observed - measurements began after 15 seconds of mixing the solution. It is probable that the rate of isomerisation in these compounds is very fast. The visible spectral data for the adduct formed together with estimates of the proportion present at equilibrium is collected in Table 8.5.

II. Measurements of Equilibrium Constants

Equilibrium constants for the formation of Meisenheimer complexes from substituted anisoles have been discussed in the preceding chapters. For the less reactive anisoles in order to achieve complete conversion to complex, media rich in dimethyl sulphoxide are used (Chapter 7). A similar approach is used for the 1-X-3,5-dinitrobenzenes, where in contrast to substituted anisoles, the formation of Meisenheimer complex takes place by the addition of nucleophile to an unsubstituted aromatic carbon. Thus thermodynamic equilibrium constants are determined using methanol-dimethyl sulphoxide mixtures for the following equilibrium:



(8.9)

(8.3)

In order to determine the thermodynamic equilibrium constants, measurements of optical densities were made in methanol-dimethyl sulphoxide mixture containing 0·098M sodium methoxide or 0·08M tetra-n-butylammonium methoxide. The resulting data, collected in Table 8.6, allows the determination of indicator ratios. As the complete conversion to complex is achieved by increasing the proportion of dimethyl sulphoxide in the solvent mixture, hence the extinction coefficient for the adduct formed is

TABLE 8.5

Visible Spectra of Methoxide Adducts of 1-X-3,5-Dinitrobenzenes in Dimethyl Sulphoxide, λ_{max} (nm) [a]

X	C_2 Adducts (8.3)		C_4 Adducts (8.4)			% of (8.4) present at equilibrium
	λ_{max}	λ_{max}	λ_{max}	λ_{max}	λ_{max}	
NO_2	431(2·8)	505(1·95)	-	431(2·8)	505(1·95)	-
CN	390(2·1)	490(2·2)	380	490	550	5[129]
SO_2Me	376(1·7)	481(2·3)	372(1·3)	485(2·2)	540(0·8)	10
CF_3	362(1·35)	490(2·6)	360(1·0)	488(1·6)	555(1·5)	7
CO_2Me	392(1·85)	496(2·2)	378(1·8)	514(1·75)	550 (1·75)	30
I	363(1·60)	513(2·5)		Not observed		< 5
$CONEt_2$	370(1·6)	510(2·7)	370(1·5)	520(1·8)	580(1·6)	< 5
SMe	366(1·4)	534(1·9)		Not observed		< 5
SO_3^-	360(1·4)	520(2·2)	360	530	600	5
H		520(2·7)		Not observed		

[a] Values of 10^4 ϵ (mole^{-1} l.cm^{-1}) accurate to ± 10% are given in parentheses

determined and used for the determination of indicator ratio (Log_{10}[Complex]/[Parent]). However as noted with less reactive anisoles (Chapter 7) a bathochromic shift in the spectrum is observed by the change in solvent from methanol to dimethyl sulphoxide, likewise extinction coefficient is also increased by changing to dimethyl sulphoxide. Thus with 1,3,5-trinitrobenzene (Table 8.6) the absorption maximum shifts from 425 to 431 nm on going from pure methanol to 70% (v/v) dimethyl sulphoxide. In addition in media where conversion to complex is virtually complete (30-70% dimethyl sulphoxide) there is an increase in extinction coefficient as the proportion of dimethyl sulphoxide is increased. Due account of these changes in extinction coefficient with solvent composition was taken in the determination of the indicator ratios for 1,3,5-trinitrobenzene and other indicators used. As before (Chapter 7) a linear correlation between wavelength of maximum absorption and extinction coefficient was found.

The attainment of equilibrium for the compounds studied is fast in the media used, this is further enhanced by increasing the proportion of methanol in the solvent mixture used. In some cases notably for cyano[130] and trifluoromethyl substituted compounds, the initial equilibrium was followed by slower irreversible substitution reaction. In such cases initial optical densities corresponding to adduct formation are determined by linear extrapolation of measured optical densities at 15 second intervals. In Figure 8.6 is given a plot of Log_{10}[Complex]/[Parent] as a function of dimethyl sulphoxide percentage in the medium. The similar slopes for the different indicators used, indicate the similar behaviour of the different 1-X-3,5-dinitrobenzenes in the medium used for this study. Hence it was possible to evaluate a J_M acidity function (Table 8.7) in methanol-dimethyl sulphoxide mixtures, and also to determine the thermodynamic equilibrium constants, referred to pure methanol as solvent.

TABLE 8.6

Indicator Ratios at 25°C with 0·098$\underline{\underline{M}}$ Sodium Methoxide for 3 x $10^{-5}$$\underline{\underline{M}}$ Parent

1,3,5-Trinitrobenzene

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
0	425	·512	0·27
5	425	·641	0·61
10	426	·700	0·86
15	426	·759	-
20	427	·775	-
30	428	·815	-
40	428	·825	-
50	429	·825	-
60	430	·835	-
70	431	·840	-

1-Cyano-3,5-dinitrobenzene

0	484	·063	-0·94
5	484	·110	-0·66
10	484	·172	-0·41
15	484	·270	-0·11
20	484	·400	+0·26
25	484	·485	+0·55
30	485	·585	-
35	486	·595	-
40	487	·616	-
50	488	·637	-
60	489	·642	-
70	490	·652	-
80	490	·655	-

1-SO_2Me-3,5-dinitrobenzene

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
5	473	·061	-0·96
10	473	·112	-0·65
15	474	·185	-0·35
20	474	·289	-0·06
25	475	·393	+0·23
30	475	·494	0·58
35	476	·558	0·89
40	477	·604	(1·22)
50	478	·651	-
60	479	·665	-
70	480	·679	-
80	481	·680	-

1-Trifluoromethyl-3,5-dinitrobenzene

25	484	·028	(-1·41)
30	485	·063	-1·04
35	485	·127	-0·70
40	486	·252	-0·31
45	486	·439	+0·12
50	487	·605	+0·54
55	488	·708	(+0·96)
60	488	·767	-
70	489	·792	-
80	489	·795	-

1-Methoxycarbonyl-3,5-dinitrobenzene

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
30	493	·036	(-1·17)
35	494	·074	-0·83
40	494	·150	-0·45
45	495	·270	-0·06
50	495	·402	+0·35
55	496	·518	+0·85
60	497	·570	-
70	498	·597	-
80	499	·603	-

1-Iodo-3,5-dinitrobenzene

45	510	·064	-1·02
50	510	·146	-0·61
55	511	·302	-0·17
60	511	·494	+0·29
65	512	·653	+0·80
70	512	·716	-
80	513	·757	-
85	513	·761	-

N,N-Diethyl-3,5-dinitrobenzamide

55	507	·064	-1·04
60	507	·158	-0·59
65	508	·331	-0·13
70	508	·550	+0·37
75	509	·700	+0·89
80	509	·752	-
86	510	·790	-
91	510	·806	-

3,5-Dinitrothioanisole

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
60	532	·043	-1·07
65	532	·113	-0·59
70	533	·251	-0·09
75	533	·411	+0·43
80	534	·534	-
85	534	·567	-
90	534	·570	-
95	534	·571	-

1,3-Dinitrobenzene

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
70	519	·015	(+1·72)
75	519	·051	-1·17
80	520	·172	-0·57
85	520	·569	+0·36
90	520	·750	(+1·06)
95	520	·815	-

3,5-Dinitrobenzenesulphonate

Dimethyl Sulphoxide % (v/v)	λ_{max} (nm)	Optical density	$\log_{10}$ (Indicator Ratio)
60	519	·022	(-1·45)
65	519	·054	-1·04
70	520	·130	-0·61
75	520	·267	-0·17
80	520	·495	+0·48
85	520	·614	-
90	520	·655	-
95	520	·665	-

Similar sets of measurements were made for solutions containing 0·080M tetra-n-butylammonium methoxide instead of sodium methoxide.

TABLE 8.7

J_M Values (25°C) for Base Addition to 1-X-3,5-Dinitrobenzenes

Dimethyl Sulphoxide (% v/v)	J_M (0·098, NaOMe)	J_M (0·080, Bu_4NOMe)
0	15·96	16·21
5	16·27	16·50
10	16·54	16·70
15	16·84	17·01
20	17·17	17·30
25	17·46	17·61
30	17·82	17·95
35	18·15	18·29
40	18·53	18·69
45	18·94	19·11
50	19·35	19·55
55	19·80	20·00
60	20·26	20·47
65	20·74	20·92
70	21·24	21·42
75	21·76	21·90
80	22·36	22·58
85	23·29	23·47

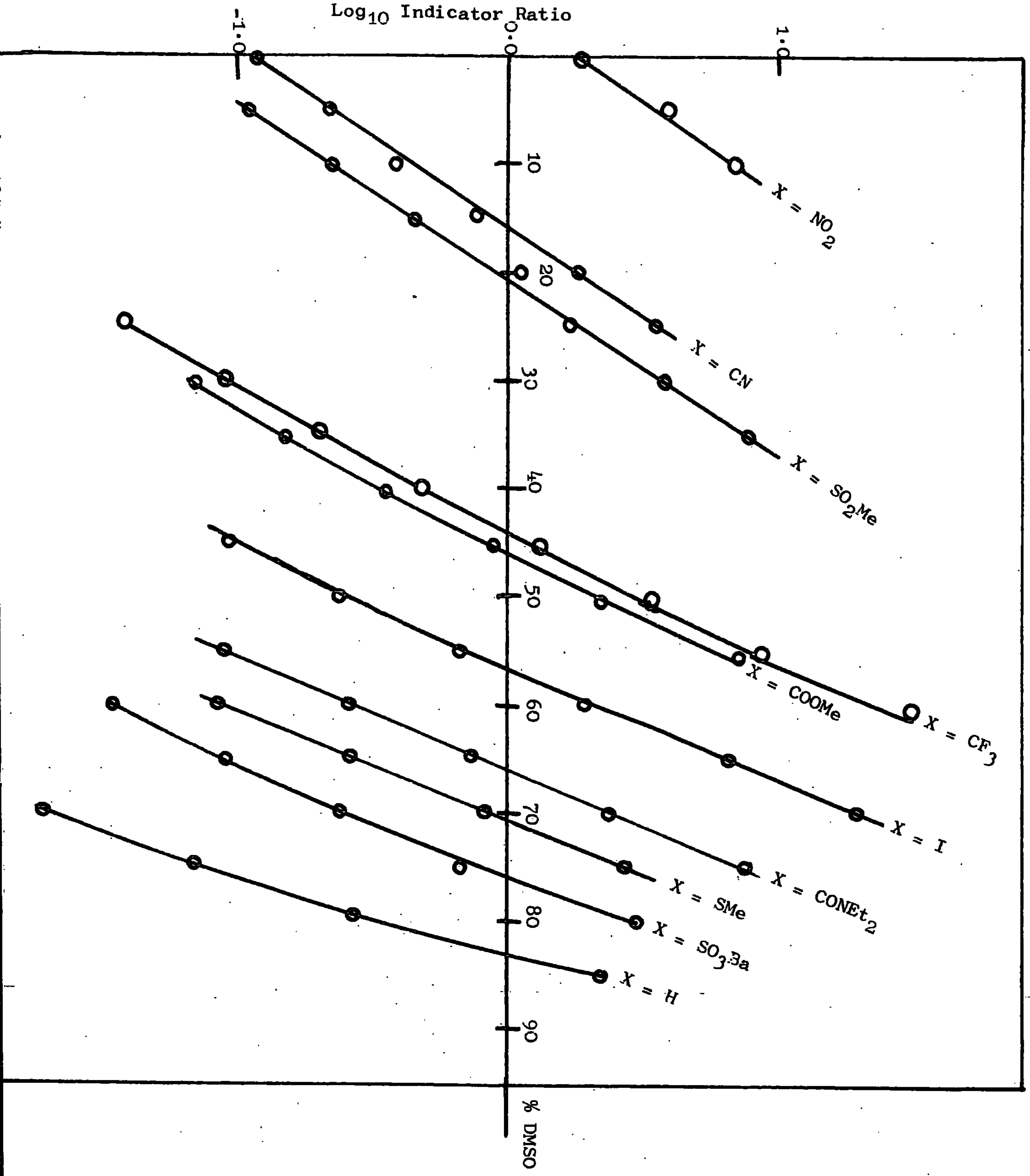


FIGURE 8.6

Variation of log$_{10}$ indicator ratio with dimethyl sulphoxide concentration

Discussion

The results of the ^{1}H n.m.r. study discussed above show the formation of Meisenheimer complexes of structure (8.3), from the different 1-X-3,5-dinitrobenzenes studied. Only in the case of 1-methoxycarbonyl-3,5-dinitrobenzene does the ^{1}H n.m.r. spectrum give evidence for the formation of isomeric complex of structure (8.4) (Figures 8.1 and 8.4). The results of the present study show that the proportion of the two isomers (8.3) and (8.4) (X = CO_2Me) present at equilibrium depends on the attacking nucleophile. With methoxide ions structure (8.3) (X = CO_2Me; Nu = OMe) is favoured over structure (8.4) (X = CO_2Me; Nu = OMe) in the approximate ratio of 70:30. However there is a statistical factor of 2:1 favouring adduct (8.3), so that in fact methoxide ions show very little discrimination for the three hydrogen-carrying ring positions in 1-methoxycarbonyl-3,5-dinitrobenzene. With acetonate ions structure (8.3) (X = CO_2Me; Nu = CH_2COCH_3) is clearly favoured over (8.4) (X = CO_2Me; Nu = CH_2COCH_3) at equilibrium, while with sulphite ions (Nu = SO_3) the amount of (8.4) present at equilibrium is below the detection limit of the present study (Figure 8.3). These differences may well be reflecting the differences in the steric requirements of the two types of adducts (8.3) and (8.4).

Visible spectroscopy results in agreement with the ^{1}H n.m.r. results, indicate that for most of the 1-X-3,5-dinitrobenzenes studied, adducts of structure (8.3) (Nu = OMe) are thermodynamically favoured (Table 8.5). However measurements with low base concentrations in dimethyl sulphoxide show that initially base addition occurs at a ring carbon para to substituent X, to give structure (8.4), then rearrangement occurs with time to give more stable adduct (8.3). Except for the methoxycarbonyl substituent the percentage of (8.4) at equilibrium is in the range of 0 to 10 (Table 8.5).

The importance of a strongly electron-withdrawing group para to the position of addition has frequently been enphasised upon, in the discussion of the stabilities of Meisenheimer complexes.[3,7] In the present case there appears to be some tendency for the proportion of adduct (8.4) present at equilibrium to increase with the electron-withdrawing ability of the substituent X (Table 8.5). Hammett σ^- values[134,135] decrease in the order $NO_2 > CN\text{-}SO_2Me > CO_2Me\text{-}CF_3 > I\text{-}SO_3^- > SMe > H$, which shows that the correlation is not very good as indicated by the fact that the greater proportion of adduct (8.4) occurs with the methoxycarbonyl substituent.

The values for the thermodynamic equilibrium constants for methoxide addition to the 1-X-3,5-dinitrobenzenes are summarised in Table 8.8, along with some previously determined values. The measured values (Table 8.8) are the sum of those for the formation of structure (8.3) and (8.4). However since with one exception ($X = CO_2Me$) the latter adduct is present only in low concentration at equilibrium (Table 8.5), the measured values for equilibrium constants are close to the values for the formation of structure (8.3).

It is of interest to compare the values of equilibrium constants obtained from 1-X-3,5-dinitrobenzenes, with those obtained from similarly activated anisoles, such data is collected in Table 8.9. The considerable greater stabilities of the adducts from the anisoles can be explained in terms of steric requirements of the two types of adducts (8.3) and (8.2). In the case of anisoles the methoxyl group suffers a considerable steric strain through two flanking ortho substituents, but on complexation this strain is largely removed as now the two methoxyl groups lie out of the plane of the ring. In the case of 1-X-3,5-dinitrobenzenes no such steric relief is observed on the formation of complex, thus the smaller difference (Table 8.9) in stabilities between the adducts from 2,4-dinitroanisoles and 1,3-dinitrobenzene reflects

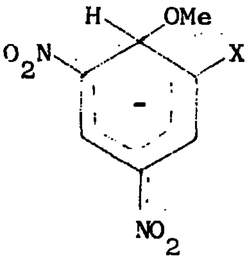
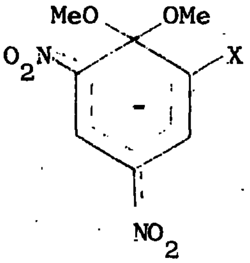
TABLE 8.8

Thermodynamic Equilibrium Constants for Methoxide Addition to 1-X-3,5-Dinitrobenzenes in Methanol at 25°C

X	K ($l.mole^{-1}$)	K ($l.mole^{-1}$) (literature)
NO_2	17	15·4 [63]; 23 [66]
CN	1·0	1·3 ; 1·9 [130]
SO_2Me	0·50	-
CO_2Me	$8{\cdot}5 \times 10^{-3}$	-
CF_3	$1{\cdot}2 \times 10^{-2}$	-
I	$8{\cdot}9 \times 10^{-4}$	-
$CONEt_2$	$1{\cdot}1 \times 10^{-4}$	-
SMe	$3{\cdot}9 \times 10^{-5}$	-
H	1×10^{-6}	5×10^{-7} [7]
SO_3^-	($10^{-4} \sim 10^{-5}$)	-

TABLE 8.9

Comparison of Equilibrium Constants for Methoxide Addition to 1-X-3,5-Dinitrobenzenes and 2-X-4,6-Dinitroanisoles

X	 K (l.mole^{-1})	 K (l.mole^{-1}) [a]	Ratio[b]
NO_2	17	17000	3000
CN	1	2600	5200
CF_3	$1{\cdot}2 \times 10^{-2}$	14	2300
CO_2Me	6×10^{-3}	10	3300
H	1×10^{-6}	$4{\cdot}6 \times 10^{-5}$	92

[a] Data from Table 4.7 (Chapter 4)

[b] In working out these ratios account has been taken of the statistical factor favouring adduct formation from 1-X-3,5-dinitrobenzenes. In general there are two equivalent ring positions leading to the formation of structure (8.3) although with 1,3,5-trinitrobenzene the factor is three.

the smaller relief of steric strain on complex formation from 2,4-dinitroanisole, where there is only one ortho substituent compared to 2,4,6-trisubstituted anisoles. These observations suggest that both electrostatic and steric requirements of the substituents play an important role in determining the stabilities of Meisenheimer complexes.

Due to the identical behaviour of ionisation for the different 1-X-3,5-dinitrobenzenes (Figure 8.6), in methanol-dimethyl sulphoxide mixtures, it was possible to define a J_M acidity function for this medium. The starting point of the scale is 0·098M sodium methoxide in methanol and the J_M value (15·96) for this solution is obtained from measurements with 1,3,5-trinitrobenzene. Values of equilibrium constant for the methoxide addition for this compound have been reported as 15·4 $l.mole^{-1}$ at zero base concentration[63] or 23 $l.mole^{-1}$ at methoxide ionic concentation of 0·2M.[66] The measurements made during this study give a value of 17 $l.mole^{-1}$ at zero ionic concentration which increases only slightly with increasing sodium methoxide concentration. The construction of the J_M scale was then carried out using the stepwise technique.[110] The agreement amongst individual indicators was excellent except for the SO_3^- substituted compound, which is of a different charge type to the other indicators, the complex being a dianion.

In order to allow for the specific effects of cations discussed in previous chapters, measurements were also made with 0·08M tetra-n-butylammonium methoxide in place of sodium methoxide. The higher starting value of the J_M scale (= 16·21) results from the non-ideal behaviour of the 1,3,5-trinitrobenzene-tetrabutylammonium methoxide system in methanol (results indicate that the stoichiometric equilibrium constant K_C increases from 17 $l.mole^{-1}$ at zero base concentration to 34 $l.mole^{-1}$ at 0·08M base concentration). However the two J_M scales are strictly parallel through the entire solvent composition range (Table 8.7). The increase in the present J_M

scale with dimethyl sulphoxide concentration is more rapid than the previous scale determined in similar media (Table 7.9) involving the methoxide addition to substituted anisoles. However it parallels exactly the acidity scale derived from the ionisation of α-cyanostilbenes, where methoxide addition occurs at a carbon atom carrying hydrogen in a conjugated system.

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PUBLICATIONS

Some of the work described in this thesis has been the subject of the following publications:

1. A Spectroscopic Study of Meisenheimer Complexes from 1-Chloro-2,6-dinitro-4-X-benzenes.

   M.R. Crampton, M.A. El Ghariani and H.A. Khan.

   Tetrahedron, 28, 3299 (1972).

2. Intermediates in Aromatic Nucleophilic Substitution Reactions: Meisenheimer Complexes from 1-Chloro-2,6-dinitro-4-X-benzenes.

   M.R. Crampton, M.A. El Ghariani and H.A. Khan.

   Chemical Comm., 1971, 834.

3. A Spectroscopic Study of the Formation of Isomeric Meisenheimer Complexes from 1-Methoxycarbonyl-3,5-dinitrobenzene.

   M.R. Crampton and H.A. Khan.

   J. Chem. Soc. Perk. II, 1972, 733.

4. The Stabilities of Meisenheimer Complexes. Part I. Adducts from Sodium Methoxide and Highly Activated Anisoles in Methanol.

   M.R. Crampton and H.A. Khan.

   J. Chem. Soc. Perk. II, 1972, 1173.

5. The Stabilities of Meisenheimer Complexes. Part II. Equilibrium Constants for the Formation of Methoxide Adducts of Low Stability and the J_M Acidity Function in Methanol-DMSO.

   M.R Crampton, M.A. El Ghariani and H.A. Khan.

   J. Chem. Soc. Perk. II, 1972, 1178.

6. The Stabilities of Meisenheimer Complexes. Part III. Specific Effects of Cations in Methanol Solution.

   M.R. Crampton and H.A. Khan.

   J. Chem. Soc. Perk. II, 1972, 2286.

7. The Stabilities of Meisenheimer Complexes. Part IV. Methoxide Adducts from 1-X-3,5-Dinitrobenzenes.

   J. Chem. Soc. Perk. II, 1973, 710.

   M.R. Crampton and H.A. Khan.